CENTER FOR DRUG EVALUATION AND RESEARCH

REMS:

APPLICATION NUMBER:

ANDA 076485Orig1s003

Name: Myorisan (Isotretinoin Capsules)
10 mg, 20 mg, 40 mg

Sponsor: VersaPharm, Inc.

Approval Date: April 30, 2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 076485Orig1s003

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 076485Orig1s003

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 076485/S-003

SUPPLEMENT APPROVAL

VersaPharm Inc.
U.S. Agent for Douglas Pharmaceuticals America Limited
Attention: John Franolic
1775 West Oak Parkway, Suite 800
Marietta, GA 30062

Dear Mr. Franolic:

Please refer to your Supplemental Abbreviated New Drug Applications (sANDAs) dated March 22, 2012, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Myorisan ® (isotretinoin capsules).

Reference is also made to your amendment dated April 12, 2012.

This supplemental application proposes modifications to the risk evaluation and mitigation strategy (REMS) for Myorisan ®.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (Package Insert and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this ANDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling

[21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Myorisan® (isotretinoin) was originally approved on January 19, 2012. The REMS consists of a Medication Guide, elements to assure safe use, and an implementation system. Your proposed modification to the REMS consists of the following:

1. removal of (b) (4) and (b) (4) from the iPLEDGE materials,

In addition, the following agreed-upon modifications are also included:

1. Relocating the Non-Compliance Action Policy from the REMS document into the REMS supporting documents
2. Relocating the following iPLEDGE website screen shots from the REMS document into the REMS supporting documents:
    a. iPLEDGE website Prescriber web pages
    b. iPLEDGE website Pharmacy web pages
    c. iPLEDGEprogram.com home page
3. Relocating the "What's New" document from the REMS document to the REMS supporting document
4. Removal of references to specific brand names, and respective sponsor names, for isotretinoin from the REMS educational materials
5. Revised "Effective Date" on the REMS educational materials to reflect the approved REMS modification approval date

Lastly, the following editorial changes have been made to the Medication Guide:

1. Deletion of "USP" from established name in product title line
2. Deletion of established name from first bullet under "What is the most important information I should know about Myorisan®?"
3. Replacing the word "one" with the number "1" in first and third bullets under the "Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby and early (premature) births."
4. Switching the order of the temperatures and parenthesis as they appear in the first bullet under "How should I store Myorisan®?"
5. Deleting the statement in brackets "[See USP Controlled Room Temperature.]" in the first bullet under "How should I store Myorisan®?"
6. Adding a hard return to create a new paragraph for the last sentence under "General Information about Myorisan®"

As required under section 505-1(i) of the FDCA, this REMS will use a single shared system for the elements to assure safe use and implementation system in the approved REMS. This single shared system, iPLEDGE, includes the following products:

ANDA 075945 Amnesteem® (isotretinoin) Capsules, 10, 20, and 40 mg
ANDA 076135 Clavaris™ (isotretinoin) Capusles, 20, 30, and 40 mg
ANDA 076356 Claravis™ (isotretinoin) Capsules, 10 mg
ANDA 076041 Sotret® (isotretinoin) Capsules, 10, 20, and 40 mg
ANDA 076503 Sotret® (isotretinoin) Capsules, 30 mg
ANDA 076485 Myorisan® (isotretinoin) Capsules, 10, 20, and 40 mg

Other products may be added to the single shared system in the future if additional applications are approved.

Your proposed modified REMS, submitted on April 12, 2012 (final REMS attachments and final REMS document), and appended to this letter, are approved.

Prominently identify future submissions containing REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

ANDA 076485
REMS ASSESSMENT
NEW SUPPLEMENT FOR ANDA 076485
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

To facilitate review of your submission, please provide a side-by-side comparison of your proposed labeling and the labeling of the reference listed drug with all differences annotated and explained. Include labeling in Final Printed Labeling (FPL) and Microsoft Word format.
If you do not submit electronically, please send 5 copies of REMS-related submissions.

REPORTING REQUIREMENTS

We remind you that, under 21 CFR 314.98, you must comply with the reporting requirements for an approved ANDA (21 CFR 314.80 and 314.81).

We also remind you of your specific reporting obligations regarding serious adverse events in patients who have received Myorisan® (isotretinoin). In addition to the usual postmarketing reporting of adverse drug experiences (21 CFR 314.80(c)), you will submit a 15-day report for each of the following:

- All pregnancy exposures to Myorisan® (isotretinoin); and
- All psychiatric events including suicides, attempted suicides, and suicidal ideation

In addition, you should continue to provide us with the following reports on an annual basis:

1. Annual Periodic Adverse Drug Experience Report
2. Special Pregnancy Periodic Biannual Report
3. Annual iPLEDGE Report (with contents as described in the attachment to this letter) to be submitted by May 1st each year
4. Non-Compliant Distribution Reports
5. Psychiatric Quarterly Report

Any changes made to the iPLEDGE Non-Compliance Action Policy should be submitted with the iPLEDGE annual report.

If you have any questions, call Carrie Lemley, Labeling Project Manager, at (240) 276-8986.

Sincerely,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

ENCLOSURES:
REMS
Annual iPLEDGE Report Contents

Initial REMS Approval: 10/2010
Most Recent Modification: 04/2012

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

The iPLEDGE Program

Single Shared System for Isotretinoin

1. GOALS

The goals of the isotretinoin risk evaluation and mitigation strategy are:

1. To prevent fetal exposure to isotretinoin
2. To inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions

2. REMS ELEMENTS

2.1. Medication Guide

A Medication Guide for isotretinoin is dispensed with each prescription for isotretinoin in accordance with 21 CFR 208.24, as described below.

A Medication Guide is enclosed with each blister package of isotretinoin to ensure that the Medication Guide is given to each patient with each prescription.

The currently approved isotretinoin Medication Guide is part of this REMS.

2.2. Elements to Assure Safe Use

2.2.1. Healthcare providers who prescribe isotretinoin are specially certified in the iPLEDGE Program.

a. Isotretinoin sponsors will ensure that healthcare providers who prescribe isotretinoin are specially certified in the iPLEDGE Program. To become certified, each prescriber must activate registration, by completing the Prescriber Enrollment Form, via the iPLEDGE website or the automated phone system. The registration and activation requires each prescriber to agree to do the following:

   i. Register each patient in the iPLEDGE Program via the iPLEDGE website or automated phone system.
   ii. Understand the risks of fetal exposure to isotretinoin and the risk factors for unplanned pregnancy.
   iii. Correctly identify and document patients as females of childbearing potential, females not of childbearing potential, or males.
   iv. Provide contraception counseling to females of childbearing potential prior to and during isotretinoin treatment, or refer females of childbearing potential to an expert for such counseling.

v. Provide scheduled pregnancy testing for females of childbearing potential and then verify and document the negative pregnancy test result prior to writing each prescription.

vi. Document the two chosen forms of contraception for each female of childbearing potential prior to writing each prescription.

vii. Prescribe no more than a 30-day supply of isotretinoin with no refills.

viii. Report any pregnancies in patients prescribed isotretinoin to iPLEDGE.

b. Isotretinoin sponsors will ensure the iPLEDGE program documents that certified prescribers/designees have performed the following responsibilities prior to initiating isotretinoin treatment and monthly prior to providing each prescription:

i. Counseled the patient about isotretinoin risks.

ii. Determined the childbearing status of all female patients prior to initiating treatment, and determined whether the childbearing status of female patients has changed.

iii. For patients who are females of childbearing potential, provided evidence or other documentation that prescribers/designees have:

a. Obtained a negative CLIA-certified pregnancy test result.

b. Determined that each female patient of childbearing potential has appropriate contraception and has been re-counseled about the importance of complying with contraceptive methods.

c. Isotretinoin sponsors will:

i. Maintain a validated and secure database of all iPLEDGE registered and activated prescribers, designees, and delegates.

ii. Monitor to ensure that only iPLEDGE certified prescribers are prescribing isotretinoin.

iii. Monitor to ensure that iPLEDGE certified prescribers correctly identify patients who are females of childbearing potential. A female of childbearing potential is defined as a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating.

iv. Monitor certified prescriber compliance with the iPLEDGE program. Certified prescriber compliance with the iPLEDGE program includes categorizing female patient risk (females of childbearing potential vs.

females not of childbearing potential), providing counseling as required, documenting contraception forms as required, and providing pregnancy testing for all females of childbearing potential treated with isotretinoin.

v. Institute appropriate corrective action according to the Non-Compliance Action Policy if the prescriber is found to be non-compliant with the iPLEDGE program.

d. The following materials are part of the REMS and are appended:

i. *The Guide to Best Practices For the iPLEDGE Program*

i. *Prescriber Contraception Counseling Guide*

ii. DVDs for prescriber use in patient counseling: *Be Prepared, Be Protected* and *Be Aware: The Risk of Pregnancy While on Isotretinoin.*

iii. Recognizing Psychiatric Disorders In Adolescents And Young Adults

iv. Request for Exemption for Patients with Serious Medical Reasons

v. Office Staff Designee Registration/Activation Form

vi. Instructions for Managing Office Staff Designees

vii. Prescriber Enrollment Form

2.2.2. Isotretinoin will only be dispensed by pharmacies that are specially certified in the iPLEDGE program.

a. Isotretinoin sponsors will ensure isotretinoin is only dispensed by pharmacies that are certified. To become certified, the pharmacy must become registered and activated in the iPLEDGE program. To become registered and activated, each pharmacy must identify a "responsible site pharmacist" who completes the Pharmacy Enrollment Form and agrees to do the following before dispensing an isotretinoin prescription:

i. Affirm that all pharmacists will comply with all iPLEDGE requirements**:**

1. Know the risk and severity of fetal injury/birth defects caused by isotretinoin.
2. Dispense only FDA-approved isotretinoin products and obtain isotretinoin only from iPLEDGE registered wholesalers.
3. Do not sell, borrow, loan, or otherwise transfer isotretinoin in any manner to or from another pharmacy.
4. Dispense only to qualified patients determined via authorization from the iPLEDGE web- or voice-based system for every isotretinoin prescription.
5. Document the Risk Management Authorization (RMA) number on each prescription.

6. Dispense no more than a 30-day supply (no refills).
7. Dispense the isotretinoin Medication Guide with each prescription.
8. Dispense prior to the "do not dispense to a patient after" date provided by the iPLEDGE program.
9. Return to the manufacturer (or delegate) any unused product if registration is revoked or if the pharmacy chooses to not reactivate.

ii. Re-activate pharmacy iPLEDGE registration annually.

b. The following materials are part of the REMS and are appended:

i. Pharmacist Guide for the iPLEDGE Program

ii. Pharmacy Enrollment Form

2.2.3. Isotretinoin sponsors will ensure that isotretinoin will only be dispensed to patients enrolled in the iPLEDGE Program with evidence or other documentation of safe-use conditions.

a. Isotretinoin sponsors will ensure that all patients treated with isotretinoin are enrolled in iPLEDGE by a registered prescriber, before isotretinoin is dispensed to them. To become enrolled, each patient or guardian must sign the appropriate Patient Information/Informed Consent form acknowledging that:

i. He or she understands the potential fetal harm with female patient exposure to isotretinoin.

ii. Enrollment in the iPLEDGE program is required.

iii. Isotretinoin must not be shared with anyone, even someone with similar symptoms.

iv. He or she cannot donate blood while on isotretinoin and for 1 month after treatment has ended.

v. He or she must fill and pick up the prescription within specified time frames.

b. Isotretinoin sponsors must ensure that isotretinoin is dispensed to females of childbearing potential only if there is evidence or other documentation that they meet the following safe-use conditions:

i. Are not pregnant or breastfeeding.

ii. Comply with the required pregnancy testing as ordered by the certified prescriber before receiving each isotretinoin prescription as follows:

1. Two urine or serum pregnancy tests before receiving the initial isotretinoin prescription. The screening test and confirmation test must be at least 19 days apart. For patients with regular menstrual cycles, the confirmation test should be done during the first 5 days of the menstrual period immediately preceding treatment. For patients with amenorrhea, irregular cycles, or using contraceptive methods that precludes withdrawal bleeding, the confirmation test must be immediately preceding treatment and at least 19 days after the screening test.
2. Monthly pregnancy testing done prior to receiving authorization to receive each isotretinoin prescription.

iii. Unless continuously abstinent, comply with the iPLEDGE requirement to use 2 forms of contraception 1 month before, during, and for 1 month after discontinuing isotretinoin treatment.

iv. Access the iPLEDGE system before receiving each isotretinoin prescription and 1 month after isotretinoin treatment concludes to answer questions about the program requirements and to enter 2 chosen forms of contraception.

v. Be informed of the purpose and importance of providing information about her pregnancy, should she become pregnant while taking, or within 1 month of the last dose of isotretinoin.

vi. Be informed of the need to immediately stop isotretinoin treatment if she engages in unprotected heterosexual intercourse.

c. Isotretinoin sponsors will ensure that there is evidence or other documentation that all iPLEDGE safe use requirements have been met for each female patient of childbearing potential prior to the patient receiving isotretinoin each month:

i. The patient is registered in the iPLEDGE program and had required pregnancy test(s).

ii. The patient entered their two chosen forms of birth control into the iPLEDGE program.

iii. The patient answered the required questions about the iPLEDGE program and pregnancy prevention.

iv. The prescriber entered into iPLEDGE the two chosen forms of contraception after re-counseling.

v. The patient has a negative pregnancy test result entered into iPLEDGE by the prescriber or designee.

d. The following materials are part of the REMS and are appended:

i. Guide to Isotretinoin for Female Patients Who Can Get Pregnant

ii. Guide to Isotretinoin for Male Patients and Female Patients who Cannot Get Pregnant

iii. The iPLEDGE Program Patient Introductory Brochure

iv. Isotretinoin Educational Kit for Males and Females of Nonchildbearing Potential

v. Isotretinoin Educational Kit for Females of Childbearing Potential

vi. Patient Information/Informed Consent for all patients

vii. Patient Information/Informed Consent for Females of Childbearing Potential

viii. Patient Monthly Comprehension Questions

2.2.4 Isotretinoin sponsors will maintain a centralized pregnancy registry for iPLEDGE enrolled female patients who become pregnant and consent to participate in a root cause analysis.

The primary objectives of the iPLEDGE Pregnancy Registry are to:

a. Determine isotretinoin exposure status for each reported pregnancy.
b. Document the outcome of each isotretinoin exposed pregnancy.
c. Determine, document, and analyze causes contributing to fetal exposure (root cause analysis).

2.3. Implementation System

The implementation system will include the following:

a. Isotretinoin sponsors will maintain a secure web- and voice-based interface for all certified entities as described in Sections 2.2.2 and 2.2.3. This includes a system and process to monitor pregnancy testing results, and to link monthly prescription authorization (risk management authorization) to collection of the following data:

i. Patient age, gender, and risk category

ii. Required counseling

iii. Prescription data (RMA numbers, dates prescription filled, quantities dispensed)

iv. For female patients of childbearing potential:

a. Baseline and monthly pregnancy tests, including 30 day post-therapy test (dates and results)

b. Chosen methods of contraception

c. Answers to monthly comprehension questions

v. For females who become pregnant:

a. Maternal and fetal outcome

b. Information from the prescriber about circumstances contributing to the fetal exposure

b. Isotretinoin sponsors will monitor wholesaler distribution data to ensure that only registered entities distribute isotretinoin. Wholesalers who distribute isotretinoin must be registered with iPLEDGE prior to distributing isotretinoin and must re-register annually thereafter. Wholesalers must register with iPLEDGE by signing and returning the iPLEDGE wholesaler agreement. By signing the agreement, wholesalers affirm that they will comply with all of the following iPLEDGE requirements:

   i. Distribute only FDA-approved isotretinoin product

   ii. Only ship isotretinoin to: 1) wholesalers registered in the iPLEDGE program with prior written consent from the manufacturer; and 2) pharmacies licensed in the US and registered and activated in the iPLEDGE program.

   iii. Notify the isotretinoin manufacturer (or delegate) of any unregistered and/or non-activated pharmacy or unregistered wholesaler that attempts to order isotretinoin.

   iv. Return to the manufacturer (or delegate) any undistributed product if registration is revoked by the manufacturer or if the wholesaler chooses to not re-register annually.

c. Isotretinoin sponsors will maintain a secure database of all certified pharmacies to ensure compliance with the following:

   i. Obtain isotretinoin only from registered wholesalers.

   ii. Dispense isotretinoin to patients only after receiving iPLEDGE authorization each month for each prescription.

   iii. Fill isotretinoin within the allowed timeframes only.

d. Isotretinoin sponsors shall develop and implement a single Non-Compliance Action Policy for handling noncompliant stakeholders (patients, pharmacies, prescribers/delegates, designees and wholesalers). The Non-Compliance Action Policy shall describe the types of non-compliance, and corresponding corrective or remedial actions (notice of non-compliance, warning, suspension, temporary or permanent deactivation) that will be taken by the iPLEDGE sponsors for each category of non-compliant stakeholder.

e. Isotretinoin sponsors will monitor registered wholesaler and certified pharmacy compliance, address deviations, and institute appropriate corrective actions according to the Non-Compliance Action Policy if the wholesaler/pharmacy is found to be non-compliant with the iPLEDGE program.

f. Isotretinoin sponsors will monitor the internet to ensure isotretinoin is not prescribed, dispensed, or otherwise obtained through the internet or any other means outside of the iPLEDGE program.

g. Based on monitoring and evaluation of the REMS elements to assure safe use, isotretinoin sponsors will take reasonable steps to work to improve implementation of these elements, as applicable.

h. Isotretinoin sponsors will maintain a call center to support prescribers, patients and pharmacies in interfacing with the iPLEDGE program.

i. The following materials are part of the REMS and are appended:

   i. iPLEDGE wholesaler agreement

   ii. Wholesaler to wholesaler shipment request form

2.4. Timetable for Submission of Assessments (Applicable only to drugs with an approved new drug application (NDA))

iPLEDGE assessments will be submitted to FDA on May 1, 2011 and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each annual submission will conclude no earlier than 60 days before the submission date for that assessment. The iPLEDGE assessment will be submitted so that it is received by FDA on or before the due date.

MEDICATION GUIDE

MYORISAN

(isotretinoin capsules)

Read the Medication Guide that comes with Myorisan before you start taking it and each time you get a prescription. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about Myorisan?

- Myorisan is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because Myorisan can cause birth defects, Myorisan is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE program.
- Myorisan may cause serious mental health problems.

1. Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. Female patients who are pregnant or who plan to become pregnant must not take Myorisan. **Female patients must not get pregnant:**

- for 1 month before starting Myorisan
- while taking Myorisan
- for 1 month after stopping Myorisan.

If you get pregnant while taking Myorisan, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE pregnancy registry at 1-866-495-0654

2. Serious mental health problems. Myorisan may cause:
- depression
- psychosis(seeing or hearing things that are not real)
- suicide. Some patients taking Myorisan have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop Myorisan and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- start to feel sad or have crying spells
- lose interest in activities you once enjoyed
- sleep too much or have trouble sleeping

- become more irritable, angry, or aggressive than usual (forexample, temper outbursts, thoughts of violence)
- have a change in your appetite or body weight
- have trouble concentrating
- withdraw from your friends or family
- feel like you have no energy
- have feelings of worthlessness or guilt
- start having thoughts about hurting yourself or taking yourown life (suicidal thoughts)
- start acting on dangerous impulses
- start seeing or hearing things that are not real

After stopping Myorisan, you may also need follow-up mental health care if you had any of these symptoms.

What is Myorisan?

Myorisan is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Myorisan can cause serious side effects (see **"What is the most important information I should know about Myorisan?"**).Myorisan can only be:

- prescribed by doctors that are registered in the iPLEDGE program
- dispensed by a pharmacy that is registered with the iPLEDGE program
- given to patients who are registered in the iPLEDGE programand agree to do everything required in the program.

What is severe nodular acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who should not take Myorisan?

- Do not take Myorisan if you are pregnant, plan to become pregnant, or become pregnant during Myorisan treatment. Myorisan causes severe birth defects. See **"What is the most important information I should know about Myorisan?"**

- Do not take Myorisan if you are allergic to anything in it. See the end of this Medication Guide for a complete list of ingredients in Myorisan.

What should I tell my doctor before taking Myorisan?

Tell your doctor if you or a family member has any of the following health conditions:

- mental problems
- asthma

- liver disease
- diabetes
- heart disease
- bone loss (osteoporosis) or weak bones
- an eating problem called anorexia nervosa (where people eat too little)
- food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Myorisan must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins and herbal supplements. Myorisan and certain other medicines can interact with each other, sometimescausing serious side effects. Especially tell your doctor if you take:

- Vitamin A supplements. Vitamin A in high doses has many of the same side effects as Myorisan. Taking both together may increase your chance of getting side effects.
- Tetracycline antibiotics. Tetracycline antibiotics taken with Myorisan can increase the chances of getting increased pressure in the brain.
- Progestin-only birth control pills (mini-pills). They may not work while you take Myorisan. Ask your doctor or pharmacist if you are not sure what type you are using.
- Dilantin (phenytoin). This medicine taken with Myorisan may weaken your bones.
- Corticosteroid medicines. These medicines taken with Myorisan may weaken your bones.
- St. John's Wort. This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with Myorisan unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How should I take Myorisan?

- You must take Myorisan exactly as prescribed. You must also follow all the instructions of the iPLEDGE program. Before prescribing Myorisan, your doctor will:
    - explain the iPLEDGE program to you
    - have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed Myorisan if you cannot agree to or follow all the instructions of the iPLEDGE program.

- You will get no more than a 30-day supply of Myorisan at a time. This is to make sure you are following the MyorisaniPLEDGE program. You should talk with your doctor each month about side effects.

- The amount of Myorisan you take has been specially chosen for you. It is based on your body weight, and may change during treatment.

- Take Myorisan 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your Myorisan capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Myorisan can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.

- If you miss a dose, just skip that dose. Do **not** take 2 doses at the same time.

- If you take too much Myorisan or overdose, call your doctor or poison control center right away.

- Your acne may get worse when you first start taking Myorisan. This should last only a short while. Talk with your doctor if this is a problem for you.

- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from Myorisan. Female patients who can get pregnant will get a pregnancy test each month.

- Female patients who can get pregnant must agree to use 2 separate forms of effective birth control at the same time 1 month before, while taking, and for 1 month after taking Myorisan. **You must access the iPLEDGE system to answer questions about the program requirements and to enter your 2 chosen forms of birth control.** To access the iPLEDGE system, go to www.ipledgeprogram.com or call 1-866-495-0654.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this free visit, which will be paid for by the company that makes Myorisan.

If you have sex at any time without using 2 forms of effective birth control, get pregnant, or miss your expected period, stop using Myorisan and call your doctor right away.

What should I avoid while taking Myorisan?

- Do not get pregnant while taking Myorisan and for 1 month after stopping Myorisan. See **"What is the most important information I should know about Myorisan?"**

- Do not breast feed while taking Myorisan and for 1 month after stopping Myorisan. We do not know if Myorisan can pass through your milk and harm the baby.

- Do not give blood while you take Myorisan and for 1 month after stopping Myorisan. If someone who is pregnant gets your donated blood, her baby may be exposed to Myorisan and may be born with birth defects.

- Do not take other medicines or herbal products with Myorisan unless you talk to your doctor. See **"What should I tell my doctor before taking Myorisan?"**

- Do not drive at night until you know if Myorisan has affected your vision. Myorisan may decrease your ability to see in the dark.

- Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using Myorisanand for at least 6 months after you stop. Myorisan can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.

- Avoid sunlight and ultraviolet lights as much as possible. Tanning machines use ultraviolet lights. Myorisan may make your skin more sensitive to light.

- Do not share Myorisan with other people. It can cause birth defects and other serious health problems.

What are the possible side effects of Myorisan?

- Myorisan can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births. See **"What is the most important information I should know aboutMyorisan?"**

- Myorisan may cause serious mental health problems. See **"What is the most important information I should know about Myorisan?"**

- serious brain problems. Myorisan can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking Myorisan and call your doctor right away if you get any of these signsof increased brain pressure:

- bad headache
- blurred vision
- dizziness
- nausea or vomiting
- seizures (convulsions)
- stroke

- skin problems. Skin rash can occur in patients taking Myorisan. In some patients a rash can be serious. Stop using Myorisanand call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like "pink eye"), a rash with a fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.

- stomach area (abdomen) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach).If your organs are damaged, they may not get better even after you stop taking Myorisan. Stop taking Myorisan and call your doctor if you get:

- severe stomach, chest or bowel pain

- trouble swallowing or painful swallowing
- new or worsening heartburn
- diarrhea
- rectal bleeding
- yellowing of your skin or eyes
- dark urine

- bone and muscle problems. Myorisan may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with Myorisan. Tell your doctor if you get:

- back pain
- joint pain
- broken bone. Tell all healthcare providers that you take Myorisan if you break a bone.

Stop Myorisan and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Myorisan may stop long bone growth in teenagers who are still growing.

- hearing problems. Stop using Myorisan and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.

- vision problems. Myorisan may affect your ability to see in the dark. This condition usually clears up after you stop taking Myorisan, but it may be permanent. Other serious eye effects can occur. Stop taking Myorisan and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking Myorisan and after treatment.

- **lipid (fats and cholesterol in blood) problems.** Myorisan can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when Myorisan treatmentis finished.

- serious allergic reactions. Stop taking Myorisan and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking Myorisan and call your doctor if you get a fever, rash, or red patches or bruises on your legs.

- blood sugar problems. Myorisan may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.

- decreased red and white blood cells. Call your doctor if you have trouble breathing, faint, or feel weak.

- The common, less serious side effects of Myorisanare dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with Myorisan. Your doctor or pharmacist can give you more detailed information. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or VersaPharm Inc. at 1-800-548-0700.

How should I store Myorisan?

- Store Myorisan at 68°-77°F (20° to 25°C). Protect from light.

- Keep Myorisan and all medicines out of the reach of children.

General Information about Myorisan

Medicines are sometimes prescribed for conditions that arenot mentioned in Medication Guides. Do not use Myorisan for a condition for which it was not prescribed. Do not give Myorisan to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about Myorisan. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Myorisan that is written for health care professionals. You can also call iPLEDGE program at1-866-495-0654 or visit www.ipledgeprogram.com.

What are the ingredients in Myorisan?

Active Ingredient: Isotretinoin
Inactive Ingredients: yellow wax, butylatedhydroxyanisole, edetate disodium, hydrogenated vegetable oil, tocopherol, and soybean oil. Gelatin capsules contain gelatin, glycerin, and non-crystallizing sorbitol solution, with the following dye systems: 10 mg – ferric oxide (yellow) and titanium dioxide; 20 mg - titanium dioxide; 40 mg - FD&C Yellow No. 6 and titanium dioxide.
The edible imprinting ink for all the capsules contains: shellac glaze, dehydrated alcohol, isopropyl alcohol, iron oxide black, N-butyl alcohol, propylene glycol, and ammonium hydroxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Dilantin is a registered trademark of Warner-Lambert Company LLC.

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The iPLEDGE Program

The Guide To Best Practices For the iPLEDGE Program

The resource to help the prescriber prepare, plan treatments, and prevent pregnancies during the course of isotretinoin therapy

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Reference ID: 3122588

The Guide To Best Practices For the iPLEDGE Program

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Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. In addition, for female patients of childbearing potential, isotretinoin is indicated only for those female patients who are not pregnant (see boxed CONTRAINDICATIONS AND WARNINGS and PRECAUTIONS sections).

Important Facts About Isotretinoin

- Isotretinoin is highly teratogenic.
- Treatment with isotretinoin during pregnancy is contraindicated. Female patients should not be pregnant or become pregnant while on isotretinoin therapy and for 1 month thereafter.
- Fetal exposure to isotretinoin may result in life-threatening congenital abnormalities.

The Guide To Best Practices For the iPLEDGE Program

This guide has been developed to assist you in fulfilling the requirements for isotretinoin pregnancy prevention risk management. Please refer to the CONTRAINDICATIONS AND WARNINGS and the PRECAUTIONS sections of the isotretinoin Package Insert.

CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE™. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see **PRECAUTIONS**).

ABOUT ISOTRETINOIN

Isotretinoin is used to treat severe recalcitrant nodular acne. Isotretinoin belongs to a class of drugs known as retinoids, commonly understood to include all natural and synthetic analogues of vitamin A. Therapy with isotretinoin should not be undertaken before conventional treatment has been tried first, including the use of systemic antibiotic therapy, and the patient has been fully counseled about the warnings and precautions in the isotretinoin package insert.

Isotretinoin is teratogenic and must not be used by pregnant women. Women should not become pregnant while taking isotretinoin or for 1 month after therapy is discontinued. A patient who becomes pregnant during treatment should stop taking isotretinoin and immediately contact her prescriber.

Isotretinoin use is associated with other potentially serious adverse events as well as more frequent, but less serious side effects. More frequent, less serious side effects include cheilitis, dry skin, skin fragility, pruritus, epistaxis, dry nose and dry mouth, and conjunctivitis.

Serious Adverse Event Warnings include psychiatric disorders* (depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors). Prescribers should read the brochure *Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide for Prescribers of Isotretinoin.* Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of Isotretinoin therapy, patients and family members should be asked about any history of psychiatric disorder, and at each visit during therapy patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary.

Other Serious Adverse Event Warnings include; pseudotumor cerebri; pancreatitis; hyperlipidemia; hearing impairment*; hepatotoxicity; inflammatory bowel disease; skeletal changes† (bone mineral density changes, hyperostosis, premature epiphyseal closure); and visual impairment (corneal opacities, decreased night vision).

Patients should be reminded to read the Medication Guide, distributed by the pharmacist at the time the isotretinoin is dispensed.

Pregnancy After Isotretinoin Therapy

The terminal elimination half-life of isotretinoin varies but is generally within 10 to 20 hours. The elimination half-life of one of the isotretinoin metabolites, 4-oxoisotretinoin, is approximately 25 hours. Since plasma elimination is host dependent, prescribers should warn patients not to become pregnant for 1 month posttreatment. Women who become pregnant during this month should be counseled as to the outcome data. In 1989, Dai et al reported the results of an epidemiologic study of pregnancies that occurred in women who conceived after discontinuing isotretinoin.[1] They studied women from 5 days to more than 60 days between the last dose of isotretinoin and conception. The incidence of birth defects in former isotretinoin patients was not significantly different from the rate in the general population.

* No mechanism of action has been established for these events

† The use of isotretinoin in patients ages 12 to 17 should be given careful consideration especially when a known metabolic or structural bone disease exists

Isotretinoin is found in the semen of male patients taking isotretinoin, but the amount delivered to a female partner would be about 1 million times lower than an oral dose of 40 mg. While the no-effect limit for isotretinoin-induced embryopathy is unknown, 20 years of postmarketing reports include 4 with isolated defects compatible with features of retinoid-exposed fetuses; however, 2 of these reports were incomplete, and 2 had other possible explanations for the defects observed.

Birth Defects

There is an extremely high risk that a deformed infant will result if pregnancy occurs while female patients are taking isotretinoin in any amount even for short periods of time. Potentially, any fetus exposed during pregnancy can be affected. Not every fetus exposed to isotretinoin has resulted in a deformed child. However, there are no accurate means of determining which fetus has been affected and which fetus has not been affected.

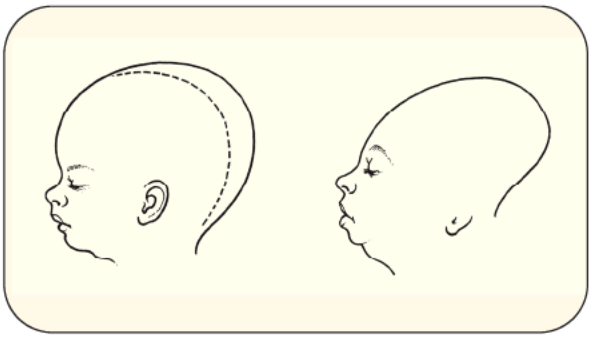
When isotretinoin is taken during pregnancy, it has been associated with fetal malformations, and there is an increased risk for spontaneous abortions and premature birth. **The following human fetal abnormalities have been documented.**

External abnormalities

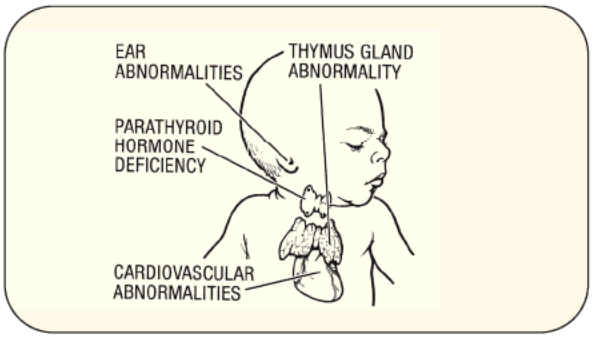
Skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Internal abnormalities

CNS abnormalities including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit; cardiovascular abnormalities; thymus gland abnormalities; parathyroid hormone deficiencies. In some cases death has occurred with certain of the abnormalities noted.



Line drawing represents the possible abnormalities of the low-set, deformed, or absent ears; wide-set eyes; depressed bridge of nose; enlarged head; and small chin.



Line drawing represents the possible abnormalities of the brain, heart, and thymus gland that may occur.

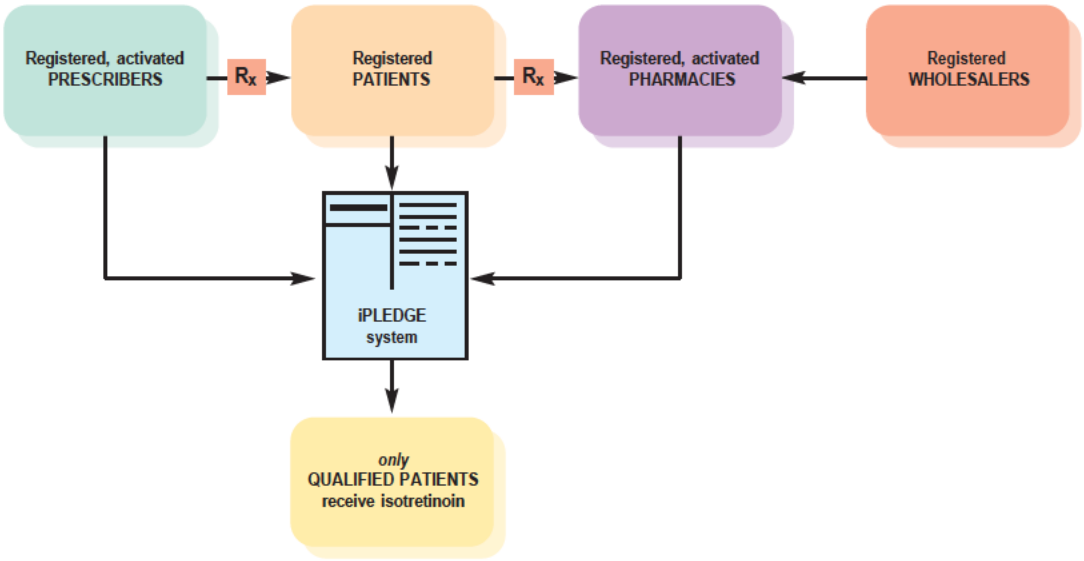
THE iPLEDGE PROGRAM

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see PRECAUTIONS).

The goals of the iPLEDGE program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions.

The iPLEDGE program is a computer-based risk management system that uses verifiable, trackable links between prescriber, patient, pharmacy, and wholesaler to control prescribing, using, dispensing, and distribution of isotretinoin.

The trackable links of the iPLEDGE program



Key Features Of The iPLEDGE Program

The iPLEDGE program has specific requirements for prescribers, patients, pharmacists, and wholesalers. Here is an overview:

- The iPLEDGE system tracks and verifies critical program elements that control access to isotretinoin.
- Only prescribers registered with and activated in the iPLEDGE program can prescribe isotretinoin.
- Prescribers or their office designee must enter required information (pregnancy test results, 2 forms of contraception used, confirmation of patient counseling) in the iPLEDGE system for patients to be qualified to receive a prescription.
- Prescribers must document that all patients—and specifically female patients of childbearing potential—meet the requirements in the iPLEDGE program.

- Only patients who are registered by prescribers in the iPLEDGE program can receive isotretinoin.
- Female patients of childbearing potential must enter required information (2 forms of contraception used, answer questions on program requirements) in the iPLEDGE system in order to be qualified to receive a prescription.
- Only pharmacies registered with and activated in the iPLEDGE program can dispense isotretinoin.
- Pharmacists must access the iPLEDGE system to receive authorization to fill and dispense every isotretinoin prescription.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE program.
- Manufacturers will only ship isotretinoin to iPLEDGE-registered entities (e.g., direct vendor pharmacies, wholesalers).
- Wholesalers must register annually in the iPLEDGE program. A registered wholesaler may distribute only FDA-approved isotretinoin product.
- Only wholesalers registered with the iPLEDGE program can distribute isotretinoin.
- Registered wholesalers can only ship isotretinoin to wholesalers registered in the iPLEDGE program with prior written consent from the manufacturer or pharmacies licensed in the US and registered and activated in the iPLEDGE program.

KEY INFORMATION FOR PRESCRIBERS

Prescribers need to follow the key points of the iPLEDGE program. These points are explained in detail in *The Guide To Best Practices For the iPLEDGE Program*. The key areas the prescriber must understand include:

- The iPLEDGE program educational materials for prescribers and patients
- Activation in the iPLEDGE automated system
- Prescriber steps required "Before," "During," and "After" treatment with isotretinoin
- Specific program criteria and procedures for female patients of childbearing potential
- Education for all patients about isotretinoin and the iPLEDGE program requirements
- Patient registration
- The initial and monthly procedures for prescribing isotretinoin and information on the requirements for pharmacists
- Information on what to do in the event of a pregnancy
- Prescriber delegates and office staff designees

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

THE iPLEDGE WEB SITE AND PHONE SYSTEM

The prescriber can access the iPLEDGE system via the program web site and automated phone system.

- Web site: **www.ipledgeprogram.com**
- Phone system: **1-866-495-0654**

The automated system is used to:

- Activate registration
- Register patients
- Confirm patient counseling monthly for all patients for each prescription
- Enter monthly pregnancy test results and contraception information for female patients of childbearing potential. **The patient cannot answer her monthly questions until the prescriber has entered the pregnancy test results in the iPLEDGE system.**
- Track the current status of a patient.
- Order additional copies of *The Guide To Best Practices For the iPLEDGE Program* and of patient and professional educational materials
- Manage delegates and designate office staff
- Find a Participating Pharmacy
- Enter and make changes to patient name, address, phone number and date of birth.
- Edit prescriber name, specialty, address, phone and fax numbers, e-mail address and preferred method of communication (US Mail or e-mail)

Logging in to either the web site or phone system requires a username and password, which are supplied upon registration.

To review and order materials

You can order additional program materials using either the web site or the phone system as follows:

1. After logging on to the web site, there are two ways to order materials:
   a. Using the navigation menu on the left side of the page, select the "Order Materials" button.

      OR

   b. Using the navigation menu on the left side of the page choose "Prescriber Information". In the "View Information Online" section, Select "To Order Educational Materials, please click here".
2. In the phone system, log in and select the option to "Request Program Information."

Materials will be shipped via ground delivery, and should arrive in 5 to 7 business days. The prescriber address in iPLEDGE at the time of the order will be used for the shipping destination. This address can be changed by the user as needed to direct shipments to specific desired locations.

PROGRAM MATERIALS

The iPLEDGE program provides educational materials for prescribers and patients. There is also a guide for pharmacists.

Prescriber Materials

It is important that the prescriber reviews the materials in the educational kit.

1. *The Guide To Best Practices For the iPLEDGE Program* describes the requirements of the iPLEDGE program for prescribers and for male and female patients.
2. *The iPLEDGE Program Prescriber Contraception Counseling Guide* is an overview of the effective forms of contraception and is a companion to the patient *iPLEDGE Program Birth Control Workbook*.
3. The brochure *Recognizing Psychiatric Disorders In Adolescents And Young Adults* contains important information about depression, suicide, and psychiatric assessment and referral of your patients.

Additional materials

Additional resource materials can be viewed on the iPLEDGE web site. These include:

- Isotretinoin Medication Guide
- Isotretinoin Package Inserts
- Prescribing Checklists
- Isotretinoin Contraception Referral Form
- Prescriber Activation Instructions
- Instructions for Registering and Managing Office Staff Designees
- Patient and Prescriber Flowcharts
- FAQ's (Frequently Asked Questions)

Patient Materials

The prescriber distributes *The iPLEDGE Program Patient Introductory Brochure* to patients considering taking isotretinoin. A patient educational kit, which provides information about the iPLEDGE program requirements, should be given to the patient when they are registered in iPLEDGE.

All kits include:

- The appropriate patient guide—*The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant* or *The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant*

- The Patient Information/Informed Consent (for all patients) form
- The patient ID card and number

Additionally, the kit for female patients of childbearing potential includes:

- *The iPLEDGE Program Birth Control Workbook*. This provides in-depth information about effective forms of contraception with iPLEDGE and their optimal use.
- *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide*. This includes the form to refer your patient to a contraception expert for counseling and a guide for the counselor about the requirements of the iPLEDGE program.
- The Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.

Educational DVD

The prescriber educational kit also includes a DVD for patients with two videos: ***Be Prepared, Be Protected*** and ***Be Aware: The Risk of Pregnancy While on Isotretinoin.*** These describe the kind of birth defects that may happen if a woman takes any amount of isotretinoin while she is pregnant and also review reasons for contraception failure.

ACTIVATING REGISTRATION

iPLEDGE registration must be activated in the iPLEDGE system before a prescriber can prescribe isotretinoin. Activation must occur annually.

The iPLEDGE system will report the expiration date of the prescriber's activation. To retrieve this information, the prescriber:

- On the web site, logs in and chooses "My Program Status" on the left navigation
- In the phone system, logs in and selects the option to hear "Program Status"

The prescriber should review *The Guide To Best Practices For the iPLEDGE Program* and *The iPLEDGE Program Prescriber Contraception Counseling Guide* to understand the program. Activation requires the prescriber to attest to the following statements in the iPLEDGE system:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I know the risk factors for unplanned pregnancy and the effective measures for avoidance of unplanned pregnancy.
- I have the expertise to provide the patient with detailed pregnancy prevention counseling or I will refer her to an expert for such counseling, reimbursed by the manufacturer.
- I will comply with the iPLEDGE program requirements described in the booklets entitled *The Guide To Best Practices For the iPLEDGE Program* and *The iPLEDGE Program Prescriber Contraception Counseling Guide*.

- Before beginning treatment of female patients of childbearing potential with isotretinoin and on a monthly basis, the patient will be counseled to avoid pregnancy by using 2 forms of contraception simultaneously and continuously 1 month before, during, and 1 month after isotretinoin therapy, unless the patient commits to continuous abstinence.
- I will not prescribe isotretinoin to any female patient of childbearing potential until verifying she has a negative screening pregnancy test and monthly negative CLIA-certified (Clinical Laboratory Improvement Amendment) pregnancy tests. Patients should have a pregnancy test at the completion of the entire course of isotretinoin and another pregnancy test 1 month later.
- I will report any pregnancy case that I become aware of while the female patient is on isotretinoin or 1 month after the last dose to the pregnancy registry.

Procedures For Activating In The iPLEDGE System

The prescriber can access the iPLEDGE system to activate registration via the web site, **www.ipledgeprogram.com**, or the automated phone system, **1-866-495-0654**. The web site is the faster and easier way to access the system. Identification in either system requires the username (DEA number or program-generated user-name) and password received with the registration materials. For information on the internet browsers compatible with the iPLEDGE web system, consult the FAQ's on the home page of the site, www.ipledgeprogram.com.

The system requires setting the prescriber's Date of Personal Significance. This is a date that the prescriber will be able to easily remember. It will be used to verify prescriber identity if needed by the iPLEDGE system or if a password is lost.

After initial activation, a prescriber must re-activate at least annually to remain active in the iPLEDGE program. The iPLEDGE system will display the "Activate" button on the Prescriber home page when the activation for a prescriber is nearing expiration. However, a prescriber can re-activate at any time using the "Prescriber Activation" button on the left-hand navigation menu on all pages.

Using the web site

The prescriber:

1. Logs in by entering username (DEA number or program-generated username) and password.
   - The system will provide prompts to change the prescriber's password and set the prescriber's Date of Personal Significance.
2. On the Prescriber home page, select "Activate My Registration". **The system will provide prompts to complete the activation process.** If your current activation is nearing expiration, the Prescriber home page will prominently display a direct link to re-activate.

Using the phone system

The prescriber:

1. Logs in and follows the prompts.
   - The system will provide prompts to change the prescriber's password and set the prescriber's Date of Personal Significance.
2. Selects the option to "Activate Your Registration." The system will provide prompts to complete the activation process.

OVERVIEW: PROGRAM REQUIREMENTS

The iPLEDGE program has specific requirements for prescribers, patients, and pharmacists. One of the prescriber's main responsibilities is knowing and educating patients about these requirements.

Prescribers are responsible for registering every patient, who meets the program requirements, in the iPLEDGE program via the automated system. They are responsible for educating patients about the side effects of isotretinoin and the high risk of birth defects for female patients of childbearing potential while taking the drug. As part of this process, they are also responsible for counseling patients about the monthly steps they must follow to receive isotretinoin.

Prescribers can only write a patient's prescription for isotretinoin for up to a maximum of a 30-day supply. Patients must plan for monthly appointments to receive their prescriptions. At each of these appointments, the prescriber must counsel the patient about the iPLEDGE program requirements and then confirm via the iPLEDGE automated system that this counseling occurred.

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient, as follows:

Female patients who can get pregnant…	Male patients and female patients who cannot get pregnant…
The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.	The prescription window is 30 days, and starts on the date the prescriber enters as the date of the office visit. This date is counted as DAY 1. To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.

After 11:59 p.m. Eastern Time on the last day of the prescription window, the patient can no longer fill and pick up their prescription, and must start the process over to get a new prescription window*

*There are generally no restrictions regarding the timing of office visits. One notable exception is that female patients of childbearing potential who do not fill and pick up their first month of therapy prescription in their first 7-day prescription window, must wait at least 19 days from their most recent pregnancy test until getting their next pregnancy test. This is based on the requirement that the most recent pregnancy test prior to beginning therapy must be conducted in the first 5 days of her menstrual cycle.

There are different program requirements for male patients and female patients who are not of childbearing potential and for female patients of childbearing potential.

The prescriber must determine if a patient is a female patient of childbearing potential (see page 18) and document that she meets the specific requirements of the program. These include taking pregnancy tests and using 2 forms of birth control consistently. Both of these requirements must be followed before, during, and after treatment.

To receive monthly prescriptions, a female patient of childbearing potential must also answer questions in the iPLEDGE system about the program requirements and pregnancy prevention. **Answering these questions can only take place after the prescriber has confirmed counseling, and entered the pregnancy test result and the patient's 2 forms of contraception (or reliance on abstinence) into the system.** In addition to answering the questions, the patient must also enter the 2 forms of birth control she is using (or indicate that she is relying on abstinence).

The pregnancy test can be obtained prior to, at the time of, or after the office visit. **However, the 7-day prescription window will begin with the date that the specimen draw was performed.**

These are the criteria the system uses to authorize a pharmacy to fill and dispense a prescription.

The Guide To Best Practices For the iPLEDGE Program includes a checklist of steps to follow before, during, and after patient treatment. (*see page 15*)

Below are the main requirements for patients and pharmacists.

Requirements For All Patients

To receive isotretinoin, all patients must meet all of the following conditions:

1. ***Must*** be registered with the iPLEDGE program by the prescriber
2. ***Must*** understand that severe birth defects can occur with the use of isotretinoin by female patients
3. ***Must*** be reliable in understanding and carrying out instructions
4. ***Must*** sign a Patient Information/Informed Consent (for all patients) form that contains warnings about the potential risks associated with isotretinoin
5. ***Must*** fill and pick up the prescription within a prescription window defined as follows:
   - Male patients and female patients who cannot get pregnant must pick up their prescription within the 30-day prescription window, counting the office visit as DAY 1.
   - Female patients who can get pregnant must pick up their prescription within 7 days of their pregnancy test, which is determined by the date of the blood draw or urine sample used in the test. The pregnancy test can be obtained before, during or after the office visit.

6. ***Must*** not donate blood while on isotretinoin and for 1 month after treatment has ended
7. ***Must*** not share isotretinoin with anyone, even someone who has similar symptoms

All patients should understand that refills are not allowed. Patients can only receive a maximum of a 30-day supply of isotretinoin per prescription. For each prescription, continuation of therapy requires the patient to satisfy the iPLEDGE program requirements to obtain a new prescription. The prescriber must also counsel the patient monthly about the iPLEDGE program requirements and then confirm via the iPLEDGE system that this counseling occurred.

Female patients of childbearing potential must:

- Have an initial pregnancy test, which may be performed in the prescriber's office
- Be counseled on contraception requirements
- Use 2 forms of contraception together for sexual intercourse for 1 month before, during, and for 1 month after treatment with isotretinoin
- There is a 30 day mandatory waiting period during which female patients of childbearing potential must be using both chosen forms of birth control before they are eligible to begin treatment with isotretinoin.
- Have a second pregnancy test, performed in a CLIA-certified laboratory, after being on 2 effective forms of contraception for 1 month and before starting isotretinoin therapy.* This second pregnancy test must be at least 19 days after the initial pregnancy test.
- Fulfill monthly requirements before receiving each prescription:
  - Have a serum or urine pregnancy test performed in a CLIA-certified laboratory*
  - Access the system to answer questions about the iPLEDGE requirements and pregnancy prevention
  - Enter into the iPLEDGE system the 2 forms of contraception being used
- Have a pregnancy test after their last dose, performed in a CLIA-certified laboratory
- Continue using 2 forms of contraception for 1 month after their last dose
- Have a pregnancy test 1 month after their last dose

About the patient questions

Prior to being able to fill and pick up a prescription, female patients of childbearing potential ***must*** answer questions about the iPLEDGE program and pregnancy prevention. **These questions must be answered after their prescriber has confirmed counseling, entered pregnancy test results and 2 contraceptive methods (or reliance upon abstinence) into iPLEDGE, but before the 7-day prescription window for their prescription expires.** Patients answer these questions via the web site or phone system. (Access information is provided in the patient guide.) The patient may use her patient guide and *The iPLEDGE Program Birth Control Workbook* to help with the answers.

* For timing information about monthly pregnancy tests, see number 1 on page 19 under "Qualification criteria for female patients of childbearing potential "

The system provides questions in several specific categories and correct answers for those questions, with references to the appropriate patient education material. A replacement question in the same category is provided for an incorrectly answered question.

If a patient misses a replacement question, the iPLEDGE system will direct her to review her materials and try again at a later time. She may also contact her prescriber so that her program education and counseling can be reinforced. The patient should also review her educational materials and then answer the questions again.

Requirements For Pharmacists

- Isotretinoin can only be obtained from pharmacies registered with and activated in the iPLEDGE program.
- Registered and activated pharmacies can obtain isotretinoin only from wholesalers registered with the iPLEDGE program.
- **The dispensing pharmacist must obtain authorization and a Risk Management Authorization (RMA) number** before filling and dispensing prescriptions.
- **Upon receiving authorization, the dispensing pharmacist can fill and dispense a prescription** for a maximum 30-day supply of isotretinoin.
- **Upon authorization, the iPLEDGE system** provides the RMA number to the dispensing pharmacist. The pharmacist should record the RMA number directly on the prescription.
- **Upon authorization, the iPLEDGE system** provides a "**Do Not Dispense To Patient After**" date to the dispensing pharmacist. This date is calculated as 30 days from the office visit for male patients and female patients not of child-bearing potential, or 7 days from the pregnancy test date for female patients of childbearing potential. The pharmacist should record this date on the prescription bag sticker.
- **The iPLEDGE system** only authorizes filling and dispensing prescriptions when patients have met the qualification criteria in the system.
- **Prescriptions** that are more than 30 days beyond the date of the office visit (for male patients and female patients not of childbearing potential) or more than 7 days beyond the pregnancy test date (for female patients of childbearing potential), will not be authorized by the iPLEDGE system.
- **Prescriptions must be picked up by the patient no later than the "Do Not Dispense To Patient After" date, and if not picked up, then the prescription is to be returned to stock.**
- **No automatic refills** are permitted.
- **Isotretinoin** comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.
- An isotretinoin Medication Guide must be given to the patient each time isotretinoin is dispensed, as required by law.

Pharmacy Information

Patients can only fill and pick up isotretinoin prescriptions at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

The web site, **www.ipledgeprogram.com**, provides a database of registered pharmacies. Patients and Prescribers can access this information by logging in and choosing the "Find a Participating Pharmacy" button on their home page.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.

iPLEDGE PROGRAM PRESCRIBING CHECKLISTS

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient, as follows:

Female patients who can get pregnant…	Male patients and female patients who cannot get pregnant…
The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.	The prescription window is 30 days, and starts on the date the prescriber enters as the date of the office visit. This date is counted as DAY 1. To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.

After 11:59 p.m. Eastern Time on the last day of the prescription window, the patient can no longer fill and pick up their prescription, and must start the process over to get a new prescription window*

*There are generally no restrictions regarding the timing of office visits. One notable exception is that female patients of childbearing potential who do not fill and pick up their first month of therapy prescription in their first 7-day prescription window, must wait at least 19 days from their most recent pregnancy test until getting their next pregnancy test. This is based on the requirement that the most recent pregnancy test prior to beginning therapy must be conducted in the first 5 days of her menstrual cycle.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Female Patients Of Childbearing Potential

Before

PLANNING

- ☐ **Plan** for office visits, counseling, pregnancy testing.
- ☐ **Educate** about isotretinoin and the contraception requirements of the iPLEDGE program.
- ☐ **Screen** with serum or urine pregnancy test, which may be performed in the prescriber's office: must be negative for patient to enter the iPLEDGE system.
- ☐ **Obtain** the Patient Information/Informed Consent (for all patients) form.
- ☐ **Register** patient in the iPLEDGE system and provide patient with an educational kit, which includes the Patient ID number on perforated, removable cards.

COUNSEL ON CONTRACEPTION

- ☐ **Counsel** patient in office or refer to healthcare professional with expertise in contraception. Please see page 22 for information on referring for contraception counseling.
- ☐ **Counsel** patient that she must use 2 effective forms of contraception simultaneously for at least 1 month before starting therapy. There is a 30 day mandatory waiting period during which she must be using both chosen forms of birth control before she is eligible to begin treatment with isotretinoin.
- ☐ **Inform** patient about confidential iPLEDGE Program Pregnancy Registry.

PRESCRIBE

- ☐ **Verify** female patient qualification criteria.
- ☐ **Order** a pregnancy test using a CLIA-certified laboratory:
  - During the first 5 days of the menstrual cycle, OR
  - For patients with amenorrhea or irregular cycles please refer to the section on "Qualification criteria for female patients of childbearing potential" (*see page 19*) for details on the timing of this test.
- ☐ **Obtain** the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.
- ☐ **Confirm** patient counseling of program requirements in the iPLEDGE system.
- ☐ **Provide** a prescription for up to a maximum 30-day supply of isotretinoin.
- ☐ **Enter** pregnancy test results and the patient's 2 forms of contraception in the iPLEDGE system within the 7-day prescription window, counting the date of specimen collection for the pregnancy test as DAY 1. Your patient will not be able to answer her comprehension questions and then fill and pick up her prescription until you have completed this task.

During
(at each monthly visit)

- ☐ **Counsel** patient on contraception adherence.
- ☐ **Order** a pregnancy test using a CLIA-certified laboratory.
- ☐ **Confirm** patient counseling of program requirements in the iPLEDGE system.
- ☐ **Provide** a prescription for up to a maximum 30-day supply of isotretinoin.
- ☐ **Enter** pregnancy test results and the patient's 2 forms of contraception in the iPLEDGE system within the 7-day prescription window, counting the date of specimen collection for the pregnancy test as DAY 1. Your patient will not be able to answer her comprehension questions and then fill and pick up her prescription until you have completed this task.

After

AFTER THE LAST DOSE

- ☐ **Counsel** patient on contraception adherence for 30 more days.
- ☐ **Counsel** patient not to give blood for at least 1 month after the last dose.
- ☐ **Order** a pregnancy test using a CLIA-certified laboratory after the last dose.
- ☐ **Enter** pregnancy test results and the patient's 2 forms of contraception in the iPLEDGE system.
  - If you do not enter the results of the pregnancy test at the conclusion of therapy, the patient will be classified as Lost to Follow Up, and both you and the patient may be contacted for additional information.

1 MONTH AFTER THE LAST DOSE

- ☐ **Order** a pregnancy test using a CLIA-certified laboratory.
- ☐ **Enter** pregnancy test results and the patient's 2 forms of contraception in the iPLEDGE system.
  - If you do not enter the results of the pregnancy test 1 month after the conclusion of therapy, the patient will be classified as Lost to Follow Up, and both you and the patient may be contacted for additional information.

Refer to page 27 for information about reporting pregnancies to the confidential iPLEDGE Program Pregnancy Registry.

Male Patients And Female Patients Who Cannot Get Pregnant

Before

PLANNING

- ☐ **Plan** for monthly office visits.
- ☐ **Educate** patients about isotretinoin and the iPLEDGE program.
- ☐ **Obtain** the Patient Information/Informed Consent (for all patients) form.
- ☐ **Register** patients in the iPLEDGE system and provide patient with an educational kit, which includes the Patient ID number on perforated, removable cards.

PRESCRIBE

- ☐ **Confirm** patient counseling about program requirements in the iPLEDGE system within the 30-day prescription window, counting the patient's office visit as DAY 1. The patient will not be able to fill and pick up his/her prescription until you have completed this task.
- ☐ **Provide** a prescription for up to a maximum 30-day supply of isotretinoin.

During
(at each monthly visit)

- ☐ **Counsel** patient on program adherence.
- ☐ **Confirm** patient counseling of program requirements in the iPLEDGE system within the 30-day prescription window, counting the patient's office visit as DAY 1. The patient will not be able to fill and pick up his/her prescription until you have completed this task.
- ☐ **Provide** a prescription for up to a maximum 30-day supply of isotretinoin.

After

AFTER THE LAST DOSE

- ☐ **Counsel** patient not to give blood for at least 1 month after the last dose.

DETERMINE CHILDBEARING POTENTIAL OF FEMALE PATIENTS

Qualification Criteria

The prescriber must determine if a female patient is of childbearing potential before enrolling her in the iPLEDGE program. The definition of a female patient of childbearing potential is a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or medically documented ovarian failure. This definition includes a young woman who has not yet started menstruating.

- A woman who has had a tubal sterilization is considered a female patient of childbearing potential in the iPLEDGE program.

Definition of menopause

Menopause can be assumed to have occurred in a woman when there is either:

1. Appropriate medical documentation of prior complete bilateral oophorectomy (i.e., surgical removal of the ovaries, resulting in "surgical menopause" and occurring at the age at which the procedure was performed), OR

2. Permanent cessation of previously occurring menses as a result of ovarian failure with documentation of **hormonal deficiency** by a certified healthcare provider (i.e., "spontaneous menopause," which occurs in the United States at a mean age of 51.5 years).

Hormonal deficiency should be properly documented in the case of suspected spontaneous menopause as follows:

1. If age >54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed;

2. If age <54 years and with the absence of normal menses: Negative serum or urine -HCG with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.

Screen patients

Data support that there are key issues in identifying female patients for treatment with isotretinoin.

The prescriber should:

1. Identify patients whose acne could be effectively managed without isotretinoin and avoid prescribing it for such patients
2. Identify those who are already pregnant when considering isotretinoin
3. Identify those who may not be reliable in avoiding pregnancy for the required period before, during, and after therapy

The patient should understand that, ultimately, it is her responsibility to avoid exposing an unborn baby to isotretinoin. The patient must understand the critical responsibility she assumes in electing to undertake therapy with isotretinoin and that any method of birth control, apart from complete abstinence, can fail.

The prescriber must verify that each individual patient receives adequate counseling about all her pregnancy prevention options (including abstinence) and that she knows how to select and use 2 separate, effective contraceptive methods.

Qualification criteria for female patients of childbearing potential

Once the prescriber decides to pursue qualification of the patient, a female patient of childbearing potential must follow these steps.

1. Female patients of childbearing potential must have had 2 negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial isotretinoin prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue qualification of the patient for isotretinoin. The second pregnancy test (a confirmation test) must be done in a CLIA-certified laboratory. The interval between the 2 tests must be at least 19 days.
   - For patients with regular menstrual cycles, the second pregnancy test must be done during the first 5 days of the menstrual period, immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for 1 month.
   - For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for 1 month.
   - The patient must be using her two forms of contraception for at least 30 days prior to beginning therapy on isotretinoin, and her second pregnancy test must occur after this 30 day period is complete.
2. The patient must sign a Patient Information/Informed Consent (for all patients) form and a Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.

3. The patient must select and commit to use 2 forms of effective contraception simultaneously, at least 1 of which must be a primary form, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy. Counseling about contraception and behaviors associated with an increased risk of pregnancy must be repeated on a monthly basis prior to issuing each prescription.

Monthly requirements

Each month of therapy, patients must have a negative result from a urine or serum pregnancy test. A pregnancy test must be repeated each month, in a CLIA-certified laboratory, prior to the female patient receiving each prescription. A pregnancy test must also be ordered at the end of therapy (after the last dose), and 1 month after the last dose. If the results of the pregnancy tests at the conclusion of therapy, and the pregnancy test 1 month after the conclusion of therapy, are not entered into the iPLEDGE system, the patient will be classified as Lost to Follow Up, and both the prescriber and the patient will be contacted for additional information. The iPLEDGE program also requires monthly counseling about contraception and behaviors associated with an increased risk of pregnancy.

In addition to their required doctor appointments, female patients of childbearing potential each month must also enter their 2 effective forms of contraception in the iPLEDGE system and answer questions about the iPLEDGE program and pregnancy prevention.

Effective Forms Of Contraception

Effective forms of contraception include both primary and secondary forms of contraception.

Primary forms	Secondary forms
• Tubal sterilization • Partner's vasectomy • Intrauterine device • Hormonal (combination oral contraceptives, transdermal patch, injectables, implantables, or vaginal ring)	*Barrier forms (always used with spermicide)* • Diaphragm • Cervical cap *Barrier forms (used with or without spermicide)* • Male latex condom *Others:* • Vaginal sponge (contains spermicide)

Unacceptable Forms Of Contraception Include:

- Progesterone-only "mini-pills," e.g.:
  - Ortho Micronor® Tablets*
- IUD Progesterone T
- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield‡

Abstinence

For this program, all female patients of childbearing potential must fully commit to pregnancy prevention. Abstinence without appropriate contraception is not recommended for patients in the iPLEDGE program who are or have been sexually active. Abstinence may be appropriate when it is a lifestyle choice (e.g., religious practice) and not just a social circumstance (e.g., not having a current partner). If, after counseling, a sexually active patient chooses abstinence without contraception, she must understand that isotretinoin is not recommended for any female patient of childbearing potential who cannot or will not follow the contraceptive requirements of the iPLEDGE program. All female patients of childbearing potential must receive contraception counseling.

Contraception Counseling

The prescriber must ensure that each individual patient receives adequate counseling about all her pregnancy prevention options (including abstinence) and that she knows how to select and use 2 separate, iPLEDGE program-effective forms of contraception that will give her the lowest failure rate.

The patient must understand the critical responsibility she assumes in electing to undertake therapy with isotretinoin and that any form of birth control, apart from complete abstinence, can fail. All female patients of childbearing potential must read the patient *iPLEDGE Program Birth Control Workbook*.

Reinforce the message

Counseling about contraception must be repeated on a monthly basis. Approximately 30% of female patients said they did not use 2 forms of contraception, even when knowing the risks and having consented.[2] Active counseling is one of the best tools toward getting patient compliance.

*Ortho Micronor is a registered trademark of Ortho-McNeil Pharmaceutical, Inc

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception See page 20

When counseling patients on contraception, the prescriber should refer to *The iPLEDGE Program Prescriber Contraception Counseling Guide*, which contains an overview of issues in contraception and the effective forms of contraception in the iPLEDGE program. It is a companion to the patient *iPLEDGE Program Birth Control Workbook*.

It is especially important to assess the patient's ability to understand her responsibilities and instructions, and to reinforce these instructions at every clinical visit. It is very important to be able to make a careful assessment of a female patient's reproductive history, contraceptive knowledge, and previous use of contraception forms. This assessment and contraceptive education should continue throughout isotretinoin treatment.

Referral for contraception counseling

Before beginning treatment, the prescriber or patient may choose referral to a healthcare professional with expertise in pregnancy prevention. The makers of isotretinoin will reimburse one visit for contraception counseling. The patient educational kit contains *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide*. The form is in the booklet; the guide outlines the contraception requirements and the effective forms of contraception of the iPLEDGE program for the birth control expert.

The referral form should be taken to the contraception counselor by the patient or sent in advance. The form instructs the counselor to fill in the appropriate information and return it to the prescriber with the patient's contraception choices to enter into the iPLEDGE system. The reverse side of the form has information for the counselor on the reimbursement process.

Referring to a gynecologist

The prescriber may want to specifically refer a patient to a gynecologist for:

- An examination prior to starting oral contraceptive agents or a hormonal transdermal patch
- Insertion of an IUD or hormonal vaginal ring
- Fitting a diaphragm or a cervical cap
- More detailed explanation of contraception options

The prescriber should also ask for gynecologic consultation under the following circumstances:

- The patient's history is suggestive of polycystic ovary syndrome (Stein-Leventhal syndrome). In addition to acne she may have:
  - Excessive facial hair growth (common when acne is present)
  - Obesity
  - Amenorrhea (no menstrual period) or irregular, heavy bleeding
  - Anovulation

- The patient has irregular menses, possibly related to pregnancy; an eating disorder; or endometriosis. It is important that the prescriber weighs the patient if there is suspicion of a potential eating disorder. Patients with eating disorders may:
  - Not admit to the problem
  - Be very underweight
- There are indications of sexual abuse found during the physical examination or counseling session.
- There is history or are symptoms of sexually transmitted disease.

Confidential birth control information

The iPLEDGE program has automated confidential birth control information that patients can use 24 hours a day, 7 days a week. Patients can call the program's toll-free number **1-866-495-0654** and obtain information on a variety of subjects, including:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

This is also a good option for patients who are vision impaired. Patients are always referred to their prescribers for additional information and clarification.

iPLEDGE PROGRAM PRESCRIBING INFORMATION

Register Patients In The iPLEDGE System

Patients may be registered in the iPLEDGE system either via the web site or phone system after obtaining the Patient Information/Informed Consent (for all patients) form and providing the patient with an ID number and ID card. The process is faster and easier using the web site.

On the web site, the prescriber logs in and chooses "Register New Patient." In the phone system, the prescriber logs in and selects the option to "Register a New Patient."

The system will request this specific patient information:

- Patient ID number
- Patient first and last name and middle initial
- Home address
- Phone number

- Date of birth
- Gender
- Last four digits of the Social Security number
- Female patient of childbearing potential (Yes or No)
- Screening pregnancy test date and results

ID number and ID card

The ID number and perforated ID cards are provided with the patient education materials. It is important that patients do not lose the cards. Prescribers should keep a record of the patient's number.

- All patients need the ID number and ID card to pick up their prescriptions, and to access the web site or automated phone line.
- Female patients of childbearing potential will need their ID number to access the iPLEDGE system to answer questions about the iPLEDGE program and preventing pregnancy.

Informed consents

Patients will need to sign the following consent forms to be in the iPLEDGE program.

- Patient Information/Informed Consent (for all patients)
- Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

For female patients of childbearing potential, signing the Patient Information/ Informed Consent About Birth Defects (for female patients who can get pregnant) form means the following.

- They understand the teratogenic risks of isotretinoin.
- They agree to follow the contraception requirements of the iPLEDGE program before, during, and for 1 month after their treatment with isotretinoin.

Prescriptions: System Requirements

Before a patient can fill and pick up a prescription for isotretinoin at a registered pharmacy, the iPLEDGE system requires that the information below be entered into the system and the timing criteria for filling and dispensing a prescription be met. This is the information that the system will use to authorize filling a prescription and to provide the Risk Management Authorization (RMA) number and the **"Do Not Dispense To Patient After"** date.

All patients

Prescriber confirms that:

- The patient is registered with the iPLEDGE program
- The patient was counseled on the iPLEDGE program requirements

Female patients of childbearing potential

Prior to the patient filling and picking up each prescription, the prescriber must access the iPLEDGE system to:

- Confirm that the patient was counseled about isotretinoin and the iPLEDGE program contraception requirements
- Enter the 2 forms of contraception that the patient is using
- Enter pregnancy result into the iPLEDGE system, within the 7-day prescription window, counting the date of blood draw or urine sample as DAY 1
- **The patient cannot answer her monthly questions and get a prescription filled until after these activities are completed by the prescriber.**

A positive pregnancy test prevents the prescription from being filled.

Patient must access the iPLEDGE system after the prescriber has entered the pregnancy test results to:

- Correctly answer the questions about the iPLEDGE program and pregnancy prevention
- Enter the 2 forms of contraception she is using

The primary form of contraception reported by both the prescriber and the patient must match.

Timing criteria for the prescription to be filled and picked up at the Pharmacy

- All patients must fill and pick up their prescriptions as follows:
  - For male and female patients who cannot get pregnant, prescriptions must be filled and picked up within the 30-day prescription window, counting the office visit as DAY 1
  - For female patients who can get pregnant, prescriptions must be filled and picked up within the 7-day prescription window counting the day of the blood draw or urine sample as DAY 1
- Patients will not be able to fill and pick up prescriptions after their prescription window has expired.

The iPLEDGE system will automatically provide the pharmacist with a "Do Not Dispense To Patient After" date, which is the end of the prescription window. The pharmacist cannot fill or dispense the patient's prescription after that date.

After The Last Dose

All patients should be reminded not to give blood for at least 1 month after their last dose.

Female patients of childbearing potential must have pregnancy tests:

- After their last dose, and
- 1 month after their last dose
- If this information is not entered, the patient will be classified as Lost to Follow Up, and both the prescriber and the patient will be contacted for more information.

It is important to stress the need for continued contraception during the 1 month after the last dose. Patients also should be reminded to enter their 2 forms of contraception.

Post Treatment iPLEDGE Requirements

When a patient will no longer be taking isotretinoin, action is required by the prescriber to record specifics of the end of therapy. Specifically the following information is required by iPLEDGE:

- If known when issuing the prescription, the prescriber will indicate that a prescription will be the last one for this patient. This will remind the prescriber of the patient requirements for post-treatment activity
- The prescriber must discontinue the patient within iPLEDGE in one of the following ways:
  - On the website, select "Manage Patients", select the patient being discontinued, and choose the button for "Discontinue Patient".
  - On the phone system, select the option to "Manage Active Patients", and then select the option to "Complete or Discontinue Patient Treatment".
- When discontinuing a patient through either the website or the phone system, the prescriber must enter the Date of Last Dose, and the reason why this patient will no longer be taking isotretinoin. This reason will be selected from a list presented by the iPLEDGE system, including Completed Therapy, Pregnancy, or Other. On the website, explanatory comments can also be provided, and may be required by the iPLEDGE system.
  - If the reason for discontinuation is related to an Adverse Event, please be as specific as possible in the comments entered in iPLEDGE.
- For female patients of childbearing potential, a final pregnancy test is required at the date of last dose, and 30 days after date of last dose.

If this information is not provided, and a patient has no activity in iPLEDGE for specific periods of time, the patient will be classified as Lost to Follow Up. If this occurs, prescribers and patients will be contacted by the iPLEDGE program.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

IN THE EVENT OF PREGNANCY

Counseling A Pregnant Patient

If a pregnancy does occur during isotretinoin treatment, isotretinoin must be discontinued immediately. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Reporting Pregnancy

The iPLEDGE Program Pregnancy Registry

The iPLEDGE Program Pregnancy Registry collects data on pregnancies that occur in female patients who become pregnant while taking isotretinoin or within 1 month of their last dose. Data from the registry are reported to the FDA and are used to assess the effectiveness of the iPLEDGE program. The data are also used to evaluate further ways to reduce fetal exposure. Information gathered in the iPLEDGE Program Pregnancy Registry will be used for statistical purposes only and will be held in the strictest confidence.

The prescriber must report to the iPLEDGE Program Pregnancy Registry any pregnancy case that he/she becomes aware of while the female patient is on isotretinoin or 1 month after the last dose. Report a pregnancy by calling **1-866-495-0654**. Select the option to "Report a Pregnancy." All pregnancies should also be reported to the FDA via the MedWatch number: 1-800-FDA-1088

In female patients taking isotretinoin

1. Positive pregnancy test results should be entered in the iPLEDGE system. A Safety Surveillance Associate will call the prescriber.
2. A prescriber should call the iPLEDGE Call Center if he or she does not have a pregnancy test result but thinks the patient is pregnant.

In partners of males being treated with isotretinoin

If the prescriber becomes aware of a pregnancy in the partner of a male patient taking isotretinoin, the prescriber should report this pregnancy to the iPLEDGE Program Pregnancy Registry. The information will be forwarded to the manufacturer of the specific isotretinoin product for follow-up.

Males And Birth Defects

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin. Approximately 3 to 5 babies in 100 (3% to 5%) are born with some kind of birth defect from other causes, not from isotretinoin.[3]

Isotretinoin also has not been shown to affect a male's ability to father children. Studies did not show effects on sperm count, how sperm look, or how well they swim and move. (For more information, see page 3.)

DELEGATES AND OFFICE STAFF

The iPLEDGE program allows the prescriber to delegate patient management to other prescribers registered with the iPLEDGE program (these are known as delegates) and to designate office staff to assist with data entry (these are known as designees).

Delegating To Another Prescriber

The prescriber must first add the name and required information for delegates into the iPLEDGE system. This function also allows the prescriber to define time frames for delegation and add or delete delegates.

To delegate to another prescriber

The prescriber:

1. Logs in to the web site, **www ipledgeprogram.com**
2. Chooses "Manage Delegates/Designees" from the Prescriber home page
3. Chooses "Manage Delegates" from the Manage Delegates and Designees page
4. Enters the desired Delegate's iPLEDGE user ID, and the date, if any, when the delegate's role is to expire.
5. Chooses "Add" new delegate for first-time entry

Designating Office Staff

The iPLEDGE program provides a unique username and password to identified office staff to allow them to perform the following activities for the prescriber:

- Register patients and maintain the patient's information in iPLEDGE
- Enter patient pregnancy results
- Confirm patient counseling
- Discontinue patients
- Manage delegates
- Check patient's program status

The following functions are available only to a prescriber:

- Prescriber registration
- Prescriber activation—initial and renewal

A prescriber may have one or more designated office staff. Designated office staff may be associated with one or more prescribers.

- They need to register only once, regardless of the number of prescribers with whom they are associated.
- They may support all the registered prescribers in a multi-physician practice.
- They have rights for any patient delegated to a delegated prescriber.

Rights to perform the functions depend on the prescriber's rights and program status.

- If a prescriber is not activated in the iPLEDGE system, neither the prescriber nor the designated office staff can register a patient.

Designated office staff may access the automated system but must provide their own user ID and date of personal significance as identifiers.

The registered and activated prescriber is responsible for all information entered and activities performed in the iPLEDGE system by the office staff designee.

To designate office staff

The prescriber:

1. Logs in to the web site, **www ipledgeprogram.com**
2. Chooses "Manage Delegates/Designees" from the Prescriber home page
3. Chooses "Register New Designee" from the Manage Delegates and Designees page
4. Fills in the required information on the registration online form
5. Selects "Save and Print" to save the new information and print the registration form

The office staff designee:

1. Signs and dates the completed form
2. Faxes or mails the completed form to the number or address provided

A username and password will be mailed to the designee upon completion of the registration process. The designee uses them:

- To log in to the automated system
- On the first log in, to reset password and choose a Date of Personal Significance as a system identifier

REFERENCES

1 Dai WS, Hsu MA, Itri LM Safety of pregnancy after discontinuation of isotretinoin *Arch Dermatol.* 1989;125:362-355

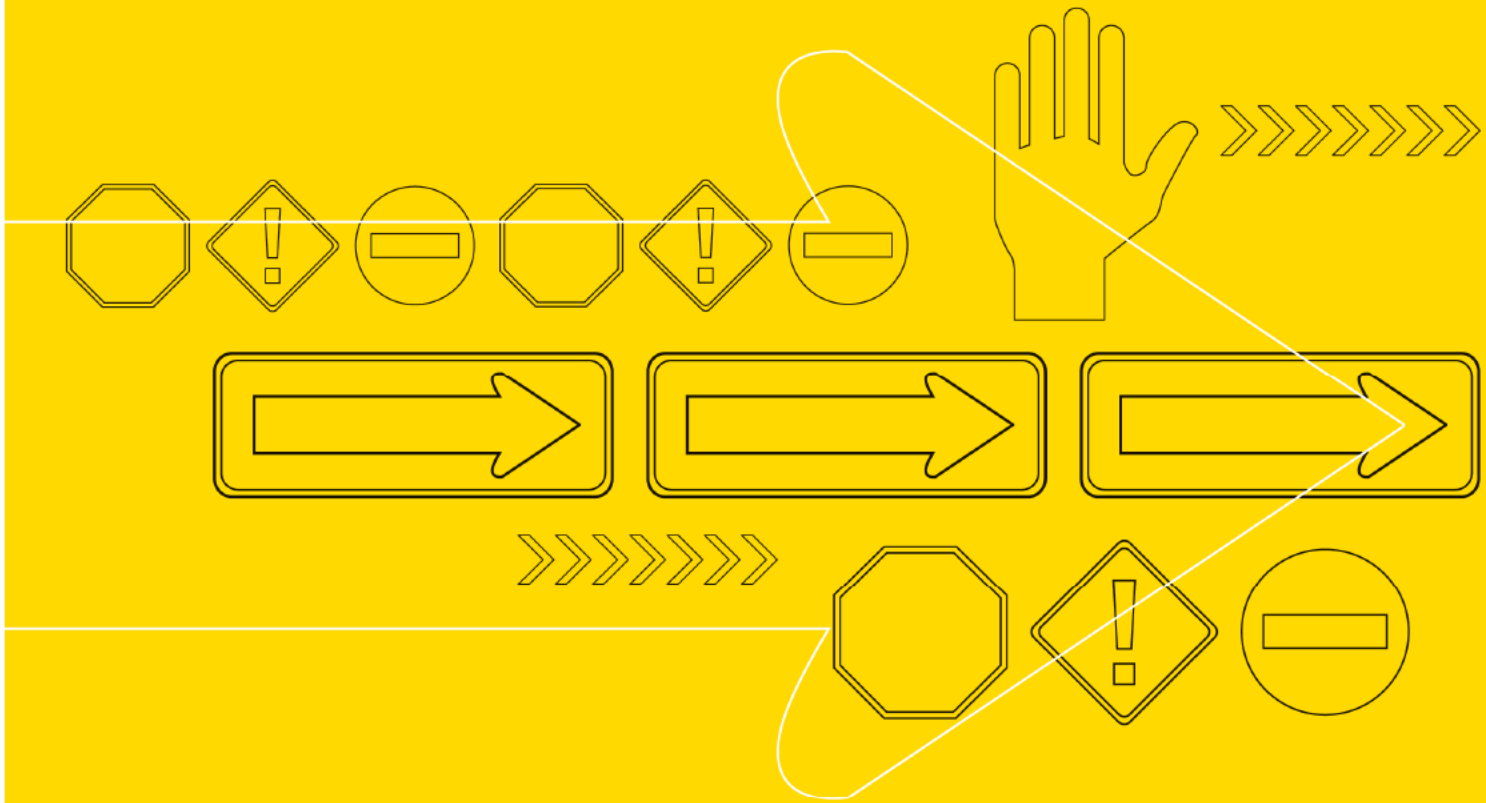
2 Mitchell, Allen A MD Isotretinoin Survey Allen A Mitchell, MD and Carla M Van Bennekom RN, MPH Slone Epidemiology Center at Boston University For presentation at FDA Advisory Committee Meeting: February 26-27, 2004

3 Centers for Disease Control and Prevention Birth defects: frequently asked questions Available at: http://www cdc gov/ncbddd/bd/faq1 htm#Whatisabirthdefect Accessed August 8, 2005

For More Information About Isotretinoin

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**



www.ipledgeprogram.com 1-866-495-0654

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

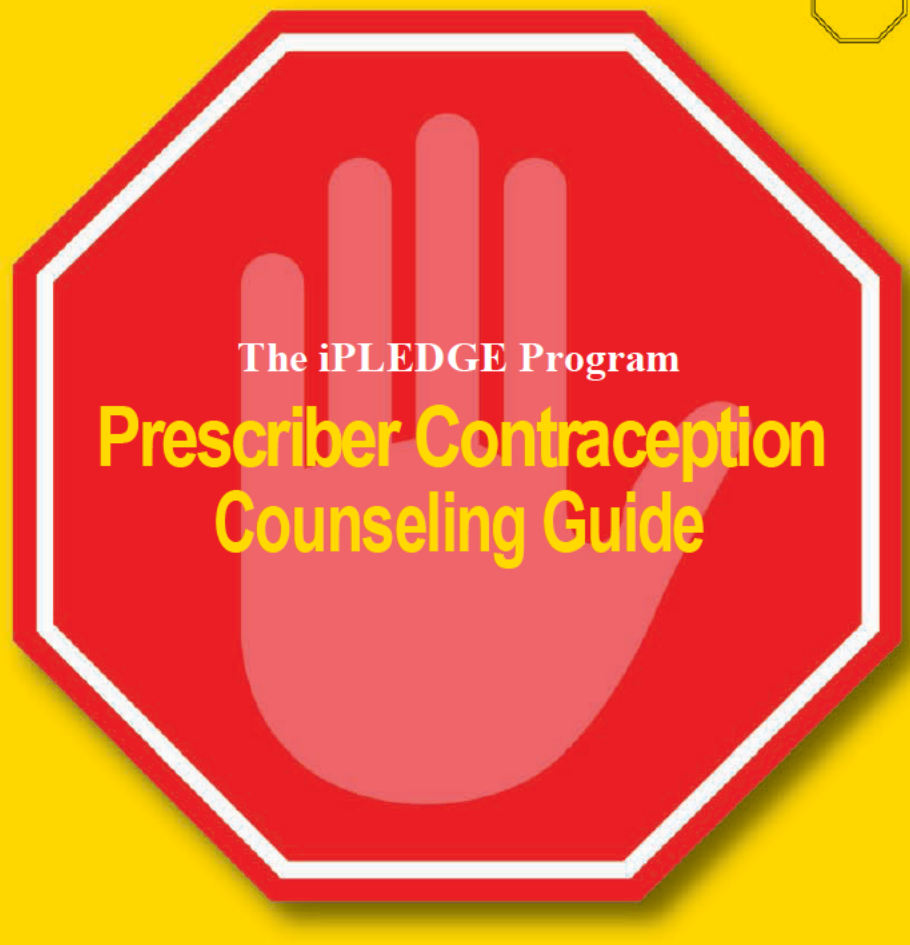
Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Most Recent Modification: April 2012



The iPLEDGE Program

Prescriber Contraception Counseling Guide

Helping patients prevent pregnancy

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iPLEDGE™
Committed to Pregnancy Prevention

Prescriber Contraception Counseling Guide

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INTRODUCTION

This *iPLEDGE Program Prescriber Contraception Counseling Guide* is intended to aid a prescriber who is not a gynecologist in counseling a female patient of childbearing potential who will be taking isotretinoin.

The patient must select and commit to using 2 forms of effective contraception simultaneously, at least 1 of which must be a primary form, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. Patients must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

It is strongly recommended that a patient use a primary form of contraception and is committed to using a second form as well, even if she says she will be abstinent for the entire required period. Isotretinoin is not recommended for sexually active female patients of childbearing potential whom you believe will not be able to maintain abstinence or will not use contraception, as the program requires.

The contraceptive that a patient selects can have a dramatic effect on her chance of becoming pregnant. A patient needs to select forms with low failure rates that she and/or her partner will use correctly each time they have intercourse. This *iPLEDGE Program Prescriber Contraception Counseling Guide* will help you enable the patient to select the 2 contraceptive forms that are consistent with the iPLEDGE program guidelines *and* that she will use correctly and consistently.

Referral For Contraception Counseling

Before beginning treatment, the prescriber or patient may choose referral to a healthcare professional with expertise in pregnancy prevention. The makers of isotretinoin will reimburse 1 visit for contraception counseling. The patient educational kit contains the *iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide*. The referral form is in the booklet; the guide outlines the contraception requirements and the effective forms of contraception of the iPLEDGE program for the birth control expert.

Contraception counseling is an important part of the patient choosing her two contraceptive forms. If practitioners are not comfortable providing this counseling, they are encouraged to take advantage of the opportunity to refer patients to a qualified counselor.

The referral form should be taken to the contraception counselor by the patient or sent in advance. The form instructs the counselor to fill in the appropriate information and return it to the prescriber with the patient's contraception choices to enter into the iPLEDGE system. The reverse side of the form has information for the counselor on the reimbursement process.

Counseling About Contraception

Please read this *iPLEDGE Program Prescriber Contraception Counseling Guide* completely before you begin your counseling session. The guide reviews the counseling goals and provides an overview of contraception choices from a pregnancy risk management context—necessary for female patients taking isotretinoin—information on obtaining a sexual and behavioral history (including additional guidance for interviewing an adolescent), and contraception reference materials.

Patients in the iPLEDGE program receive *The iPLEDGE Program Birth Control Workbook*, which contains information on effective primary and secondary forms of contraception. It is not complete information on any of the forms, and the patient is encouraged to ask questions about specific forms or issues. The workbook has questions on such issues as medication adherence and lifestyle choices for the patient to think about in choosing contraception. Please review her responses with her.

COUNSELING GOALS

Ensure that the patient:

- Understands the risk of having a child with significant birth defects from exposure to isotretinoin.
- Understands the need for using 2 forms of contraception together consistently and correctly and knows when to contact her prescriber for emergency contraception (see page 27).
- Chooses the forms of contraception that will work best for her, that will provide her with the lowest practical failure rate, and that she and her partner will actually use. Adherence impacts the failure rate of hormonal combination oral contraceptives more strongly than other primary forms. (Please see "Hormonal Combination Oral Contraceptives As A Primary Form" on page 5.)
- Commits fully to not becoming pregnant and to using 2 forms of contraception simultaneously, consistently, and correctly. In previous isotretinoin risk management programs, patients understood the need for 2 forms of contraception; however, they did not comply, despite adequate information about the risk to the fetus. If, after counseling, the patient recognizes she will not be able to commit fully, encourage her to not take isotretinoin or do not prescribe.
- Is able and willing to maintain abstinence, if that is her choice after counseling. If a patient who has ever been sexually active chooses abstinence, and you believe that she will not be able to maintain abstinence and will not use contraception, encourage her to not take isotretinoin.

Counseling younger teens

For younger teens, it is important to stress the following aspects of contraception for the iPLEDGE program during counseling:

- The birth control forms that are effective as primary and secondary forms.
- Why it is important to use 2 forms of birth control. Younger teens may need more emphasis on this point to fully understand it and comply.
- The role of emergency contraception. Young teens may need more explanation from you about the need to take immediate action if they had unprotected sex. If she is under 18 years old, she may require a prescription or other assistance from a healthcare provider in order to use emergency contraception.

CONTRACEPTION REQUIREMENTS

Using 2 Forms Of Contraception Provides More Protection

Use of 2 forms of contraception simultaneously substantially reduces the chances that a female will become pregnant over the risk of pregnancy with either form alone.

In addition, it is not known if hormonal contraceptives are less effective when used with isotretinoin.[1] Because of this possibility, and the fact that all contraceptive forms are less than 100% effective, the iPLEDGE program requires the additional protection of a second form of contraception.

Selecting An Effective Primary Form Of Contraception

Table 1 lists, by typical use failure rate, the primary forms of contraception acceptable in the iPLEDGE program.

Table 1: Primary Forms of Contraception by Typical Use Failure Rate

	Percentage of Females Experiencing an Unintended Pregnancy Within the First Year of Use[a]	
Method	**Perfect Use**	**Typical Use**
Implantable Hormones	0.05%	0.05%
Partner's Vasectomy	0.10%	0.15%
Hormonal IUD (LNg 20)	0.20%	0.20%
Tubal Sterilization	0.50%	0.50%
Non-hormonal IUD (Copper T380A)[b]	0.60%	0.80%
Hormonal Injectable (single)	0.30%	3.00%
Hormonal Transdermal Patch	0.30%	8.00%
Hormonal Vaginal Ring	0.30%	8.00%
Hormonal Combination Oral Contraceptives[b]	0.30%	8.00%

a Adapted from Trussell J Contraceptive efficacy In: Hatcher RA, Trussell J, Stewart F, et al, eds *Contraceptive Technology*. Nineteenth Revised Edition, New York, NY: Ardent Media 2007

b The IUD Progesterone T and progestin-only "mini-pills" are not acceptable for the iPLEDGE program (See "Unacceptable Forms Of Contraception" on page 7)

The single most important decision in contraception for the iPLEDGE program is selecting a primary form with a very low failure rate that the patient can and will use as perfectly as possible. Other important factors to consider in selecting a primary form include side effects, contraindications, and willingness and ability to use perfectly. (Perfect use is defined as the use of the form correctly and consistently covering every act of intercourse. Typical use reflects the practices of the average user.) All of these factors influence compliance and the chance of unwanted pregnancy.

Hormonal Combination Oral Contraceptives As A Primary Form

If the patient is currently taking or planning to take oral contraceptives, review that section in *The iPLEDGE Program Birth Control Workbook* with her. Her answers to questions on consistency and medication adherence will provide insight into potential issues with iPLEDGE program adherence.

Other contraception not requiring daily activity may be a better choice for a patient who is not likely to take oral contraceptives perfectly. For example, if such a patient chooses an IUD, she reduces her chances of becoming pregnant by up to approximately 90%.[1] It is critical that such a patient choose a form other than oral contraceptive agents.

Selecting An Effective Secondary Form Of Contraception

Table 2 lists the acceptable secondary forms of contraception in the iPLEDGE program. There are 2 forms of secondary contraception: barrier and other. Barrier forms include the diaphragm and the cervical cap (both of which are always used with spermicide) and the male latex condom (which can be used with or without spermicide). The other form is the vaginal sponge, which contains spermicide.

Table 2: Secondary Forms of Contraception Listed by Typical Use Failure Rate

	Percentage of Women Experiencing an Unintended Pregnancy Within the First Year of Use[a]	
Form	**Perfect Use**	**Typical Use**
Barrier Forms		
Male Latex Condom[b]	2%	15%
Diaphragm*	6%	16%
Cervical Cap*,[d]	9%	20%
Other Forms		
Vaginal Sponge[c]	9%	16%

a Adapted from Trussell J Contraceptive efficacy In: Hatcher RA, Trussell J, Stewart F, et al, eds *Contraceptive Technology*. Nineteenth Revised Edition, New York, NY: Ardent Media 2007
b Male Latex Condom failure rates are for use without spermicide Female condoms are not acceptable for the iPLEDGE program (See "Unacceptable Forms Of Contraception"on page 7)
c Failure rate for nulliparous women The rate is approximately double for parous women
d Adapted from Trussell J Contraceptive efficacy In: Hatcher RA, Trussell J, Stewart F, et al, eds *Contraceptive Technology*. 17th Edition, New York, NY: Irvington Publishers 1998

* Failure rates for Diaphragm and Cervical Cap are for forms including the use of spermicide

The most important issue for a secondary form is whether it will be used each time the patient has intercourse (i.e., will it be in place when the first form fails).

Help the patient select a secondary form that she and/or her partner can fully commit to using correctly each time they have intercourse. If it is apparent that more than 1 of the forms would be equally suited, select the form with the lower or lowest perfect use failure rate, as this will reduce the overall likelihood of becoming pregnant.

Unacceptable Forms Of Contraception

The following forms of contraception are not acceptable for the iPLEDGE program:

- Progesterone-only "mini-pills," e.g.:
  - Ortho Micronor® Tablets*
- IUD Progesterone T

Typical use and perfect use failure rates (2.0%, 1.5%) are unacceptably high compared with other available IUDs.

- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield, a silicone disc with a one-way air valve that creates suction to adhere to the cervix‡

Patients currently using these forms of contraception must switch to effective forms of contraception. They must use 2 effective forms together consistently and correctly for at least 30 days and have a negative pregnancy test before beginning isotretinoin.

Emergency Contraception

- Review this section in *The iPLEDGE Program Birth Control Workbook* with the patient. (Also, see page 27 in this *iPLEDGE Program Prescriber Contraception Counseling Guide.*) She should know when to call her prescriber for possible emergency contraception. She should also realize that emergency contraception should not be used on a regular basis as a replacement for the other contraceptive forms she selected.
- If she is under 18 years old, she may require a prescription or other assistance from a healthcare provider in order to use emergency contraception.

Abstinence

If a female patient of childbearing potential cannot commit completely to abstinence while taking isotretinoin, she must use 2 separate, effective forms of birth control at the same time. The only exceptions are if she has had a hysterectomy, or had both of her ovaries removed (bilateral oophorectomy), or if she has been medically confirmed as post-menopausal.

* Ortho Micronor is a registered trademark of Ortho-McNeil Pharmaceutical, Inc

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception See page 26

REFERRING TO A GYNECOLOGIST

You may want to refer your patient to a gynecologist for:

- An examination prior to starting oral contraceptive agents or a hormonal transdermal patch
- Insertion of an IUD or hormonal vaginal ring
- Fitting a diaphragm or a cervical cap
- More detailed explanation of contraception options

You should also ask for gynecologic consultation under the following circumstances:

- Your patient's history is suggestive of polycystic ovary syndrome (Stein-Leventhal syndrome). In addition to acne she may have:
  - Excessive facial hair growth (common when acne is present)
  - Obesity
  - Amenorrhea (no menstrual period) or irregular, heavy bleeding
  - Anovulation
- Your patient has irregular menses, possibly related to pregnancy; an eating disorder; or endometriosis. It is important to weigh your patient. Patients with eating disorders may:
  - Not admit to the problem
  - Be very underweight
- There are indications of sexual abuse found during the physical examination or counseling session.
- There is history or symptoms of sexually transmitted disease.

OBTAINING A SEXUAL AND BEHAVIORAL HISTORY

There are several reasons to take a sexual and behavioral history. You need to know about sexual promiscuity, risk-taking behavior, reactions to previous contraceptive medication, and current contraceptive practices to assess whether your patient is appropriate for the iPLEDGE program. This information may help you eliminate unsuitable patients or refer those whose contraceptive needs require gynecologic referral.

General Interview Information

Preparation

Insure that your patient feels safe and comfortable.

- This is important for an effective counseling session.
- Allow time for taking the history, answering questions, and decision-making.
- A private office is more conducive to counseling than an examination room. This may permit a more open and personal exchange.
- Interruptions by other staff members and telephone calls should be discouraged.

Use open-ended questions to encourage discussion.

- Your patient may be reluctant or embarrassed to answer questions about her sexual history.
- It may help to start asking about less sensitive material.

Being objective and nonjudgmental is important in building rapport. Make sure your patient understands your questions and the information you are giving her. Listen to her use of language and tailor your language to be sure she understands.

Sexual history questions

1. Does she menstruate? Does she menstruate regularly?
   - Most females (95%) have their menstrual period every 21 to 35 days and usually in a recurrent and regular pattern. A female whose menses vary by a week or more from month to month or vary in length or quantity of flow would qualify as irregular.
2. Has she had a hysterectomy or oophorectomy?
3. Is she still menstruating?
4. Is she postmenopausal?
5. Is she sexually active?
   - If not, is there any possibility of a sexual relationship developing?
6. If she is sexually active, are her partners men, women, or both?
7. Has she ever used contraception? Does she currently use contraception?
   - If yes, what form(s) and for how long?
   - Specifically question the use of unacceptable forms such as the Progesterone T IUD, progesterone-only mini-pills, or female condom.
8. If she uses oral contraceptives, does she take them exactly as prescribed? If so, which brands?
9. Does she use a secondary form of contraception every time she has sex? If so, which forms?
10. How many sexual partners has she had in the past 6 months? How many sexual partners does she currently have?

11. How long has she been with her current partner(s)? Is she monogamous?
12. Has she ever had a sexually transmitted disease? Has she ever been sexually abused?
13. Has she ever been pregnant? Does she have children?
14. Has she ever had an unintended pregnancy? What was the outcome?

Behavioral history questions

1. Does she engage in risk-taking behavior, such as using drugs or alcohol?
2. How is she doing in school/at work?
3. How is her relationship with her parents? With her siblings?
4. What is her cohabitational status? Is she married? Living with a partner?
5. Is she currently using any prescription or non-prescription medications, herbal supplements, or vitamins?

Additional Guidance For Interviewing An Adolescent*

This section offers guidance on how to approach an adolescent to obtain a sexual and behavioral history, taking into consideration concerns adolescents have about independence, parental oversight, and privacy.

Discuss confidentiality first

- Inform the patient that she has a private and privileged relationship with you.
- Identify restrictions for which you may need to breach confidentiality, such as reporting physical or sexual abuse to health authorities.
- Tell her that you will not talk with her parent or parents about something she has said without discussing it with her first.

Start gently when asking about personal history

- Start with non-threatening topics and gradually move to more sensitive issues.
- Explain that you ask all of your patients about sexual activity and tell her why this information is important.
- Consider using one of the following questions to initiate the discussion about the patient's sexual history.
  - Are you dating anyone?
  - Are you intimate with anyone?
  - Are you physically close with anyone?

* Adapted from: Sexual History Taking American College of Obstetrics and Gynecology, Committee on Adolescent Health Care, ACOG Committee Opinion No 300 October 2004 p3

Identify risk behaviors

- Leave room for discussing casual sex partners (who, for example, may not be perceived as "boyfriends").
  - Did you choose to have sex?
  - Has anyone forced you to have sex?
- Establish the sex of partner or partners first. Do not assume heterosexual behavior.
- Ask about oral and anal sex, and describe what you mean by this, if necessary.
  - Anal intercourse may be used by some teenagers to preserve virginity and protect against pregnancy, so they may not be using their secondary forms.
- Ask about the number of partners, STDs (sexually transmitted diseases) and pregnancy prevention methods used.
  - Specifically, ask what methods the patient is using.
  - Find out if they are using unacceptable forms of contraception such as the progesterone-only mini-pill, Progesterone T IUD, female condom, or withdrawal.

Keep the lines of communication open

- Encourage adolescents to discuss these issues with their parents. You can assist the adolescent in telling her parents about her sexual activity and her need to use 2 forms of contraception for the iPLEDGE program.
- Congratulate the patient for showing ability to think about her sexual health and be responsible.

CONTRACEPTION REFERENCE MATERIAL

The following sections contain some pertinent details, advantages, and disadvantages of the **primary** and **secondary** forms of effective contraception. This is not complete product information. Please refer to individual product labeling for contraindications, warnings and precautions, instructions for use, adverse events, and other product-specific information.

The percentages that follow for perfect use and typical use of a contraceptive are percentages of females having an unintended pregnancy during the first year of use, expressed as "1 female in X years."[2] Perfect use is defined as the use of the form correctly and consistently covering every act of intercourse. Typical use reflects the practices of the average user.

PRIMARY FORMS OF CONTRACEPTION

The effective primary forms of birth control fall into 3 categories:

- Combination Hormonal Contraceptives
- Single Hormonal Contraceptives
- Non-Hormonal Contraceptives

None of the primary forms protect against STDs (sexually transmitted diseases) or HIV (AIDS).

Combination Hormonal Contraceptives

Combination hormonal contraceptives include combination oral contraceptives, the transdermal patch, the vaginal ring, and hormonal implants. They use estrogen and a progestin in combination to suppress ovulation. In general, these forms have similar contraindications and adverse event profiles.

Hormonal Combination Oral Contraceptives[3]

With perfect use, the failure rate for combination oral contraceptives is equal to that of the best currently available contraceptive measure. **With typical use, oral contraceptives have the highest failure rate of the effective primary forms (Table 1).** Do not prescribe combination oral contraceptives for patients whom you do not think will take them exactly as prescribed. Other primary forms that do not require daily action by the patients, such as an IUD, may be a better choice for reducing the likelihood of pregnancy.

Note: Progesterone-only contraceptives (mini-pill), such as Ortho Micronor® Tablets, are not acceptable for the iPLEDGE program. If your patient is using them, she will have to choose another effective primary form of birth control.

Rate of unintended pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 8.00% (1 female in approximately 12 will become pregnant)

Mechanism of action

Suppression of ovulation

Contraindications

- Thrombophlebitis disorders, history of deep vein thrombosis (DVT), or thromboembolic disorder
- Cerebral vascular or coronary artery disease
- Migraine with focal aura
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Acute or chronic hepatocellular disease with abnormal liver function
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy
- Hypersensitivity to product

Other warnings

- Female patients with significant hypertension should not be started on oral contraceptives.
- Female patients who have had major surgery with immobilization or any leg surgery should not be started on oral contraception.
- Cigarette smoking increases the risk of serious cardiovascular adverse events with oral contraceptives. Female patients who use oral contraceptives should be strongly advised not to smoke. This risk is increased for female patients over 35 and those who smoke more than 15 cigarettes a day.

Instructions for use

Once daily for hormone pills for a specified time period, often followed by placebos for a specified number of days. The patient should take oral contraceptives exactly as prescribed.
Missed pill(s):

- Any missed pills: discontinue intercourse for the remainder of the cycle
- Missed more than 2 pills: instruct the patient to call as soon as she realizes that she has missed 2 or more pills; she should be evaluated for possible emergency contraception, depending on her sexual activity. The patient should be counseled not to have intercourse for the rest of the cycle.

Advantages

- May decrease the risk of the following:
  - endometrial and ovarian cancer
  - functional ovarian cysts
  - pelvic inflammatory disease
  - benign breast disease
  - ectopic pregnancy
- May decrease the incidence of dysmenorrhea and acne

Disadvantages

- Combination oral contraceptives do not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- Common adverse events include breakthrough bleeding, nausea and vomiting, and headaches
- Associated with an increased risk of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease
- Less effective with medications affecting hepatic metabolism such as anticonvulsants; may be less effective with the antibiotics rifampin and griseofulvin,* possible interaction with St. John's Wort
- Isotretinoin may make hormonal forms less effective
- If pills are skipped or missed, the risk of pregnancy is very high

Hormonal Transdermal Patch[4]

Rate of unintended pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 8.00% (1 female in approximately 12 will become pregnant)

Contraindications

See "Contraindications," page 13.

Instructions for use

One patch is used per week for 3 consecutive weeks, on the same day of the week. The fourth week is patch-free. Menses occurs at this time.

If the female patient is starting the patch for the first time, she should wait until the day she begins her menstrual period.

*Adapted from ACOG Practice Bulletin, Number 18, July 2000

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Slipped or missed patches:

- If the patch falls off or is partially detached for less than 24 hours, the patient can reapply in the same place. Otherwise, replace with a new patch immediately. Change patches on the original schedule.
- If the patch is detached for more than 1 day or the patient is not sure how long the patch was detached, she should start a new cycle with a new change day by applying a new patch. It will not be effective for contraception for the first week.
- The patient should be instructed not to have intercourse during this first week.

Advantages

- It is not necessary to remember to take a daily pill
- Many female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the patch is stopped

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS); less effective in female patients over 198 pounds
- Not effective if it becomes loose or falls off for more than 24 hours or if the same patch is left on the skin for more than 1 week
- Has the same labeling for contraindications, warnings, and precautions as oral contraceptives
- Common side effects include breakthrough bleeding, nausea, headaches and breast tenderness.
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective
- Possible increased risk of blood clots

Hormonal Vaginal Ring[5,6]

Rate of unintended pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 8.00% (1 female in approximately 12 will become pregnant)

Contraindications

See "Contraindications," page 13.

Instructions for use

Patient inserts ring in the vagina, where it should remain for 3 weeks. She removes ring for 1 week to bring on menses. A new ring is used each month for continuous contraception.

Advantages

- It is not necessary to remember to take a daily pill
- It does not need to be fitted by a clinician
- Many female patients have more regular, lighter, and shorter periods
- Fertility returns quickly when the ring is stopped

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- The ring cannot be used with a diaphragm or cervical cap
- Some female patients may have trouble inserting the ring
- It has the same labeling for contraindications, warnings, and precautions as oral contraceptives
- Efficacy of the ring is lessened if:
  - The unopened package containing the ring is put into direct sunlight or exposed to very high temperatures
  - It slips out of the vagina and is not replaced in 3 hours
  - It does not stay in the vagina for 3 weeks
  - It is left in the vagina for more than 3 weeks
- Common side effects include breakthrough bleeding, nausea and vomiting, and headaches.
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Single Hormone Contraceptives (Progestin-only)

Single hormone forms contain a progestin that can suppress ovulation, thicken cervical mucus, and produce endometrial atrophy. Accepted forms include single hormone injection, the LNg20 IUD, and implantable hormones. **Note: oral contraceptives containing no estrogen (progestin-only "mini-pills" see page 7) are not an acceptable form of contraception during isotretinoin therapy. The Progesterone T IUD is also not an acceptable form for the iPLEDGE program.**

Single Hormone Injections[3]

Rate of unintended pregnancies

Perfect Use: 0.3% (1 female in approximately 333 will become pregnant)
Typical Use: 3.00% (1 female in approximately 33 will become pregnant)

Contraindications

Pregnancy, unexplained abnormal vaginal bleeding, breast cancer or significant liver problems

Instructions for use

Injection every 12 weeks (150 mg/1 cc IM)

Advantages

- It works for 12 weeks at a time
- There is no daily pill to take
- It is good for female patients who cannot take estrogen

Disadvantages

Black Box Warning: Prolonged use of this [drug] may result in significant loss of bone density, and loss is greater the longer the drug is administered. Bone density loss may not be completely reversible after discontinuation of the drug. A female should only use this [drug] as a long-term birth control form (for example, longer than 2 years) if other birth control forms are inadequate for her.

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- It can cause irregular bleeding
- It requires healthcare professional visit for injection every 12 weeks
- If patient is planning to get pregnant *after* she finishes isotretinoin treatment, it may take up to 18 months for return of ovulation.
- Isotretinoin may make single hormonal forms less effective

LNg20 Intrauterine Device (IUD)[3,7]

The LNg20 IUD is indicated for contraception in female patients who have had at least 1 child, are in a monogamous relationship, and are at low risk for STDs (sexually transmitted diseases).

Note: The Progesterone T IUD is not an acceptable primary form of birth control for the iPLEDGE program. If your patient is using it, she will have to choose another effective primary form of birth control.

Rate of unintended pregnancies

Perfect Use: 0.2% (1 female in 500 will become pregnant)
Typical Use: 0.2% (1 female in 500 will become pregnant)

Contraindications

- Pregnancy or suspicion of pregnancy
- Congenital or acquired uterine anomaly, including fibroids if they distort the uterine cavity
- Acute pelvic inflammatory disease (PID) or history of PID without subsequent intrauterine pregnancy
- Postpartum endometritis or infected abortion in the past 3 months
- Known or suspected uterine or cervical neoplasia or unresolved, abnormal Pap smear
- Carcinoma of the breast
- Genital bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, lower genital tract infections
- Acute liver disease or liver tumor (benign or malignant)
- Female patient or her partner has multiple sexual partners
- Conditions associated with increased susceptibility to infections with microorganisms
- Genital actinomycosis
- Previously inserted IUD that has not been removed
- History of ectopic pregnancy or condition that would predispose to ectopic pregnancy

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Instructions for use

The IUD is inserted by a healthcare professional. The patient should check for IUD strings often in the first few months after insertion and after each period. If the patient cannot find the strings, the strings feel shorter or longer, she can feel the IUD itself, there are any signs of symptoms of PID, or she misses a period, instruct her to call her prescriber.

Advantages

- It can be used for long-term contraception (5 years) and is relatively quickly reversible (i.e., return to fertility).

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- It requires insertion and removal by a healthcare professional
- Common adverse events include menstrual changes, lower abdominal pain and cramping, acne or other skin problems, back pain, breast tenderness, headache, mood changes, nausea
- Enlarged ovarian follicles have been diagnosed in about 12% of LNg20 users; most disappear spontaneously during 2 to 3 months of observation
- All types of IUDs may increase the risk of pelvic inflammatory disease (PID); side effects of all types of IUDs may include cramps and heavier and longer periods in the first few months after it is placed
- IUD may be expelled, often during menses
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective

Implantable Hormones[3]

Description

Implantable hormones (etonogestrel implant) are a long acting (up to 3 years), reversible method of progestin only contraception. This form of contraception involves a sterile rod(s), the size of a matchstick, for subdermal insertion under the skin on the inner side of the upper arm during a minor in-office surgical procedure.

Rate of Unintended pregnancies

Perfect Use: 0.05% (1 female in 2000 will become pregnant)
Typical Use: 0.05% (1 female in 2000 will become pregnant)

Contraindications

- Known or suspected pregnancy
- Current or past history of thrombosis or thrombotic disorders
- Hepatic tumors (benign or malignant), active liver disease
- Undiagnosed abnormal genital bleeding
- Known or suspected carcinoma of the breast or personal history of breast cancer
- Hypersensitivity to any of the components of the implant

Advantages

- Effective birth control for up to 3 years
- It is not necessary to remember to take a daily pill
- Fertility may return quickly when Implant is removed
- Can be used in patients who cannot take estrogen

Disadvantages

- Implant does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- May cause irregular and unpredictable bleeding or amenorrhea.
- Other side effects can include headache, acne, dysmenorrhea and emotional lability
- Associated with an increased risk of myocardial infarction, thromboembolism, stroke, hepatic neoplasia and gall bladder disease
- Complications of insertion can include: swelling, redness, pain, bruising, scarring, infection, paresthesias, bleeding, and hematoma
- Complications of removal include: a broken rod, scar tissue making removal more difficult
- Rarely, it can be difficult or impossible to remove which may result in a surgical procedure

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

- If pregnancy occurs, there is a higher chance of an ectopic pregnancy
- Ovarian cysts that usually disappear spontaneously
- Studies were not done in women who weighed more than 130% of their ideal body weight or patients who are chronically taking medication that induce liver enzymes, and it is possible that the implant may be less effective in women who are overweight
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective

If you use an implant, always verify its presence in the patient's arm immediately after insertion by palpation. Until you confirm proper insertion, your patient must use a nonhormonal contraceptive method and is not eligible to start isotretinoin.

Non-hormonal Contraceptives[3,8]

Accepted non-hormonal forms of contraception include the Cu T 380A IUD, tubal sterilization, and partner's vasectomy. These non-hormonal forms do not protect against STDs (sexually transmitted diseases) or HIV.

Cu T 380A IUD

Perfect Use: 0.6% (1 female in approximately 166 will become pregnant)
Typical Use: 0.8% (1 female in 125 will become pregnant)

Description

Made of polyethylene covered with copper

Mechanism of action

Prevents fertilization by altering tubal and uterine transport of sperm

Contraindications

- Pregnancy or suspicion of pregnancy
- Abnormalities of the uterus resulting in distortion of the uterine cavity
- Acute pelvic inflammatory disease (PID) or a history of PID
- Postpartum endometritis or infected abortion in the past 3 months
- Known or suspected uterine or cervical malignancy, including unresolved, abnormal Pap smear
- Genital bleeding of unknown etiology

- Untreated acute cervicitis or vaginitis, including bacterial vaginosis, until infection is controlled
- Diagnosed Wilson's disease
- Known allergy to copper
- Female patient or her partner has multiple sexual partners
- Genital actinomycosis
- A previously inserted IUD that has not been removed

Instructions for use

Patient should check for IUD strings often in first few months after insertion and after each period. If patient cannot find the strings, the strings feel shorter or longer, she can feel the IUD itself, there are any signs of symptoms of PID, or she misses a period, she should call her prescriber.

Advantages

- Female patients who cannot take hormones can use it
- It can be used for long-term contraception (10 years) and is relatively quickly reversible (i.e., return to fertility)

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- It requires insertion and removal by a healthcare professional
- It should be used in female patients who are not at risk for STDs (sexually transmitted diseases)
- All types of IUDs may increase the risk of pelvic inflammatory disease (PID)
- Side effects of all types of IUDs may include cramps, and heavy, longer periods
- The IUD may be expelled, often during menses

Sterilization[3]

Female sterilization may be accomplished using a variety of techniques. They are all considered to be very effective, virtually permanent methods of pregnancy prevention and, with the exception of hysteroscopic tubal sterilization, are immediately effective. For purposes of the iPLEDGE program, a patient should not be permitted to consider her hysteroscopic tubal sterilization as an accepted method of contraception unless she has had a confirmatory hysterosalpingogram (HSG) or other confirmation.

A partner's vasectomy involves the mechanical blocking of the vasa deferentia in males. This is an effective primary form of contraception which prevents fertilization by keeping sperm from entering the seminal fluid. Males should have semen analysis after 15 to 20 ejaculations to be sure semen is free from sperm. If the patient has more than 1 partner, each partner must be sterilized for male sterilization to be effective as the patient's only primary form. If the patient uses male sterilization as a primary form, she should be encouraged to choose another primary form as a second form.

Rates of unintended pregnancies

Tubal sterilization

Perfect Use: 0.5% (1 female in 200 will become pregnant)
Typical Use: 0.5% (1 female in 200 will become pregnant)

Partner's vasectomy

Perfect Use: 0.1% (1 female in 1,000 will become pregnant)
Typical Use: 0.15% (1 female in approximately 666 will become pregnant)

Advantages (for tubal sterilization)

- Very effective, virtually permanent means of contraception

Disadvantages (for tubal sterilization)

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- Difficult to reverse
- Requires surgery
- If a pregnancy does occur, there is an increased risk of an ectopic pregnancy

Advantages (for partner's vasectomy)

- Very effective, virtually permanent means of contraception

Disadvantages (for partner's vasectomy)

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- Low success rate in reversing
- Requires surgery
- Not effective right away

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

SECONDARY FORMS OF CONTRACEPTION

Most of the secondary forms are barrier contraceptives that prevent sperm from entering the vagina (condom) or cervix (diaphragm and cervical cap). Barrier forms include the diaphragm and the cervical cap, both of which must be used with spermicide. The male latex condom can be used with or without spermicide. The vaginal sponge is a delivery system for spermicide and has spermicide embedded in it. Female condoms are not acceptable for the iPLEDGE program.

Diaphragms, and cervical caps are barrier contraceptives that are considered moderately effective when used in combination with a spermicide. The male latex condom is a barrier contraceptive that is considered moderately effective when used with or without spermicide. The vaginal sponge is also considered moderately effective. The most important issue is whether the secondary form will be used each time the patient has intercourse. If the patient selects a secondary form as the second form of contraception, she must understand how it is used and be fully committed to using it each time she has intercourse.

Female patients under 30 and female patients who have intercourse 3 or more times per week may have a higher failure rate with vaginal secondary forms.

Note: The female condom, a thin, flexible plastic tube that covers the cervical os, is not an acceptable secondary form for the iPLEDGE program.

Male Latex Condom Used With or Without Spermicide[3]

If the patient does not feel she can convince her partner(s) to use a latex condom (with or without spermicide) each time they have intercourse, she would need to select another secondary form where she has the control or select a second primary form.

Rate of unintended pregnancies

Perfect Use: 2% when used without spermicide (1 female in 50 will become pregnant)
Typical Use: 15% when used without spermicide (1 female in 7 will become pregnant)

Male condom (Latex) may be used with or without spermicide

Instructions for use

Unrolled onto erect penis before there is any contact with female genitals; use only water-based lubricants with latex condoms

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Advantages

- Protects against STDs (sexually transmitted diseases) and HIV (AIDS)
- Easy to buy, no doctor appointment needed, no pelvic exam needed
- Easy to tell when it breaks or slips, important for seeking emergency contraception
- May lower risk of cervical dysplasia and cancer[12]

Disadvantages

- Condoms can break or slip during sex
- May decrease sensitivity and spontaneity, may have trouble maintaining erection
- Must remember to use every time

Diaphragm Used With Spermicide[3,9]

Rate of unintended pregnancies

Perfect Use: 6% when used with spermicide (1 female in approximately 17 will become pregnant)
Typical Use: 16% when used with spermicide (1 female in approximately 6 will become pregnant)

Description

Dome-shaped rubber cap with a flexible rim available in many sizes (50-95 mm diameter) and different styles

Warnings

- There is an association between Toxic Shock Syndrome (TSS) and diaphragm use.
- A diaphragm must be removed after 6 to 8 hours to decrease the risk of TSS.
- There may be increased risk of urinary tract infections, candidiasis, or bacterial vaginosis.
- A diaphragm may cause allergic reactions in females sensitive to latex or rubber.

Advantages

- Female patients can easily carry a diaphragm with them and have control of its use
- Immediately effective
- No hormones
- No interruption of sex play; can be inserted any time before intercourse and must stay in place for at least 6 to 8 hours after intercourse; a diaphragm should not be worn for more than 24 hours
- May lower risk of cervical dysplasia and cancer
- Can be used during a menstrual period

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- Requires a prescription, pelvic examination, and periodic refitting; lasts about 1 to 2 years

- Some female patients find it hard to insert
- Spermicide must be inserted in the vagina if there is repeated intercourse
- Can get pushed out of place during sex
- Must be checked for holes after sex and cleaned after use

Cervical Cap Used With Spermicide[3,10]

Rate of unintended pregnancies in nulliparous females

Perfect Use: 9% when used with spermicide (1 female in approximately 11 will become pregnant)

Typical Use: 20% when used with spermicide (1 female in 5 will become pregnant)

The failure rate is double in parous females.

Description

Deep rubber cap with firm rim and a groove inside the rim that fits snugly around the cervix

Advantages

- Same as diaphragm
- No need to add more spermicide if female patient has repeated intercourse
- Continuous protection for 48 hours

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- Some female patients find it harder to insert than a diaphragm
- It cannot be used during a menstrual period
- Patient needs a prescription and a pelvic examination to fit a cervical cap; a cap lasts about 1 year.
- Must be checked for holes and tears after sex and cleaned after use
- Less effective with multiparous females

Vaginal Sponge (Contains Spermicide)[3,11]

Rate of unintended pregnancies in nulliparous females:

Perfect Use: 9% (product contains spermicide) (1 female in approximately 11 will become pregnant)

Typical Use: 16% (product contains spermicide) (1 female in approximately 6 will become pregnant)

The failure rate is double in parous females.

Description

Soft, disposable, non-abrasive polyurethane foam that is a delivery system for 1 gram of the spermicide, Nonoxynol-9

Advantages

- Female patients can easily carry a vaginal sponge with them and have control of its use
- Immediately effective
- No hormones
- No interruption of sex play; can be inserted any time before intercourse and is effective for up to 24 hours
- No need to put in more spermicide with repeated intercourse
- No special fitting, available over the counter
- Not associated with TSS

Disadvantages

- Does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- Less effective with multiparous females

EMERGENCY CONTRACEPTION[3]

Emergency contraception is indicated after sex without adequate protection:

- No contraception is used
- A secondary form slips or breaks
- Missed pill or injection
- Rape

Emergency contraception is provided as either emergency hormonal contraception or insertion of a Cu T 380A IUD.

Emergency Contraception Pills (ECPs)

Emergency contraception is a sequence of 2 high doses of combination oral contraceptives beginning within 72 hours of unprotected sex and taken 12 hours apart. Progestin-only pills must be started within 72 hours of unprotected sex. Patients must understand that the sooner ECPs are started, the more likely they are to be effective. Common side effects include nausea and vomiting. Consider prescribing medication to reduce these side effects.

Please check product specific labeling for dosing and related adverse events for emergency contraception alternatives.

Insertion of Cu T 380A IUD

The IUD is inserted within 5 days of unprotected sexual intercourse. IUD insertion for emergency contraception is not recommended for female patients who have not had a child or are at risk for sexually transmitted infections. These include female patients with more than 1 sex partner or whose partners have more than 1 partner, female patients with new partners, and female patients who have been raped.

The names and phone numbers of emergency contraception prescribers in your area can be obtained by calling toll free: 1-888-NOT-2-LATE (1-888-668-2528).

REPORTING A PREGNANCY

The iPLEDGE Program Pregnancy Registry

The iPLEDGE Program Pregnancy Registry collects data on pregnancies that occur in female patients who become pregnant while taking isotretinoin or within 30 days of their last dose. Data from the registry are reported to the FDA and are used to assess the effectiveness of the iPLEDGE program. The data are also used to evaluate further ways to reduce fetal exposure. Information gathered in the iPLEDGE Program Pregnancy Registry will be used for statistical purposes only and will be held in the strictest confidence.

The prescriber must report to the iPLEDGE Program Pregnancy Registry any pregnancy case that he/she becomes aware of while the female patient is on isotretinoin or 1 month after the last dose. Report a pregnancy by calling **1-866-495-0654**. Select the option to **"Report a Pregnancy."** All pregnancies should also be reported to the FDA via the MedWatch number: 1-800-FDA-1088.

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NOTES:

For More Information About Isotretinoin And The iPLEDGE Program

If you have questions about the iPLEDGE program, visit the iPLEDGE program web site at **www.ipledgeprogram.com**, or call **1-866-495-0654**.

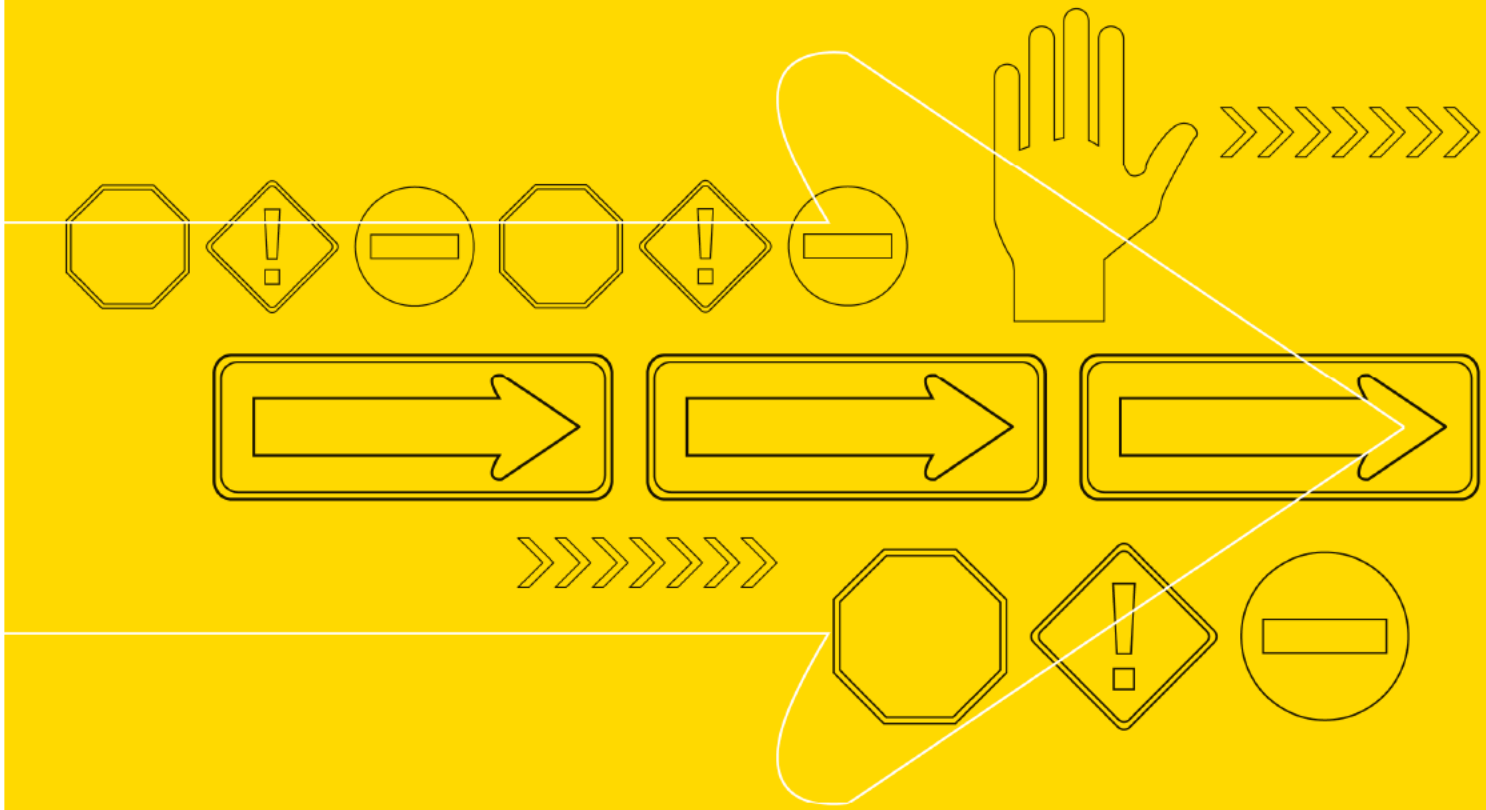
Confidential birth control information can be obtained via the iPLEDGE automated phone line 24 hours a day, 7 days a week at **1-866-495-0654**. The subjects include:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**



www.ipledgeprogram.com 1-866-495-0654

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™
Committed to Pregnancy Prevention

 PRE_BOOK05 (R-1 0312)

Be Prepared, Be Protected

VIDEO SCRIPT

SCENE 1: ABSTINENCE

FEMALE 1: I thought I was abstinent. I guess I didn't know what abstinence really means. Now I do.

ANNOUNCER: It's important to know what abstinence means. Not having sex. Not once, twice, or ever. Just because you're not having sex now, doesn't mean you will have always be abstinent. You're only abstinent if you know you won't be tempted to have sex. And this becomes especially important when you are taking a drug that may cause birth defects to your unborn baby. Think about it: Are you *really* abstinent?

SCENE 2: UNPREPARED PREGNANCY

FEMALE 2: I can't believe I'm pregnant. It was just that one time. And I have been so careful. This can't be right.

ANNOUNCER: You have to be sure if you are having sex at any time you can't use any excuses. It doesn't matter if your periods are irregular, or if you think you can't get pregnant, or if you don't have sex frequently. And if you are on a medication that could be harmful to your unborn baby, you need to be especially and extremely careful. Once can be enough.

SCENE 3: WITHDRAWAL

FEMALE 3: We used withdrawal for a long time. But this time withdrawal just didn't work.

ANNOUNCER: Withdrawal is unreliable. Use effective birth control such as the contraceptive pill, diaphragm, condom, and if you are taking a medication that may cause birth defects to your unborn baby, use a combination of two. If you don't like the pill, you have other options such as long lasting contraceptive implants, injectables, and intrauterine devices—IUDs. Always practice safe birth control using reliable effective methods to avoid pregnancy.

SCENE 4: BEING UNPREPARED

FEMALE 4: This is so nice. (Thoughts of Female 4) *I didn't think this would happen. I mean at least not tonight. I'm so surprised and unprepared.*

ANNOUNCER: Be prepared and protected. Think about it before hand. You may have sex and you might get pregnant? Don't assume your partner will take responsibility. And if you are on a medication that may cause birth defects—think about your unborn baby. Be prepared and ready to use reliable effective forms of birth control.

SCENE 5: BIRTH CONTROL CAN FAIL

FEMALE 5: I can't believe this. There's a hole in my diaphragm. What if I get pregnant? What am I going to do?

ANNOUNCER: Your doctor or nurse can help you find out if you are really pregnant. If you are, they can give you advice. Always make sure your birth control is reliable and effective. And if you are on a drug that may cause birth defects, be sure you are doubly protected.

If you have any questions you should speak to your doctor or nurse. Carefully follow instructions provided by your prescriber, and consult with them if you have any questions about pregnancy, birth control, or your medical treatment.

[TYPE—NO VOICE]

Frame 1:

Complete Contraceptive Certainty = Be prepared Be protected

Frame 2:

You have just seen five scenarios with the most common reasons women have unwanted or ill-timed pregnancies.

Frame 3:

If you are not being completely abstinent, then

- Use birth control regularly
- Use the most effective types of birth control
- Be sure the method you choose is reliable
- Be prepared and be protected

Frame 4:

Brought to you as an educational service.

Opening Segment
"ISOTRETINOIN CANNOT BE TAKEN BY WOMEN WHO ARE PREGNANT, BECAUSE ISOTRETINOIN CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY.

In this video we will see what can happen to an unborn baby if the baby's mother takes isotretinoin.

A woman must not take isotretinoin at any time during pregnancy.

Storyboard P2
Isotretinoin is usually prescribed for males and females to treat the most severe form of acne called nodular acne. This type of acne cannot be cleared up by any other acne treatments, including antibiotic pills. Nodular acne has many red, swollen, tender lumps that form in the skin. These lumps are the size of a pencil eraser or larger and can result in permanent scars if not treated.

Because of serious side effects and birth defects, patients should use isotretinoin only if other treatments including antibiotic pills have not worked.

Storyboard P3
"FEMALE PATIENTS MUST NOT TAKE ISOTRETINOIN IF THEY ARE PREGNANT, PLAN TO BECOME PREGNANT OR BECOME PREGNANT DURING THERAPY. TO AVOID PREGNANCY, WOMEN MUST USE TWO FORMS OF EFFECTIVE CONTRACEPTION ONE MONTH BEFORE STARTING ISOTRETINOIN, WHILE TAKING ISOTRETINOIN, AND FOR ONE MONTH AFTER STOPPING ISOTRETINOIN UNLESS THEY ARE ABSOLUTELY ABSTINENT, NEVER HAVING SEX, OR HAVE HAD THEIR UTERUS OR WOMB REMOVED".

Storyboard P4
"ISOTRETINOIN CAPSULES BREAK DOWN IN THE BODY AND THE MEDICINE ENTERS INTO THE BLOODSTREAM

Storyboard P5
"AND THE BLOOD IS CARRIED INTO THE PLACENTA WHERE IT REACHES THE UNBORN FETUS.

The medicine can cause severe birth defects."

Storyboard P6
"It is highly possible that the unborn baby may die because the baby's mother took isotretinoin."

Storyboard P7
"If the fetus lives, as the fetus develops, several birth defects can begin to take place.

These birth defects may be caused by taking isotretinoin during pregnancy".

Storyboard P8
"One of these birth defects may be abnormal skull development". "Use of isotretinoin during pregnancy may cause an under development or over development of the skull".

Storyboard P9
"Development of the ears may also be affected". "The ears may not fully develop if isotretinoin is used during pregnancy. The outer ear may be deformed and the ear canal may be very small or absent entirely causing deformity".

Storyboard P10
"The eyes also may not develop fully".
"The eye socket may be very small or not develop at all causing facial deformity

Storyboard P11
"As face structure begins to form the fetus can have a flattening of the nose and a twisting of the mouth. These birth defects could happen from using isotretinoin during pregnancy".

Storyboard P12
"The baby may also be born with a separation of the roof of the mouth and sometimes the lips which is known as a cleft palate".

Storyboard P13
IN ADDITION TO THE VISIBLE DEFECTS, SEVERAL INTERNAL SERIOUS AND LIFE-THREATENING BIRTH DEFECTS MAY DEVELOP IN THE HEART AND IN THE ENTIRE HEART AND BLOOD FLOW SYSTEM.

One of these defects can include an abnormal heart that has the arteries and veins in the wrong position.

Storyboard P14
"The system that helps to fight infection may also be affected. One of the glands in this system - the thymus gland may not develop and the baby then would have trouble fighting infections." "In addition, another gland -the parathyroid gland may not develop. The parathyroid gland helps the baby to form bones by controlling the amount of calcium in the body.

Storyboard P15
Brain and nervous system defects including an abnormal brain may occur…" OR AN UNDERDEVELOPMENT OF THE BRAIN. IT HAS ALSO BEEN REPORTED THAT SOME CHILDREN HAVE LOW IQ SCORES".

Storyboard P17
In summary, taking isotretinoin during pregnancy can result in any or all of these birth defects:

The skull may over- or under- develop.

FACIAL DYSMORPHIA CAN OCCUR, CAUSING A FLATTENING OF THE NOSE AND DISTORTION OF FACIAL STRUCTURE.

Enlargement of the brain may occur.

Eye sockets may be very small or not develop at all.

The brain can also under-develop.

Ears may not fully develop.

The thymus gland may not develop, affecting an infant's ability to fight off disease.

Abnormalities in the heart and entire cardiac system can be life threatening.

A cleft palate may form.

Storyboard P18
UNLIKE THE BIRTH DEFECTS THAT ARE SEEN IN THE BABIES WHEN MOTHERS TAKE ISOTRETINOIN, THERE IS NO PATTERN OF BIRTH DEFECTS WHEN FATHERS TAKE ISOTRETINOIN.

"But men who take isotretinoin should be careful in other ways." Men might not realize that they should not donate blood during, and for a period of one month following, the end of their isotretinoin treatment".

Storyboard P19
"As discussed earlier, isotretinoin is carried through the bloodstream and a pregnant woman could, unknowingly accept a blood transfusion from a man or a woman who took isotretinoin. The blood and medicine could then pass into the placenta possibly harming an unborn baby".

Therefore, it is extremely important that both men and women taking isotretinoin do not donate blood during treatment and for a period of at least one month following the end of their isotretinoin treatment.

Storyboard P 20
"Neither men nor women should *ever* share their isotretinoin with another woman..."

Storyboard P 21
"...BECAUSE OF THE RISK THAT SHE MAY BE PREGNANT."

"No one should ever share any medicine with anyone else, because the medicine may harm the other person."

Black Box

YOU MUST NOT BECOME PREGNANT WHILE TAKING ISOTRETINOIN, OR FOR ONE MONTH AFTER YOU STOP TAKING ISOTRETINOIN.

Isotretinoin can cause severe birth defects in babies of women who take it while they are pregnant, even if they take isotretinoin for only a short time.

There is an extremely high risk that your baby will be deformed or will die if you are pregnant while taking isotretinoin. Taking isotretinoin also increases the chance of miscarriage and premature births.

Female patients will not get their first prescription for isotretinoin unless there is proof they have had two negative pregnancy tests. The first test must be done when your prescriber decides to prescribe isotretinoin. The second pregnancy test must be done during the first five days of the menstrual period right before starting isotretinoin therapy, or as instructed by your prescriber. Each month of treatment, you must have a negative result from a urine or serum pregnancy test. Female patients cannot get another prescription for isotretinoin unless there is proof that they have had a negative pregnancy test.

WHILE YOU ARE TAKING ISOTRETINOIN, YOU **MUST** USE EFFECTIVE BIRTH CONTROL. **YOU MUST USE 2 SEPARATE, EFFECTIVE FORMS OF BIRTH CONTROL AT THE SAME TIME** FOR AT LEAST ONE MONTH BEFORE STARTING ISOTRETINOIN, WHILE YOU TAKE IT, AND FOR ONE MONTH AFTER YOU STOP TAKING IT. YOU CAN EITHER DISCUSS EFFECTIVE BIRTH CONTROL METHODS WITH YOUR PRESCRIBER OR GO FOR A FREE VISIT TO DISCUSS BIRTH CONTROL WITH ANOTHER PHYSICIAN OR FAMILY PLANNING EXPERT. YOUR PRESCRIBER CAN ARRANGE THIS FREE VISIT, WHICH WILL BE PAID FOR BY THE MANUFACTURER.

You must use two separate forms of effective birth control because any method, including birth control pills and sterilization, can fail. There are only 2 reasons that you would not need to use 2 separate methods of effective birth control:

1. You have had your womb removed by surgery – a hysterectomy or
2. You are absolutely certain you will not have genital-to-genital sexual contact with a male before, during and for one month after isotretinoin treatment.

IF YOU HAVE SEX AT ANY TIME WITHOUT USING TWO FORMS OF EFFECTIVE BIRTH CONTROL, GET PREGNANT, OR MISS YOUR PERIOD, STOP USING ISOTRETINOIN AND CALL YOUR PRESCRIBER RIGHT AWAY.

Recognizing Psychiatric Disorders In Adolescents And Young Adults

A Guide For Prescribers Of Isotretinoin

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Recognizing Psychiatric Disorders In Adolescents And Young Adults: A Guide For Prescribers Of Isotretinoin

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CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE™. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see **PRECAUTIONS**).

Warnings

Psychiatric Disorders: Isotretinoin may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. No mechanism of action has been established for these events (see ADVERSE REACTIONS: Psychiatric). Prescribers should read the brochure, *Recognizing Psychiatric Disorders In Adolescents And Young Adults: A Guide For Prescribers Of Isotretinoin*. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin therapy, patients and family members should be asked about any history of psychiatric disorder, and at each visit during therapy patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary. Signs and symptoms of depression, as described in the brochure *Recognizing Psychiatric Disorders In Adolescents And Young Adults,* include sad mood, hopelessness, feelings of guilt, worthlessness or helplessness, loss of pleasure or interest in activities, fatigue, difficulty concentrating, change in sleep pattern, change in weight or appetite, suicidal thoughts or attempts, restlessness, irritability, acting on dangerous impulses, and persistent physical symptoms unresponsive to treatment. Patients should stop isotretinoin and the patient or a family member should promptly contact their prescriber if the patient develops depression, mood disturbance, psychosis, or aggression, without waiting until the next visit. Discontinuation of isotretinoin therapy may be insufficient; further evaluation may be necessary. While such monitoring may be helpful, it may not detect all patients at risk. Patients may report mental health problems or family history of psychiatric disorders. These reports should be discussed with the patient and/or the patient's family. A referral to a mental health professional may be necessary. The physician should consider whether isotretinoin therapy is appropriate in this setting; for some patients the risks may outweigh the benefits of isotretinoin therapy.

Pseudotumor Cerebri: Isotretinoin use has been associated with a number of cases of pseudotumor cerebri (benign intracranial hypertension), some of which involved concomitant use of tetracyclines. Concomitant treatment with tetracyclines should therefore be avoided. Early signs and symptoms of pseudotumor cerebri include papilledema, headache, nausea and vomiting, and visual disturbances. Patients with these symptoms should be screened for papilledema and, if present, they should be told to discontinue isotretinoin immediately and be referred to a neurologist for further diagnosis and care (see ADVERSE REACTIONS: Neurological).

Adverse Reactions

Neurological: pseudotumor cerebri (see WARNINGS: Pseudotumor Cerebri), dizziness, drowsiness, headache, insomnia, lethargy, malaise, nervousness, paresthesia, seizure, stroke, syncope, weakness

Psychiatric: suicidal ideation, suicide attempts, suicide, depression, psychosis, aggression, violent behaviors (see WARNINGS: Psychiatric Disorders), emotional instability

Of the patients reporting depression, some reported that the depression subsided with discontinuation of therapy and recurred with reinstitution of therapy.

Reporting adverse events

Specific information about adverse events that may occur during isotretinoin therapy may be reported to the individual makers of isotretinoin and/or to the Food and Drug Administration MedWatch Program at 1-800-FDA-1088 or via www.fda.gov/medwatch/report.htm.

The contact information for specific brands of isotretinoin can be obtained by calling 1-866-495-0654 or via www ipledgeprogram.com.

Isotretinoin

Isotretinoin is a retinoid related to vitamin A. Patients should be advised against taking vitamin supplements containing vitamin A to avoid additive toxic effects.

Introduction

Mental health problems are underdiagnosed and undertreated.[1] Dermatologists and other isotretinoin prescribers often see patients who are otherwise healthy, and they may be among the only professionals who have opportunities to evaluate patients' mental health. Healthcare providers who recognize the signs and symptoms of psychiatric illness and respond appropriately can improve, and perhaps even save, their patients' lives.

Isotretinoin may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors. Although causality has not been established for these reports, awareness of signs and symptoms may save your patient's life. This brochure provides an overview of depression. The goal of this brochure is to help you identify when a psychiatric consult is advisable.

You and your staff may feel uncomfortable evaluating your patients' mental health status. It is often difficult to distinguish clinical depression from other responses. It may also be difficult to decide whether erratic behavior may warrant psychiatric evaluation, especially if that behavior seems to be age-appropriate in a teenager. However, as with any specialized problem, you may identify patients who seem to need more than dermatologic care, and you may need to refer them to a specialist. Knowing when to make a referral for a patient who may be at psychiatric risk can make a major difference in the patient's life. In extreme cases, it can mean the difference between life and death.

Depression

Depression and suicidal tendencies are two important psychiatric conditions that may be observed in dermatology and family practice settings. This brochure provides an overview of depression because depression is the most commonly reported psychiatric adverse event in patients taking isotretinoin and is also a well established risk factor for suicidal behavior.

Depression is characterized by symptoms that include intense, persistent sadness; anxiety; loss of pleasure from usual activities; and loss of energy.[2] These feelings can be normal responses to a negative life event, but clinical depression is either not triggered by such an event or is disproportionate to the trigger.[3]

Depression can be episodic. According to the National Comorbidity Survey, 16.2% (between 32.6 and 35.1 million) of Americans will experience depression at some point during their lives, and 6.6% (between 13.1 and 14.2 million) are depressed in any given month.[4,5] Several epidemiological studies reported that up to 8.3% of adolescents in the United States suffer from depression.[6] Older adolescents experience more depressive symptoms than adults and comparable symptom persistence, suggesting that these adolescents may be at the highest risk for depression.[7]

Depression can take several forms: three of the most common are dysthymia, major depression, and bipolar disorder.[2] These three disorders are characterized by various combinations of the symptoms listed in Table 1. Not every patient exhibits all depressive symptoms. Some patients, especially adolescents, may display irritability instead of sadness.

TABLE 1. Symptoms of depression

- Persistent sad, anxious, or "empty" mood
- Feelings of hopelessness, pessimism
- Feelings of guilt, worthlessness, helplessness
- Loss of interest or pleasure in hobbies and activities that were once enjoyed, including sex
- Decreased energy, fatigue, being "slowed down"
- Difficulty concentrating, remembering, making decisions
- Insomnia, early-morning awakening, or oversleeping
- Appetite and/or weight loss or overeating and weight gain
- Thoughts of death or suicide; suicide attempts
- Restlessness, irritability
- Persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders, and chronic pain
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

Table 1 modified from National Institute of Health "Depression" Available at: http://www nimh nih gov/publicat/depression cfm#ptdep1 Accessed February 23, 2005

Dysthymia has characteristics similar to those of major depression but is not as disabling. People with dysthymia often function adequately but not at previous wellness levels, and are at risk for episodes of major depression. In major depression, a combination of symptoms prevents the patient from working, studying, and/or engaging in normal activities.

In bipolar disorder, the patient alternates between periods of depression (severe lows) and episodes of mania (severe highs).[2]

Symptoms of mania[2]

- Abnormal or excessive elation
- Unusual irritability
- Decreased need for sleep
- Grandiose notions
- Increased talking
- Racing thoughts
- Increased sexual desire
- Markedly increased energy
- Poor judgment
- Inappropriate social behavior

Causes of depression

The causes of depression are often multifactorial and may include:

- Genetic predisposition[2]
- Stress at home, work, or school[2]
- Loss of a parent or loved one[8]
- Alcohol or substance abuse[9]
- Breakup of a romantic relationship[10]
- Medications[11]

Suicide

Suicide accounts for more than 30,000 American deaths each year. It is the third leading cause of death (after accidents and homicide) among people aged 15 to 24, which makes it responsible for more deaths in this age group than any physical illness.[12–14] Of the total number of suicides among people ages 15 to 24 in 2001, 86% were male and 14% were female.[15, 16] Healthcare providers often miss the warning signs because patients may hide suicidal intent very successfully. In fact, 60% of people who commit suicide had seen a physician within 1 month of their deaths.[9] Suicidal tendencies rarely arise spontaneously; 93% of people who commit suicide suffer from depression, schizophrenia, and/or substance abuse.[17]

Up to 60% of adolescents and young adults think about suicide at some point,[12] but fortunately these thoughts usually pass. Few people who have suicidal thoughts make the attempt, and most attempts at suicide are unsuccessful.[13] The following are some elements of a suicide risk assessment that can be used to determine the individual's risk level for suicide[18]:

- Ideation (thoughts of death or suicide)
- Suicidal intent
- Plan (specific time, place, and method)
- Means (e.g., a firearm in the house or a supply of drugs)

Women are twice as likely as men to attempt suicide, but men are four times more likely to be successful. Women usually use means from which they may be rescued, such as a drug overdose,[19] whereas men tend to use firearms or automobiles. Firearms are used in 55% of all completed suicides.[13]

Despite a patient's attempt to hide suicidal thoughts, he or she may send deliberate warning signals, some of which can be explicit.[2] Every mention or discussion of "killing myself" should be treated with utmost seriousness.

Evaluating And Referring Patients For Psychiatric Disorders

Although only 5% of the population is depressed at any given time,[20] the incidence has been found to be closer to 15% to 20% in primary care settings.[21] Given that 1 in 5 patients who come to your office may have some degree of depression, a few questions can identify patients who may be at risk.

It is important to find out whether a patient is under care or has ever been under care for an emotional problem or psychiatric disorder, particularly depression. Knowing a patient's current medications, for example, if he or she is taking antidepressants, can further identify those patients who may be at even greater risk than the general population.

Talking About Depression

Although it can be awkward to explain to a patient that he or she may have signs of depression (or any mental illness), the awkwardness can be minimized by reminding the patient that:

- Depression is very common
- It matches some of the symptoms the patient described
- It is treatable

Assessments: Depression

While taking a history, the prescriber should suspect the likelihood of depression if the patient has symptoms such as[6]:

- Persistent sad or irritable mood
- Loss of interest in activities once enjoyed
- Significant change in appetite or body weight
- Difficulty sleeping or oversleeping
- Psychomotor agitation or retardation
- Loss of energy
- Feelings of worthlessness or inappropriate guilt
- Difficulty concentrating
- Recurrent thoughts of death or suicide

In children and young adolescents, other signs to look for include[6]:

- Frequent, vague, non-specific physical complaints such as headaches, muscle aches, stomach aches, or tiredness
- Frequent absences from school or poor performance in school
- Talk of or efforts to run away from home
- Outbursts of shouting, complaining, unexplained irritability, or crying
- Being bored
- Lack of interest in playing with friends
- Alcohol or substance abuse
- Social isolation, poor communication
- Fear of death
- Extreme sensitivity to rejection or failure
- Increased irritability, anger, or hostility
- Reckless behavior
- Difficulty with relationships

The prescriber should also discuss with the patient:

- Alcohol or substance abuse
- Chronic pain
- Real or perceived disfigurement

Studies indicate that acne is associated with symptoms such as social embarrassment, low self-esteem, and anxiety, but an association of acne with frank depressive disorders has not been established, nor has treatment of acne by itself been shown to ameliorate frank depressive disorders.[22-24]

Assessments: Suicide

Psychiatric specialists have identified several factors for suicide risk. These include[19]:

- Presence or history of depression, bipolar disorder, or other psychiatric disorder
- Access to firearms in the home
- Family history of suicide or violence, including abuse
- Poor physical health, chronic illness, or chronic pain
- Alcohol or substance abuse
- Previous suicide attempt

It is important to note that depression itself is a major risk factor for suicidal behavior.[19] Thus, special attention is needed when prescribing drugs that may cause depression. An association with isotretinoin should be considered in patients with signs and symptoms of depression, even in the presence of other life stressors. Discontinuation of isotretinoin may be insufficient intervention and a formal psychiatric evaluation should be conducted. It is also important to note that signs and symptoms of depression are not included in all reported cases of suicidal behavior. It is not known if this means the signs were masked by the patient, unrecognized by observers, or if the suicidal tendency arose impulsively. It is important that patients taking isotretinoin be made aware of this so that they might recognize any such signs and symptoms. Patients (and parents, if the patient is a minor) should be instructed to stop isotretinoin and seek immediate medical help.

Talking with patients about suicide does not encourage or remind them that suicide is an option.[19]

Knowing When To Refer

You should refer the patient to a psychiatric specialist for further evaluation if any of the following apply:

- Risk factor(s) for suicide is (are) present
- The patient has, or may have, clinical depression or bipolar disorder, or if the prescriber believes that there may be a problem but cannot classify it
- The patient has expressed interest in, or spontaneously mentioned, suicide
- There is any question about the patient's safety

Summary

Prescribers who are alert to the warning signs of psychiatric disorders can guide patients to receive the help they need. Observing patients for signs of depression and suicidal ideation, and referring appropriate patients to a psychiatric specialist, need not be complicated. The benefits to patients can be immense, even life saving.

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Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

 10266-9 SEP05

iPLEDGE™
Committed to Pregnancy Prevention

REQUEST FOR EXEMPTION FOR PATIENTS WITH SERIOUS MEDICAL REASONS

NOTE: This form **MUST** be filled out and signed by the requesting prescriber or office staff designee. **All** required information (*) must be provided. If requested by the office staff designee, please provide the office staff designee name and iPLEDGE ID. Please FAX this completed form to **866-486-7001**.

*Prescriber ID	**"[click here and enter the prescriber's iPLEDGE ID]"**
*Prescriber Name	**"[click here and enter the prescriber's name]"**
*Patient ID	**"[click here and enter the patient's iPLEDGE ID]"**
*Patient Date of Birth	**"[click here and enter the patient's date of birth]"**
Office Staff Designee ID	**"[click here and enter the designee's iPLEDGE ID]"**
Designee Name	**"[click here and enter the designee's name]"**
*Office Telephone Number	**"[click here and enter your telephone number]"**

☐ I request iPLEDGE to authorize an exemption from the iPLEDGE requirements to change the status of the patient identified above to "Requires Confirmation". I understand that this would provide a 7 day window for the patient to fill their prescription from the date of specimen collection for the pregnancy test upon successful demonstration of comprehension.
This exemption applies only to this prescription.

☐ I request iPLEDGE to authorize an exemption from the iPLEDGE requirements to change the status of the patient identified above to "Qualified to Receive Drug". I understand that this request indicates that the patient is not capable of demonstrating comprehension based on mental and/or physical limitations.
This exemption applies only to this prescription.

- I understand that my signature below indicates that the patient identified above for serious medical reasons should not delay the initiation of isotretinoin and is not pregnant as of the date of this request.
- I will contact the pharmacy regarding this request and alert the pharmacy to access the iPLEDGE system for authorization.
- I understand that a copy of this form should be maintained with the patient's medical chart.

*Signature _____

*Date of Request _____

PLEASE FAX COMPLETED COPY TO 866-486-7001

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE – Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

OFFICE STAFF DESIGNEE REGISTRATION FORM

(Please Print All Information)

Note: Only One Registration Per Office Staff Designee Is Required

Please complete the information below. All information is **required** and any missing information will delay the completion of your registration. You can also register office staff on the program web site, **www ipledgeprogram.com.** Log in and choose **"Manage Delegates/Designees"** on the Prescriber home page and then select **"Register New Designee"**. Once you have completed all information, select the **"Save and Print"** button on the registration page to save the new information and print the registration form. The Office Staff Designee must sign and date the completed form.

Designee Last Name _____

Designee First Name _____ Middle Initial _____

Last Four Digits of Social Security Number _____ Date of Birth _____ (mm/dd/yyyy)

Office Address _____

City _____ State _____ ZIP _____

Office Telephone _____ Office Fax _____

E-mail _____

Preferred method of contact (Please select only one)

☐ Phone ☐ E-mail

Signature (Designee) _____

Date _____ (mm/dd/yyyy)

To Register:

1. Fax this completed form to **1-866-495-0660**, or
2. Mail this completed form to:

   iPLEDGE – Committed to Pregnancy Prevention
   P.O. Box 29094
   Phoenix, AZ 85038

Your username and password will be mailed to you upon completion of the registration process. You will need your username and password to log in to the system on the web or phone. Once a prescriber has designated you as his or her Office Staff Designee, you will be able to perform all patient activities in the iPLEDGE system for that prescriber.

iPLEDGE – Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

REGISTERING AND MANAGING OFFICE STAFF DESIGNEES

As a registered prescriber, you may designate a member of your office staff to perform all patient activities for you in the iPLEDGE system. An Office Staff Designee must be registered in the iPLEDGE program and receive a unique username and password. You may assign a member of your staff as your Office Staff Designee once the registration process has been completed. A registered and designated Office Staff Designee may perform all patient activities for you in the iPLEDGE system.

The registered prescriber is responsible for all information entered and activities performed in the iPLEDGE system by the Office Staff Designee.

Registering An Office Staff Designee

Go to **www.ipledgeprogram.com** and log in by entering your username (DEA number or program-generated username) and password. You will be presented with the Prescriber home page. Select the **"Manage Delegates/Designees"** button. The Manage Delegates and Designees page will be displayed. Select the **"Register New Designee"** button. The Office Staff Designee Registration form will be presented. Have the Office Staff Designee follow the registration instructions on the form to complete the registration.

Managing Office Staff Designees

Go to **www.ipledgeprogram.com** and log in by entering your username (DEA number or program-generated username) and password. You will be presented with the Prescriber home page. Select the **"Manage Delegates/Designees"** button. The Manage Delegates and Designees page will be presented. Select the **"Manage Designees"** button to display the Manage Designees page. On the Manage Designees page, enter the Office Staff Designee's iPLEDGE username and select **"Add."**

It is important to note the following:

- Your Office Staff Designee's access to activities in the iPLEDGE system is dependent on your access to the system. Specifically, if you have not been activated in the system or if your activation has expired, your Office Staff Designee will not be able to perform activities in the iPLEDGE system.
- Although several prescribers may utilize the same Office Staff Designee, the Office Staff Designee only needs to register in the iPLEDGE program once.

Reference ID: 3122588

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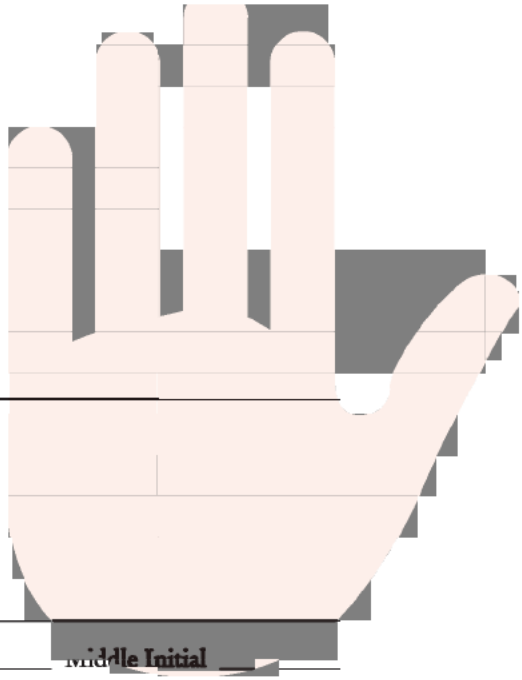

PRESCRIBER REGISTRATION FORM

(Please Print All Information)

Prescriber DEA Number _____

Your DEA number will be used as your username.

Check the box below if you do not have a DEA number.

☐ I do not have a DEA number. Please generate a username for me.

Prescriber Last Name _____

First Name _____ Middle Initial ___

Degree ☐ ___ ☐ ___ ☐ NP ☐ ___ ☐ Other ___

Prescriber Primary Specialty (Please select only one)

☐ ___ ☐ Pediatrics ☐ FP/GP ☐ Internal Medicine

☐ ___ ☐ OB/GYN ☐ Other _____

Prescriber Office Address _____

City _____ State ___ ZIP _____

Telephone (___) _____ Fax (___) _____

E-mail _____

Preferred method of contact (Please select one) ☐ U.S. mail ☐ E-mail

Prescriber Signature _____

Date _____

To Register:

1. Fax this completed form to **1-866-495-0660,** or
2. Mail this completed form to:

iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Most Recent Modification: April 2012

The iPLEDGE Program

The Pharmacist Guide For the iPLEDGE Program

The resource to help the pharmacist understand and comply with the iPLEDGE program for isotretinoin therapy

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Reference ID: 3122588

The Pharmacist Guide For the iPLEDGE Program

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For iPLEDGE Program Information

Call Center hours: Monday through Saturday, 9AM–12AM (midnight) EST
1-866-495-0654

www.ipledgeprogram.com

CONTRAINDICATIONS AND WARNINGS

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for short periods of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

Birth defects which have been documented following isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system, and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion, and premature births have been reported.

Documented external abnormalities include: skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate. Documented internal abnormalities include: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); cardiovascular abnormalities; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted.

If pregnancy does occur during treatment of a female patient who is taking isotretinoin, isotretinoin must be discontinued immediately, and she should be referred to an Obstetrician-Gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Special Prescribing Requirements

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE™. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see **PRECAUTIONS**).

ABOUT ISOTRETINOIN

Isotretinoin is used to treat severe recalcitrant nodular acne. Isotretinoin belongs to a class of drugs known as retinoids, commonly understood to include all natural and synthetic analogues of vitamin A. Therapy with isotretinoin should not be undertaken before conventional treatment has been tried first, including the use of systemic antibiotic therapy, and the patient has been fully counseled about the warnings and precautions in the isotretinoin package insert.

Isotretinoin is teratogenic and must not be used by pregnant women. Women should not become pregnant while taking isotretinoin or for 1 month after therapy is discontinued. A patient who becomes pregnant during treatment should stop taking isotretinoin and immediately contact her prescriber.

Isotretinoin use is associated with other potentially serious adverse events as well as more frequent, but less serious side effects. More frequent, less serious side effects include cheilitis, dry skin, skin fragility, pruritus, epistaxis, dry nose and dry mouth, and conjunctivitis.

Serious Adverse Event Warnings include psychiatric disorders* (depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors). Prescribers should read the brochure *Recognizing Psychiatric Disorders in Adolescents and Young Adults: A Guide for Prescribers of Isotretinoin*. Prescribers should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of isotretinoin therapy, patients and family members should be asked about any history of psychiatric disorder, and at each visit during therapy patients should be assessed for symptoms of depression, mood disturbance, psychosis, or agression to determine if further evaluation may be necessary.

Other Serious Adverse Events include pseudotumor cerebri; pancreatitis; hyperlipidemia; hearing impairment*; hepatotoxicity; inflammatory bowel disease; skeletal changes† (bone mineral density changes, hyperostosis, premature epiphyseal closure); and visual impairment (corneal opacities, decreased night vision).

Patients should be reminded to read the Medication Guide, distributed by the pharmacist at the time the isotretinoin is dispensed as required by law.

* No mechanism of action has been established for these events

† The use of isotretinoin in patients 12 to 17 should be given careful consideration especially when a known metabolic or structural bone disease exists

Pregnancy After Isotretinoin Therapy

The terminal elimination half-life of isotretinoin varies but is generally within 10 to 20 hours. The elimination half-life of one of the isotretinoin metabolites, 4-oxoisotretinoin, is approximately 25 hours. Since plasma elimination is host dependent, prescribers should warn patients not to become pregnant for 1 month post treatment. Women who become pregnant during this month should be counseled as to the outcome data. In 1989, Dai et al reported the results of an epidemiologic study of pregnancies that occurred in women who conceived after discontinuing isotretinoin.[1] They studied women from 5 days to more than 60 days between the last dose of isotretinoin and conception. The incidence of birth defects in former isotretinoin patients was not significantly different from the rate in the general population.

Isotretinoin is found in the semen of male patients taking isotretinoin, but the amount delivered to a female partner would be about 1 million times lower than an oral dose of 40 mg. While the no-effect limit for isotretinoin-induced embryopathy is unknown, 20 years of postmarketing reports include 4 with isolated defects compatible with features of retinoid-exposed fetuses; however, 2 of these reports were incomplete, and 2 had other possible explanations for the defects observed.

Birth Defects

There is an extremely high risk that a deformed infant will result if pregnancy occurs while female patients are taking isotretinoin in any amount even for short periods of time. Potentially, any fetus exposed during pregnancy can be affected. Not every fetus exposed to isotretinoin has resulted in a deformed child. However, there are no accurate means of determining which fetus has been affected and which fetus has not been affected.

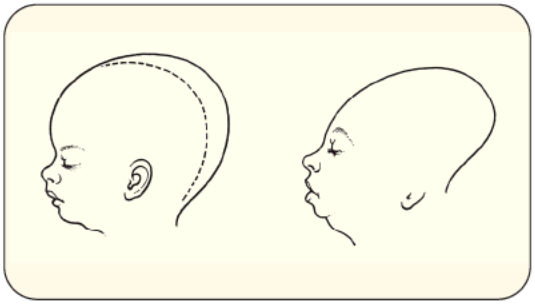
When isotretinoin is taken during pregnancy, it has been associated with fetal malformations, and there is an increased risk for spontaneous abortions and premature birth. **The following human fetal abnormalities have been documented.**

External abnormalities

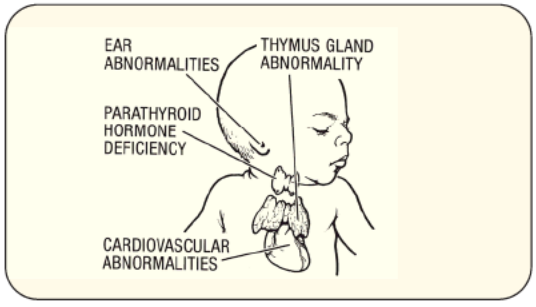
Skull abnormality; ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); facial dysmorphia; cleft palate.

Internal abnormalities

CNS abnormalities including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit; cardiovascular abnormalities; thymus gland abnormalities; parathyroid hormone deficiencies. In some cases death has occurred with certain of the abnormalities noted.



Line drawing represents the possible abnormalities of the low-set, deformed, or absent ears; wide-set eyes; depressed bridge of nose; enlarged head; and small chin.



Line drawing represents the possible abnormalities of the brain, heart, and thymus gland that may occur.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

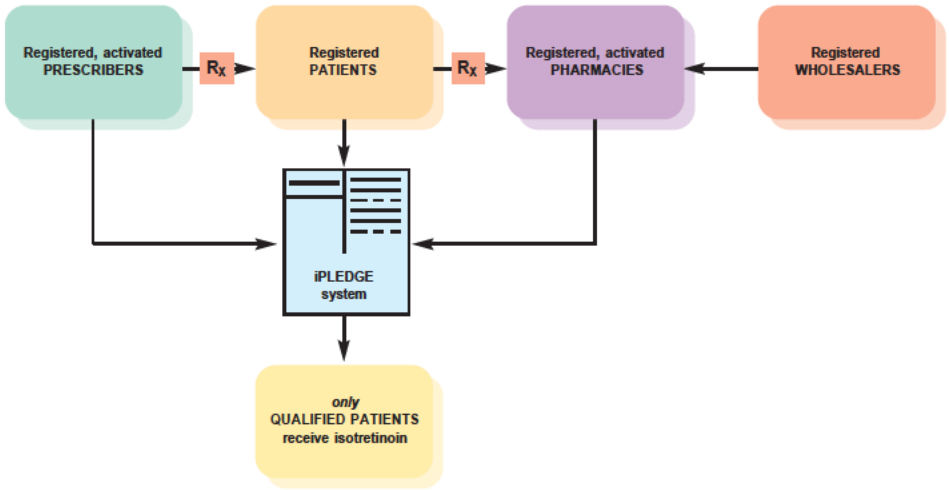
THE iPLEDGE PROGRAM

Because of isotretinoin's teratogenicity and to minimize fetal exposure, isotretinoin is approved for marketing only under a special restricted distribution program approved by the Food and Drug Administration. This program is called iPLEDGE. Isotretinoin must only be prescribed by prescribers who are registered and activated with the iPLEDGE program. Isotretinoin must only be dispensed by a pharmacy registered and activated with iPLEDGE, and must only be dispensed to patients who are registered and meet all the requirements of iPLEDGE (see PRECAUTIONS).

The goals of the iPLEDGE program are to prevent fetal exposure to isotretinoin and to inform prescribers, pharmacists, and patients about isotretinoin's serious risks and safe-use conditions.

The iPLEDGE program is a computer-based risk management system that uses verifiable, trackable links between prescriber, patient, pharmacy, and wholesaler to control prescribing, using, dispensing, and distribution of isotretinoin.

The trackable links of the iPLEDGE program



Key Features Of The iPLEDGE Program

The iPLEDGE program has specific requirements for prescribers, patients, pharmacists, and wholesalers. Here is an overview:

- The iPLEDGE system tracks and verifies critical program elements that control access to isotretinoin.
- Only prescribers registered with and activated in the iPLEDGE program can prescribe isotretinoin.
- Prescribers must ensure that all patients—and specifically female patients of childbearing potential—meet the requirements to be registered in the iPLEDGE program.

- Prescribers and patients must enter required information (i.e., pregnancy test results, 2 forms of contraception used, confirmation of patient counseling) in the iPLEDGE system for patients to be qualified to receive a prescription.
- Only patients who are registered by prescribers in the iPLEDGE program can receive isotretinoin.
- Only pharmacies registered with and activated in the iPLEDGE program can dispense isotretinoin.
- Pharmacists must access the iPLEDGE system to receive authorization to fill and dispense every prescription.
- Manufacturers will only ship to iPLEDGE-registered entities (e.g., direct vendor pharmacies, wholesalers).
- Wholesalers must register annually in the iPLEDGE program. A registered wholesaler may distribute only FDA-approved isotretinoin product.
- Only wholesalers registered with the iPLEDGE program can distribute isotretinoin. (See page 9 for information on how to find a registered wholesaler.)
- Registered wholesalers can only ship to wholesalers registered in the iPLEDGE program with prior written consent from the manufacturer or pharmacies licensed in the US and registered and activated in the iPLEDGE program.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE program.

PHARMACIES AND THE iPLEDGE PROGRAM

The iPLEDGE program includes specific requirements that pharmacies must follow in order to dispense isotretinoin. These include:

- Designating a Responsible Site Pharmacist (*see page 10*)
- Following the procedures to fill and dispense prescriptions (*see page 14*)

Key Information For Pharmacists

- **The Responsible Site Pharmacist must register and activate the pharmacy** in the iPLEDGE system.
- **The dispensing pharmacist must get authorization and a Risk Management Authorization (RMA) number** before filling and dispensing prescriptions.
- **Upon receiving authorization, the dispensing pharmacist can fill and dispense a prescription** for a maximum 30-day supply of isotretinoin.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

- **Upon authorization, the iPLEDGE system** provides the RMA number to the dispensing pharmacist. The pharmacist should record the RMA number directly on the prescription.
- **Upon authorization, the iPLEDGE system provides a "Do Not Dispense To Patient After"** date to the dispensing pharmacist. This date is calculated as 30 days from the office visit for male patients and female patients not of child-bearing potential, or 7 days from the pregnancy test date for female patients of childbearing potential. The pharmacist should record this date on the prescription bag sticker. Patients who present a prescription beyond this date will not be authorized in the iPLEDGE system to receive isotretinoin.
- **Prescriptions must be picked up by the patient no later than the "Do Not Dispense To Patient After" date, and if not picked up, then the prescription is to be returned to stock.**
- **The iPLEDGE system** only authorizes filling and dispensing prescriptions when patients have met the qualification criteria in the system.
- **Prescriptions** that are more than 30 days beyond the date of the office visit (for male patients and female patients not of childbearing potential) or more than 7 days beyond the pregnancy test date (for female patients of childbearing potential) will not be authorized by the iPLEDGE system.
- **No automatic refills** are permitted.
- Telephone, fax, and electronic transmission (e.g., e-mail) prescriptions are permitted in the iPLEDGE program.
- **Isotretinoin** comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.
- An isotretinoin Medication Guide must be given to the patient each time isotretinoin is dispensed, as required by law.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.

About Authorization Criteria

Prior to each prescription, the prescriber and patient must enter required patient information into the iPLEDGE system. The pharmacist is not responsible for entering this information. When the pharmacist begins the authorization process, the system automatically checks this information to ensure that the patient has met the criteria to receive a prescription. (See page 19 for the specific criteria.)

THE iPLEDGE WEB SITE AND PHONE SYSTEM

The pharmacist can access the iPLEDGE system via the program web site and automated phone system:

- Web site: **www ipledgeprogram.com**
- Phone system: **1-866-495-0654**

The iPLEDGE system is used for:

- Activation of the pharmacy registration
- Authorization to fill and dispense prescriptions
- Reversal of approved prescriptions
- Ordering additional copies of *The Pharmacist Guide For the iPLEDGE Program* and patient and professional educational materials
- Finding a wholesaler registered in the iPLEDGE Program
- Finding a pharmacy participating in the iPLEDGE Program
- FAQ's (Frequently Asked Questions)

To log in to either the web site or the phone system, the dispensing pharmacist needs the pharmacy username and password supplied upon registration. The pharmacy's Responsible Site Pharmacist can supply this information.

It is important that the Responsible Site Pharmacist does not forget the iPLEDGE username, password, and date of personal significance for the pharmacy. All of these items should be communicated to other pharmacists working at the pharmacy.

(Note: Date of Personal Significance is chosen by you, and can be any date that is easy for you to remember)

To Review And Order Materials

You can order additional program materials using either the web site or the phone system as follows:

1. After logging on to the web site, there are two ways to order materials:
   a. Using the navigation menu on the left side of the page, select the "Order Materials" button.

      OR

   b. Using the navigation menu on the left side of the page choose "Pharmacy Information." In the "View Information Online" section, select "To Order Educational Materials, please click here."
2. In the phone system, log in and select the option to "Request Program Information." Additional bag stickers can also be ordered using this process.

To Find A Registered Wholesaler

On the web site, log in and choose "Find Wholesaler" in the left navigation. A list of registered wholesalers and distributors will be presented.

THE RESPONSIBLE SITE PHARMACIST

Each pharmacy in the iPLEDGE program must designate a pharmacist as the Responsible Site Pharmacist. The Responsible Site Pharmacist is the point of contact for the pharmacy and the iPLEDGE program. The Responsible Site Pharmacist performs the following tasks:

- Registers the pharmacy with the iPLEDGE program
- Activates the pharmacy registration initially and annually; attests to program requirements
- Trains all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions and keeps a log or record of the staff who have been trained
- Ensures that all pharmacy staff using iPLEDGE are aware of the pharmacy's username, password and date of personal significance for the iPLEDGE System.

Registration

The Responsible Site Pharmacist registers the pharmacy in the iPLEDGE program. Only one registration is needed for each pharmacy. After the Responsible Site Pharmacist registers the pharmacy, the pharmacy will receive a system password by mail. The NCPDP number is the username for the entire pharmacy.

Activation

Before a pharmacist can fill and dispense prescriptions for isotretinoin, the Responsible Site Pharmacist must activate the registration in the iPLEDGE system. The program activation expires annually. The Responsible Site Pharmacist, representing the pharmacy, must activate the automated registration annually to continue ordering, filling, and dispensing isotretinoin. If your activation expires, and you do not intend to reactivate, you must return all unused isotretinoin immediately to the manufacturer or delegate.

The iPLEDGE system will report the expiration date of a pharmacy's registration. To retrieve this information on the web site, log in and choose "My Program Status" on the left navigation; in the phone system, log in and select the option to hear "Current Program Status."

Review *The Pharmacist Guide For the iPLEDGE Program* to ensure an understanding of the program. Activation requires attesting to the following statements in the iPLEDGE system:

- I know the risk and severity of fetal injury/birth defects from isotretinoin.
- I will train all pharmacists, who participate in the filling and dispensing of isotretinoin prescriptions, on the iPLEDGE program requirements.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

- I will comply and seek to ensure all pharmacists who participate in the filling and dispensing of isotretinoin prescriptions comply with the iPLEDGE program requirements described in the booklet entitled *The Pharmacist Guide For the iPLEDGE Program.*
- I will only obtain isotretinoin product from only iPLEDGE-registered wholesalers.
- I will not sell, buy, borrow, loan, or otherwise transfer isotretinoin in any manner to or from another pharmacy.
- I will return to the manufacturer (or delegate) any unused product if registration is revoked by the manufacturer or if the pharmacy chooses to not reactivate annually.
- I will not fill isotretinoin for any party other than a qualified patient.

Procedures For Activating In The iPLEDGE System

Access the iPLEDGE system to activate the pharmacy's registration via the web site, **www ipledgeprogram.com**, or the automated phone system, **1-866-495-0654**. Both the web site and the phone system provide prompts to log in and complete the initial activation. Identification in either system requires the username (NCPDP number) and the password received upon registration.

The web site is the faster and easier way to access the system. After initial activation, a pharmacy must re-activate at least annually to remain active in the iPLEDGE program.

The iPLEDGE system will display the "Activate" button on the Pharmacy home page when the activation for a pharmacy is nearing expiration. However, a pharmacy can re-activate at any time using the "Activate Pharmacy Registration" button on the left-hand navigation menu on all pages.

The system requires setting the pharmacy's Date of Personal Significance.

- The date of personal significance is a date that is easily remembered and will be used to verify the pharmacy's identity if required by the iPLEDGE system or if the pharmacy's password is lost.
- The same date of personal significance will be used by all pharmacists in the pharmacy when contacting the iPLEDGE Call Center.
- **The date of personal significance should be a date that will be known by all the pharmacists at the pharmacy.**
- It is important that you remember the selected date of personal significance. It is used to verify Pharmacy identity for some functions within iPLEDGE, as well as to obtain assistance from the iPLEDGE Call Center. The selected date should be communicated to other pharmacists in your pharmacy that will be using iPLEDGE.
- If you change the date of personal significance for your pharmacy, you should communicate this change to others at your pharmacy that will be using the iPLEDGE System.

Using the web site

The Responsible Site Pharmacist:

1. Logs in by entering the pharmacy username (NCPDP number) and password.
2. Changes the pharmacy password and sets the date of personal significance.
3. Selects "Activate Pharmacy Registration" from the Pharmacy home page. The system will provide prompts to complete the activation process. If the current activation for a pharmacy is nearing expiration, the Pharmacy home page will prominently display a direct link to re-activate.

Using the automated phone system

The Responsible Site Pharmacist:

1. At the main menu, selects the option to log in and follows the prompts to enter the pharmacy username (NCPDP number) and password.
2. Changes the pharmacy password and sets the date of personal significance.
3. At the pharmacy menu, selects the option to begin the activation process

Training Pharmacists

The Responsible Site Pharmacist is responsible for the training, and the documentation of training, of all pharmacists in a registered pharmacy. The pharmacy's standard operating procedures for training may be followed in training pharmacists on the iPLEDGE program requirements.

The training objectives for all dispensing pharmacists include:

- Knowing about isotretinoin teratogenicity and the contraception and program requirements of the iPLEDGE program
- Being able to access the iPLEDGE system and obtain authorization to fill and dispense a prescription
- Correctly using the RMA number and **"Do Not Dispense To Patient After"** date

Training begins by providing *The Pharmacist Guide For the iPLEDGE Program* to all pharmacists. Additional copies can be requested through the automated system.

The Responsible Site Pharmacist should review the following sections with each pharmacist after he/she has read the material:

- Isotretinoin teratogenicity and measures to reduce fetal exposure (*see "About Isotretinoin," page 3*)
- Accessing the iPLEDGE system via web site and phone system, using username (NCPDP number) and system password (*see page 14*)
- iPLEDGE program procedures for filling and dispensing prescriptions (*see page 14*)

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

- Time limitations on dispensing (*see page 15*)
- Prescription bag sticker requirements (*see page 15*)
- Patient qualification criteria (*see page 16*)
- Effective primary and secondary forms of contraception (*see page 18*)
- Additional contraception information and counseling about pregnancy (*see page 21*)

After reviewing the material, the Responsible Site Pharmacist should:

- Review the steps with the pharmacist for accessing the iPLEDGE system and the procedures for obtaining authorization to fill a prescription (*see page 14*)
- Ensure that pharmacists have the date of personal significance, username, and password necessary to log in to the iPLEDGE system
- Record the date of training, have the pharmacist sign a log or record of training, and co-sign this training record; verification of training records may be requested and reviewed as part of the iPLEDGE program

To Change The Responsible Site Pharmacist

The pharmacy can change its designated Responsible Site Pharmacist at any time. The new Responsible Site Pharmacist or the former Responsible Site Pharmacist can make the change on the automated phone line, **1-866-495-0654**.

The new Responsible Site Pharmacist:

- Selects the option to continue in English
    - Pharmacy support is only available in English
- Logs in with the pharmacy's username and password
- Selects #0 to transfer to the Call Center, then presses 1 at the prompt
- Selects the option for pharmacies
- The Responsible Site Pharmacist will be connected with an operator, who will assist with the change.
- The new Responsible Site Pharmacist must re-activate the pharmacy in the iPLEDGE program (for activation information, see page 11)
    - If your activation expires, and you do not intend to reactivate, you must return all unused isotretinoin immediately to the manufacturer or delegate.

PROCEDURE FOR FILLING AND DISPENSING PRESCRIPTIONS

Access the iPLEDGE system

The dispensing pharmacist:

- Accesses the iPLEDGE system via the web site, **www ipledgeprogram.com** or the automated phone system, **1-866-495-0654**
- Logs in using the pharmacy username (NCPDP number) and the pharmacy password
  - On the web site, chooses "Fill Prescriptions" from the left navigation
  - In the phone system, selects the option to "Obtain Approval to Fill or Reverse a Prescription"
- Enters the patient ID number from the patient ID card
- Enters the patient's date of birth

Confirm patient qualification and obtain authorization

- The iPLEDGE system automatically checks patient qualification criteria for you.
- Prescriptions will be authorized only for those patients who meet all criteria.
- If authorized to fill and dispense, the pharmacist enters the:
  - NDC Code
  - Number of days to be dispensed
  - Amount dispensed
- System provides:
  - An RMA number to be recorded on the prescription
  - A **"Do Not Dispense To Patient After"** date for the prescription bag sticker (*see next page*)

Additional fills for the prescription to achieve the desired dosage can be entered by the pharmacist immediately after the prescription is authorized. If not added immediately, the prescription must be reversed and then re-authorized if the dosage is not correct.

- The pharmacist may proceed with normal insurance adjudication only if the iPLEDGE system has authorized dispensing.
- The pharmacist may not proceed with normal insurance adjudication and may not dispense isotretinoin if dispensing is not authorized in the iPLEDGE system.
- If not authorized to fill and dispense:
  - The system will provide information or instructions for the patient (e.g., "Please contact your doctor")

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Dispense the prescription

- Only FDA-approved products may be dispensed.
- The system will automatically calculate and provide the **"Do Not Dispense To Patient After"** date to the pharmacist. The pharmacist must not dispense the prescription after this date.
- A maximum 30-day supply of isotretinoin may be dispensed.
- Refills are not allowed. Monthly continuation of therapy requires the patient to satisfy the iPLEDGE program requirements to obtain a new prescription.

Prescription bag stickers

- The bag sticker has space for the **"Do Not Dispense To Patient After"** date.
- The iPLEDGE system provides the **"Do Not Dispense To Patient After"** date.
- The pharmacist should write the date on the sticker and put the sticker on the prescription bag.
- Additional stickers can be ordered. (*see page 9*)

DO NOT DISPENSE ISOTRETINOIN AFTER THE DATE ON THE BAG STICKER

Non-dispensed prescriptions

If the prescription is not dispensed for any reason (e.g., the patient did not pick up, dispense date expired, third party did not authorize payment, etc.) the authorization to dispense must be reversed in the system. The pharmacist must call the iPLEDGE program at **1-866-495-0654**, log in, and select the option to "Obtain Approval to Fill or Reverse a Prescription," or log in to the web site and select "Reverse Prescription."

iPLEDGE PROGRAM GENERAL INFORMATION

The following section covers general aspects of the iPLEDGE program.

Determining Childbearing Potential Of Female Patients

The prescriber must determine if a female patient is of childbearing potential before registering the patient in the iPLEDGE program.

The definition of a female patient of childbearing potential is a nonmenopausal female who has not had a hysterectomy, bilateral oophorectomy, or documented ovarian failure. This definition includes a young woman who has not yet started menstruating.

A woman who has had a tubal sterilization is considered a female patient of childbearing potential in the iPLEDGE program.

Definition of menopause

Menopause can be assumed to have occurred in a woman when there is either:

1. Appropriate medical documentation of prior complete bilateral oophorectomy (i.e., surgical removal of the ovaries, resulting in "surgical menopause" and occurring at the age at which the procedure was performed), OR
2. Permanent cessation of previously occurring menses as a result of ovarian failure with documentation of **hormonal deficiency** by a certified healthcare provider (i.e., "spontaneous menopause," which occurs in the United States at a mean age of 51.5 years).

Hormonal deficiency should be properly documented in the case of suspected spontaneous menopause as follows:

1. If age >54 years and with the absence of normal menses: Serum FSH (Follicle Stimulating Hormone) level elevated to within the post-menopausal range based on the laboratory reference range where the hormonal assay is performed;
2. If age <54 years and with the absence of normal menses: Negative serum or urine -HCG with concurrently elevated serum FSH (Follicle Stimulating Hormone) level in the post-menopausal range, depressed estradiol (E2) level in the post-menopausal range, and absent serum progesterone level, based on the laboratory reference ranges where the hormonal assays are performed.

All Patients

To receive isotretinoin, all patients must meet all of the following conditions:

1. ***Must*** be registered with the iPLEDGE program by the prescriber
2. ***Must*** understand that severe birth defects can occur with the use of isotretinoin by female patients
3. ***Must*** be reliable in understanding and carrying out instructions

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

4. ***Must*** sign a Patient Information/Informed Consent (for all patients) form that contains warnings about the potential risks associated with isotretinoin
5. ***Must*** fill and pick up the prescription within their prescription window as follows:
   - Male patients and female patients who cannot get pregnant, prescriptions must be filled and picked up within the 30-day prescription window, counting the office visit as DAY 1.
   - Female patients who can get pregnant, prescriptions must be filled and picked up within the 7-day prescription window, counting the day of the blood draw or urine sample as DAY 1.
6. ***Must*** not donate blood while on isotretinoin and for 1 month after treatment has ended
7. ***Must*** not share isotretinoin with anyone, even someone who has similar symptoms

All patients should understand that refills are not allowed. Patients can only receive a maximum of 30-day supply of isotretinoin per prescription. For each prescription, continuation of therapy requires the patient to satisfy the iPLEDGE program requirements to obtain a new prescription. The prescriber must also counsel the patient each month about the iPLEDGE program requirements and then confirm via the iPLEDGE automated system that this counseling occurred.

Female Patients Of Childbearing Potential

Once the prescriber decides to pursue qualification of the patient, a female patient of childbearing potential must follow these steps.

1. Female patients of childbearing potential ***must*** have had 2 negative urine or serum pregnancy tests with a sensitivity of at least 25 mIU/mL before receiving the initial isotretinoin prescription. The first test (a screening test) is obtained by the prescriber when the decision is made to pursue qualification of the patient for isotretinoin. The second pregnancy test (a confirmation test) must be done in a CLIA-certified laboratory. The interval between the 2 tests must be at least 19 days.
   - For patients with regular menstrual cycles, the second pregnancy test must be done during the first 5 days of the menstrual period immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for 1 month.
   - For patients with amenorrhea, irregular cycles, or using a contraceptive method that precludes withdrawal bleeding, the second pregnancy test must be done immediately preceding the beginning of isotretinoin therapy and after the patient has used 2 forms of contraception for 1 month.
   - The patient must be using their two forms of birth control for at least 30 days prior to beginning to take isotretinoin, and their second pregnancy test must occur after this 30 day period is complete.
2. The patient must sign the Patient Information/Informed Consent (for all patients) form and the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form.
3. The patient must select and commit to use 2 forms of effective contraception together, at least 1 of which must be a primary form, unless continuous abstinence is chosen. Patients must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

Requirements For Each Prescription

In addition to the requirements for all patients, the female patient of childbearing potential has additional requirements. Prior to each prescription, they must have a negative result from a urine or serum pregnancy test. A pregnancy test must be repeated, in a CLIA-certified laboratory, prior to the female patient receiving each prescription. A pregnancy test must also be obtained at the end of therapy (after the last dose) and 1 month after the last dose. Before each prescription, the iPLEDGE program also requires monthly counseling about contraception and behaviors associated with an increased risk of pregnancy.

In addition to their required doctor appointments, female patients of childbearing potential must also report their 2 forms of birth control in the iPLEDGE system and answer questions about the iPLEDGE program and pregnancy prevention.

Effective forms of contraception

Effective forms of contraception include both primary and secondary forms of contraception.

Primary forms	Secondary forms
• Tubal sterilization • Partner's vasectomy • Intrauterine device • Hormonal (combination oral contraceptives, transdermal patch, injectables, implantables, or vaginal ring)	*Barrier forms (always used with spermicide)* • Diaphragm • Cervical cap *Barrier form (used with or without spermicide)* • Male latex condom *Others:* • Vaginal sponge (contains spermicide)

Unacceptable forms of contraception

- Progesterone-only "mini-pills," e.g.:
  - Ortho Micronor® Tablets*
- IUD Progesterone T
- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield‡

*Ortho Micronor is a registered trademark of Ortho-McNeil Pharmaceutical, Inc

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Abstinence

For this program, all female patients of childbearing potential must fully commit to pregnancy prevention. Abstinence without appropriate contraception is not recommended for patients in the iPLEDGE program who are or have been sexually active. Abstinence may be appropriate when it is a lifestyle choice (e.g., religious practice) and not just a social circumstance (e.g., not having a current partner). If, after counseling, a sexually active patient chooses abstinence without contraception, she must understand that isotretinoin is not recommended for any female patient of childbearing potential who cannot or will not follow the contraceptive requirements of the iPLEDGE program. All female patients of childbearing potential must receive contraception counseling.

Patient Criteria For Authorization To Fill And Dispense

This is the information that must be entered by prescribers and patients into the iPLEDGE system for all patients and, specifically, for female patients of childbearing potential. This is the information the system uses to authorize filling a prescription and to provide the RMA number and the **"Do Not Dispense To Patient After"** date.

All patients

Prescriber confirms that:

- The patient is registered with the iPLEDGE program
- The patient was counseled about the iPLEDGE program requirements

Female patients of childbearing potential

Prescriber:

- Confirms that the patient was counseled about the iPLEDGE program contraception requirements
- Enters the 2 forms of contraception that the patient is using
- Enters pregnancy test results to start the 7-day prescription window, counting the date of the specimen collection as DAY 1.

Patient:

- Correctly answers the questions about pregnancy prevention and the iPLEDGE program
- Enters the 2 forms of contraception she is using

The primary form of contraception reported by both the prescriber and the patient must match.

Note: The system will automatically provide the pharmacist with the "Do Not Dispense To Patient After" date.

Note: the following is provided to the pharmacist for information purposes only. No action is required by the Pharmacist for a patient to fulfill the requirements of iPLEDGE and become qualified to fill and pick up a prescription.

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient, as follows:

Female patients who can get pregnant…	Male patients and female patients who cannot get pregnant…
The prescription window is 7 days and starts on the date that the urine or blood sample is taken for a pregnancy test. This date is counted as DAY 1. To determine the end date of their 7-day prescription window, these patients should add 6 days to the date of the blood or urine sample being taken.	The prescription window is 30 days and starts on the date that the prescriber enters as the date of the office visit. This date is counted as DAY 1. To determine the end date of their 30-day prescription window, these patients should add 29 days to the date of their office visit.

After 11:59 p m. Eastern Time on the last day of the prescription window, the patient can no longer fill and pick up their prescription, and must start the process over to get a new prescription window.*

* There are generally no restrictions regarding the timing of office visits. One notable exception is that female patients of childbearing potential who do not fill and pick up their first month of therapy prescription in their first 7-day prescription window, must wait at least 19 days from their most recent pregnancy test until getting their next pregnancy test. This is based on the requirement that the most recent pregnancy test prior to beginning therapy must be conducted in the first 5 days of her menstrual cycle.

ADDITIONAL CONTRACEPTION INFORMATION

The iPLEDGE program has *The iPLEDGE Program Prescriber Contraception Counseling Guide* available. This is the professional companion piece to the patient's *iPLEDGE Program Birth Control Workbook*. Copies can be requested through the iPLEDGE system. (See page 9 for instructions.)

Patients can also be directed to the phone system for confidential birth control information. They can call **1-866-495-0654**, log in, and select the option to hear "Confidential Birth Control Information."

The following subjects are covered:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

Counseling A Potentially Pregnant Patient

If a patient expresses concern that she may be pregnant, tell her to stop taking isotretinoin immediately and call her prescriber.

Males And Birth Defects

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin. Approximately 3 to 5 babies in 100 (3% to 5%) are born with some kind of birth defect from other causes, not from isotretinoin.[2]

Isotretinoin also has not been shown to affect a male's ability to father children. Studies did not show effects on sperm count, how sperm look, or how well they swim and move. (For more information, see page 3.)

REFERENCES

1 Dai WS, Hsu M-A, Itri LM Safety of pregnancy after discontinuation of isotretinoin *Arch Dermatol* 1989;125:362-355

2 Centers for Disease Control and Prevention Birth defects: frequently asked questions Available at: http://www cdc gov/ncbddd/bd/faq1 htm#Whatisabirthdefect Accessed August 8, 2005

For More Information About Isotretinoin

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.

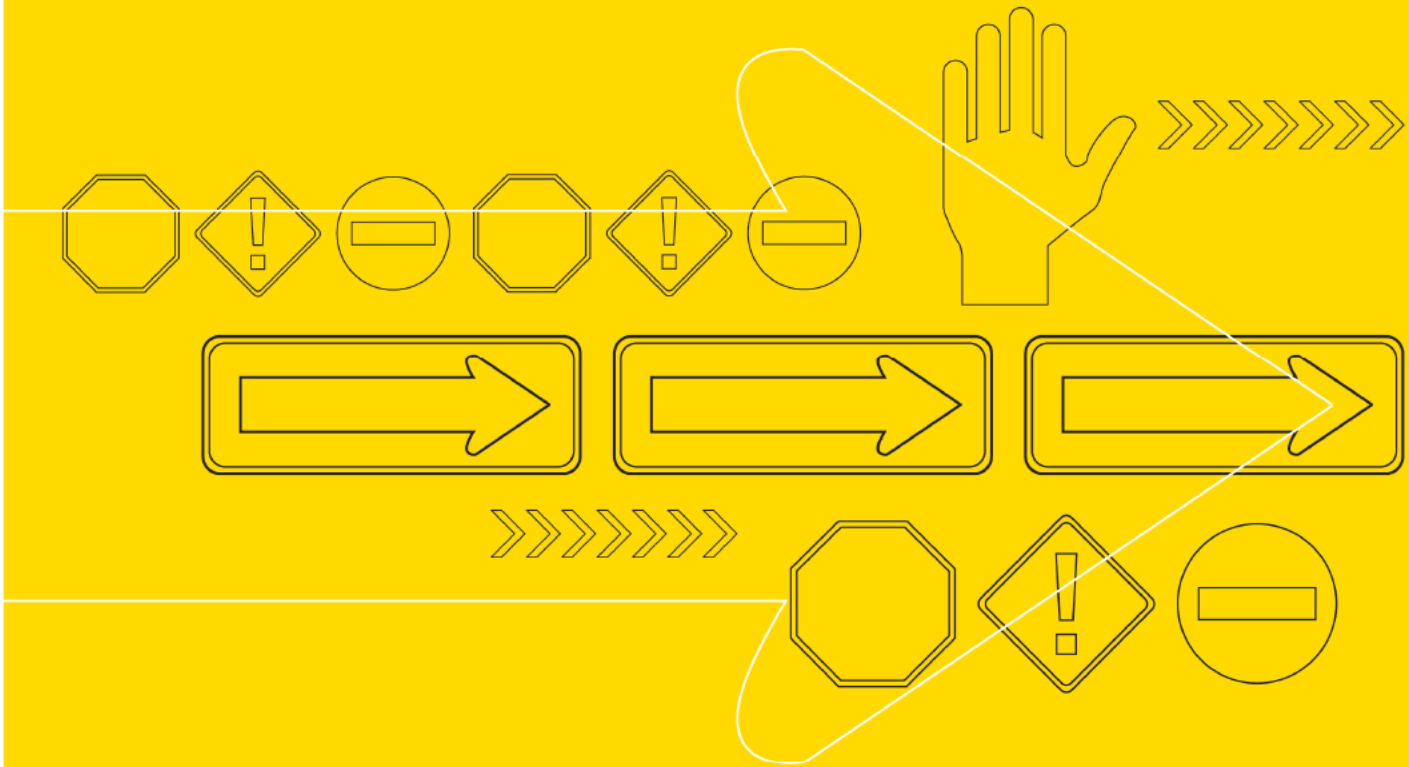
For iPLEDGE Program Information

Call Center hours: Monday through Saturday, 9AM–12AM (midnight) EST

1-866-495-0654

www.ipledgeprogram.com

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**



www.ipledgeprogram.com 1-866-495-0654

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE – Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

PHARMACY REGISTRATION FORM

(Please Print All Information)
Note: Only One Registration Per Pharmacy Is Required

Pharmacy NCPDP Number _____ (eg xxx-xx)

Pharmacy DEA Number _____

Pharmacy Name _____

Pharmacy Address _____

City _____ State _____ ZIP _____ format: xxxxx-xxxx

Pharmacy Telephone _____ format: xxx-xxx-xxxx

Pharmacy Fax _____ format: xxx-xxx-xxxx

Pharmacy E-mail _____

Preferred method of contact? Please select only one method.

☐ U.S. mail ☐ E-mail

Responsible Site Pharmacist (RSP) Information

RSP First Name _____ Please Print

RSP Last Name _____ Please Print

RSP License Number _____

☐ This pharmacy orders isotretinoin directly from one or more of the manufacturers of isotretinoin

RSP Signature _____ Date _____ (mm/dd/yyyy)

To Register:

1. **Fax this completed form to 1-866-495-0660**

Or

2. **Mail this completed form to:**

iPLEDGE – Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Reference ID: 3122588

Most Recent Modification: April 2012

The iPLEDGE Program

Guide To Isotretinoin For Female Patients Who Can Get Pregnant

The Importance Of Avoiding Pregnancy On Isotretinoin

The resource to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment. Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Guide To Isotretinoin For Female Patients Who Can Get Pregnant

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ABOUT ISOTRETINOIN

Isotretinoin (eye-soh-tret-in-OH-in) treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months.

Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby's mother takes isotretinoin. The goal of the iPLEDGE program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin. The program involves a set of steps that you, your doctor, and your pharmacist must follow for you to take isotretinoin.

Before starting isotretinoin, talk with your doctor about how isotretinoin can help your skin and about the side effects. Read this *iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant* and the other materials in this educational kit. Your doctor also has an educational DVD for you to watch.

Make sure you understand the requirements of the iPLEDGE program. Then, decide if isotretinoin is right for you.

ISOTRETINOIN AND BIRTH DEFECTS: FOR FEMALE PATIENTS WHO CAN GET PREGNANT

Here are 2 key messages of the iPLEDGE program:

Do NOT take isotretinoin if you are pregnant.

Do NOT get pregnant before starting isotretinoin, while taking it, and for 1 month after your last dose.

If you get pregnant while taking isotretinoin, there is a very high chance that your baby will be deformed, born too early, or die before being born. This can happen even if you only take isotretinoin for a short time.

Prevent Pregnancy And Birth Defects

Here are some key steps you must follow in the iPLEDGE program to take isotretinoin:

Have 2 negative pregnancy tests before you start isotretinoin.

Have a negative pregnancy test before you fill and pick up each monthly prescription.

Use 2 forms of birth control together.

You must use 2 forms of birth control together correctly all the time for 1 month before you start isotretinoin, while you are taking isotretinoin, and for 1 month after your last dose. These forms of birth control must be effective in the iPLEDGE program.

Any form of birth control can fail. Using 2 forms of birth control together all the time drastically reduces the chance that you will get pregnant.

Your doctor will talk with you about birth control or refer you to a gynecologist, a family doctor, or a birth control expert for counseling.

Reasons you would not have to use 2 forms of birth control

There are 2 reasons you would not have to use 2 effective forms of birth control.

- You commit to not having any heterosexual sexual intercourse with a male for 1 month before, during, and for 1 month after your isotretinoin treatment (abstinence).
- You are unable to get pregnant because:
  - You have entered menopause, and your doctor has confirmed this.
  - You have had both of your ovaries or uterus taken out by surgery, and your doctor has confirmed this.

If you have any questions about being able to get pregnant, talk with your doctor.

Do Not Donate Blood

Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant woman receives blood that you donated. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone

You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

See the *Safety Information* section on page 14 for more detailed information about other serious side effects, precautions, and warnings for isotretinoin.

THE iPLEDGE WEB SITE AND PHONE SYSTEM

The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant and your patient educational kit are resources for the information you need about isotretinoin and the iPLEDGE program. The iPLEDGE program also has a web site and an automated phone system.

- Web site: **www.ipledgeprogram.com**
- Phone system: **1-866-495-0654**

The information on the phone system is available in English and Spanish. You can get general information about isotretinoin and the iPLEDGE program right away. When you start taking isotretinoin, your doctor will give you a patient ID number and ID card, and other program materials. You use these to log in to the system. *(see page 9)* You will use the system to meet some of the monthly requirements of the program.

After you have been registered in iPLEDGE by your doctor, you will receive your iPLEDGE password in the mail in 5 to 10 business days. Follow the instructions that come with the password to access the iPLEDGE system.

KEY INFORMATION FOR PATIENTS

The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant explains the key information about the iPLEDGE program before, during, and after your isotretinoin treatment. Here is a general overview:

1. Learn about the iPLEDGE program and the isotretinoin side effects and risks in pregnancy.
2. Sign the Patient Information/Informed Consent forms.
3. Plan for treatment and for monthly appointments and pregnancy tests.
4. Choose 2 forms of effective birth control for the iPLEDGE program; use them all of the time.
5. Take blood or urine pregnancy tests.
6. Answer monthly educational questions to show you understand about the iPLEDGE program and about preventing pregnancy.
7. Follow requirements for pregnancy testing and follow-up after your last dose.
8. Do not donate blood during your treatment or for 1 month after your last dose.
9. Do not share isotretinoin.

This information and details of the program are described in the sections to follow. The section on page 6 reviews the forms of effective birth control in the iPLEDGE program.

You can always use the checklist on the next page as a quick reminder of the program information.

THE iPLEDGE PROGRAM CHECKLIST

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient.

Female patients who can get pregnant…

The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for your pregnancy test. This date is counted as DAY 1.

To determine the end date of your 7-day prescription window, you should add 6 days to the date of the blood or urine sample being taken.

After 11:59 p m. Eastern Time on the last day of the 7-day prescription window, you can no longer fill and pick up your prescription, and must start the process over to get a new 7-day prescription window.

Before Starting Treatment

PLANNING

- ☐ **Plan** your course of treatment (about 4 to 5 months). (*see page 8*)
- ☐ **Talk** with your doctor about the iPLEDGE program.
- ☐ **Sign** the Patient Information/Informed Consent (for all patients) form.
- ☐ **Have** your first urine or blood pregnancy test, which can be performed at the doctor's office.
- ☐ **Get** your patient ID cards containing your patient ID number from your doctor. (*see page 8*)

BIRTH CONTROL (*see page 6*)

- ☐ **Read** *The iPLEDGE Program Birth Control Workbook.*
- ☐ **Talk** with your dermatologist, gynecologist, family doctor, or a birth control expert about effective birth control options.
- ☐ **Choose** 2 effective forms of birth control.
- ☐ **Start** using the 2 forms of birth control together for at least 1 month before you start isotretinoin.

YOUR FIRST PRESCRIPTION

- ☐ **Have** a second pregnancy test within the first 5 days of your menstrual period.
- ☐ **Sign** the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form. (*see page 9*)
- ☐ **Answer** questions about the iPLEDGE program and confirm your 2 forms of birth control. (*see page 10*) **This cannot be completed until after your doctor has entered your pregnancy test result in the iPLEDGE System.**
- ☐ **Fill and Pick up** your prescription for up to a maximum of a 1-month supply. (*see page 11*)
- ☐ **Fill and Pick up** your prescription within the 7-day prescription window, counting the date of the pregnancy test as DAY 1. (*see page 12*)
  - If you are not able to fill and pick up your first prescription within the 7-day prescription window, you will be required to wait a minimum of 19 days before you can start this process again.
- ☐ **Use** 2 effective forms of birth control together all the time.
- ☐ **Keep** your appointments every month to get a prescription.
- ☐ **See** your doctor for a monthly pregnancy test.
- ☐ **Answer** different questions each month about the iPLEDGE program.

During Treatment

- ☐ **Use** 2 effective forms of birth control together all the time.
- ☐ **See** your doctor for a monthly pregnancy test.
- ☐ **Keep** your appointments every month to get a prescription.
- ☐ **Confirm** your 2 forms of birth control by entering them into the iPLEDGE System. (*see page 10*)
- ☐ **Answer** different questions each month about the iPLEDGE program. **This cannot be completed until after your doctor has entered your pregnancy test result in the iPLEDGE System.**
- ☐ **Fill and Pick up** your prescription for up to a maximum of a 30-day supply. *(see page 11)*
- ☐ **Fill and Pick up** your prescription within the 7-day prescription window counting the day of the pregnancy test as DAY 1. (*see page 12*)
  - If you do not fill and pick up your prescription within the 7-day prescription window, you will need to go back to your doctor to start this process again.
- ☐ **Do not donate** blood.

After Treatment

RIGHT AFTER YOUR LAST DOSE (*see page 13*)

- ☐ **Get** a pregnancy test after your last dose.
- ☐ **Continue** using your birth control for 1 month.
- ☐ **Do not donate** blood for 1 month after your last dose.
- ☐ **Ensure** that your doctor has entered the results of this pregnancy test into the iPLEDGE System.

1 MONTH AFTER YOUR LAST DOSE

- ☐ **Have** a final pregnancy test at 1 month after your last dose.
- ☐ **Ensure** that your doctor has entered the results of this pregnancy test into the iPLEDGE System.

EFFECTIVE FORMS OF BIRTH CONTROL

Not all forms of birth control are acceptable while you are taking isotretinoin. Choosing birth control is a very personal decision. It helps to get all the information you need and then talk with your doctor to help you decide what to do.

Read The iPLEDGE Program Birth Control Workbook

To find out what birth control is effective for the iPLEDGE program, read *The iPLEDGE Program Birth Control Workbook*. Discuss this information with someone you trust. Discuss it with your partner. Think about what forms of birth control you would really use, and then talk with your doctor or a birth control expert.

Talk With An Expert

If you want to talk to a birth control expert, your gynecologist, or family doctor about birth control, the doctor who prescribes isotretinoin for you can refer you. The makers of isotretinoin will pay for a visit for you to talk about birth control. *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide* is in this booklet.

- Make an appointment with a birth control expert, your gynecologist, or family doctor.
- Take *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide* with you. It has important information that the birth control expert, gynecologist, or family doctor needs to talk about, including the forms of effective birth control for the iPLEDGE program.
- The healthcare professional providing contraception counseling will fill out the Contraception Referral Form included in the guide after he/she talks with you and then mail or fax it back to the doctor who prescribes your isotretinoin.

Changing Your Birth Control

If you need to change forms of birth control during your isotretinoin treatment, you need to tell the doctor who prescribes your isotretinoin. You do not want to take isotretinoin if you are not protected against pregnancy all the time.

You may have to stop having sex until your new form of birth control is working. You may have to stop isotretinoin and wait until you have been on the new form for at least 1 month and have a negative pregnancy test.

Changing From Abstinence

If you have been abstinent (not having any sexual activity) and you decide to start having sexual activity, you must tell the doctor who prescribes your isotretinoin. You and your doctor must make a plan to start birth control and be sure you are not pregnant before you continue isotretinoin.

One of the most common reasons that women get pregnant is that they do not avoid sexual activity when they plan to be abstinent.

DVD: *Be Prepared, Be Protected, And Be Aware: The Risk Of Pregnancy While On Isotretinoin*

Your doctor has a DVD that shows the kinds of birth defects that may happen if a woman takes any amount of isotretinoin while she is pregnant. It also reviews the steps for preventing pregnancy.

THE iPLEDGE PROGRAM CHECKLIST INFORMATION

Plan Your Course Of Treatment

Pregnancy tests

To start isotretinoin, you need to have 2 negative pregnancy tests. They can be urine or blood tests. You will need to plan with your doctor when and where to take your pregnancy tests.

- You take the first test when you decide to take isotretinoin.
- You take the second test in an approved lab during the first 5 days of the menstrual period right before you start isotretinoin. The interval between the two tests must be at least 19 days. You must use 2 effective forms of birth control together all the time for at least 1 month before you can take this second test.

You also take a pregnancy test in an approved lab during treatment. You take a pregnancy test each month, during treatment, after your last dose, and 1 month after your last dose. You will need to plan with your doctor when to take your pregnancy test each month.

Prescriptions

The most isotretinoin you can get at any one time is up to a maximum of a 30-day supply. You will need to see your doctor each month to get a new prescription, and meet the monthly program requirements.

Get Your Patient ID Number And Cards

Your doctor will give you your patient ID number and cards when you start the iPLEDGE program. The ID cards are included in the back of this booklet. Tear out one card and keep it in a safe place. You can use the other cards in the booklet if you lose your card. It is important not to lose these cards. Write your number down as soon as you receive it and keep it where you will be able to find it.

You need your ID number and card:

- When you take your prescription to be filled at the pharmacy
- When you log in to the iPLEDGE program automated system, either the web site, **www.ipledgeprogram.com**, or automated phone line, **1-866-495-0654**

About The iPLEDGE Automated System

The first time you login to iPLEDGE (either the web site or phone line) you will be asked to select a personal password and select a Date of Personal Significance. The selection of a personal password is a security feature that ensures that only you will know your password. A Date of Personal Significance is collected by the system to be used in verifying your identity should you require assistance from the iPLEDGE Call Center while using iPLEDGE.

Both your password and your Date of Personal Significance should be something that you will find easy to remember.

You can access the system to:

- Find a pharmacy where you can fill and pick up your prescription
- Change to a new doctor
- Get information about isotretinoin
- Answer your Comprehension Questions, required before you can fill and pick up your prescription
- View information about your current status, your 7-day prescription window, and next steps required in the program
- View FAQ's (Frequently Asked Questions)

If you lose your patient ID cards, and cannot remember your patient ID number, contact your doctor.

Informed Consents

You sign 2 consent forms to be in the iPLEDGE program.

1. **Patient Information/Informed Consent (for all patients)**

Signing the Patient Information/Informed Consent (for all patients) form means you understand that there are risks with isotretinoin.

2. **Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)**

Your doctor will talk to you about the risks of isotretinoin during pregnancy. You must also get this information in writing. You must understand that a baby exposed to isotretinoin could have severe birth defects. Signing the consent form means the following:

- You understand the risks of isotretinoin for unborn babies.
- You agree to use 2 effective forms of birth control, as the iPLEDGE program requires. *The iPLEDGE Program Birth Control Workbook* has the list of effective forms.

The iPLEDGE Program Pregnancy Registry

Because isotretinoin causes such severe birth defects, it is very important for us to know about all the pregnancies that happen during treatment and within 1 month after the last dose. The confidential iPLEDGE Program Pregnancy Registry is a way to collect that information. It may help us prevent more pregnancies in the future.

Your doctor will tell you about the confidential iPLEDGE Program Pregnancy Registry. You are encouraged to contact the iPLEDGE Program Pregnancy Registry, if you get pregnant.

Answering Questions About The iPLEDGE Program And Preventing Pregnancy

The iPLEDGE Program requires you to answer comprehension questions before picking up every prescription. These questions will demonstrate your understanding of the iPLEDGE program requirements, the birth control that you have chosen and the risks associated with isotretinoin. **You will not be able to answer your questions until your doctor has entered your pregnancy test result in the iPLEDGE System.** You may not fill and pick up your prescription until you have correctly answered the questions. You may use your iPLEDGE educational kit as a resource as you answer the questions.

Your First Month Taking Isotretinoin

The first month that you answer your questions, you will be asked a series of questions about iPLEDGE information and counseling provided to you. There are no wrong answers to these questions. The answers are used to determine how often the iPLEDGE materials are shared with patients.

Birth Control Verification

You must enter the 2 forms of birth control you are using. Your doctor will also separately enter the 2 forms of birth control you told him or her you are using. This information must be in the iPLEDGE system and must match for you to fill and pick up your prescription.

Comprehension Questions

Before each prescription can be filled and picked up at the Pharmacy, you will have different questions about the iPLEDGE program and preventing pregnancy to answer. You answer the questions in the iPLEDGE program system using the web site, **www.ipledgeprogram.com**, or automated phone line, **1-866-495-0654** within the 7-day prescription window.

You can use *The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant* and *The iPLEDGE Program Birth Control Workbook* to help you with the answers.

You need your patient ID number and password to log in to the iPLEDGE system.

To answer questions on the iPLEDGE web site:

1. Log in
2. Click on the button under "Answer the Questions"
3. Enter the 2 forms of birth control you are using
4. Follow the prompts to answer the questions

To answer the questions on the iPLEDGE phone system:

1. Log in
2. Select the option to "Demonstrate Your Program Knowledge"
3. Follow the prompts to enter the 2 forms of birth control you are using
4. Follow the prompts to answer the questions

The system will let you know if you answered correctly. If you missed any questions, you will get to try other questions like the ones you missed. You must answer the questions correctly before you will be able to fill and pick up your prescription.

If you miss a question again, the system will tell you where to look in *The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant* or *The iPLEDGE Program Birth Control Workbook* to find answers. You can answer the questions again later. You may also talk with your doctor about questions you missed.

Fill And Pick Up Your Prescription

Fill and pick up your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

The web site, **www.ipledgeprogram.com**, has a list of registered and activated pharmacies. Log in and choose "Finding a Participating Pharmacy" on the Patient home page.

The pharmacist will contact the iPLEDGE system before filling the prescription. The system tells your pharmacist if you can get isotretinoin. It will not tell the pharmacist any personal information about you.

You can only fill and pick up your prescription for isotretinoin if:

- Your pregnancy test was negative
- Your doctor entered your 2 forms of birth control in the iPLEDGE system

- You answered your questions correctly. **This can only be done after your doctor has entered your pregnancy test result in the iPLEDGE System.**
- You also entered your 2 forms of birth control

You **fill** the prescription ***and*** **pick it up** within the 7-day prescription window (1 week) of the date of your pregnancy test, counting the date of the pregnancy test as DAY 1.

To figure out the last date you can pick up your prescription, add 6 to the date of your pregnancy test. For example:

Day 1 Day of the pregnancy test	Day 2–Day 6	Day 7 – Last day to fill and pick up prescription
(Friday, March 1)	(Saturday–Wednesday)	(Thursday, March 7)

The 7-day prescription window expires at 11:59 p m. Eastern Time on Day 7 of the prescription window. Your pharmacist will not be able to fill your prescription after this time. If your 7-day prescription window expires before you fill and pick up your prescription, you can start a new 7-day prescription window right away (unless it is your first prescription window), but you must repeat the program requirements to get another prescription. Additional information regarding the specific dates of your 7-day prescription window, and other information about your current status can be found by selecting "My Program Status" on the website from the Patient home page (after you log in).

Note: Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.

After Your Last Dose

It is very important that you:

- Get a pregnancy test.
- Keep using 2 effective forms of birth control together all the time for 1 month after your last dose. It takes time for isotretinoin to leave your bloodstream.
- Go back to your doctor 1 month after your last dose for your last pregnancy test, even if you think you are not pregnant. If you miss this appointment, you will receive a reminder notification.
- Do not give blood for 1 month after your last dose.
- If your doctor does not enter the results of the pregnancy test after your last dose, and does not enter the pregnancy test 1 month after your last dose, both you and your doctor will be contacted for additional information.

Changing To A New Doctor

You can change your doctor (Primary Prescriber) in the iPLEDGE system. Once you make the change, you will not be able to get any more prescriptions from your original doctor.

You can change your doctor through the iPLEDGE web site, **www.ipledgeprogram.com**, or automated phone line, **1-866-495-0654**. You need your patient ID number to log in to the system.

To change your doctor on the iPLEDGE web site:

1. Log in
2. Choose "Change Primary Prescriber" from the menu
3. You need to enter the following information about your new doctor:
   - First and last name
   - City
   - Phone number

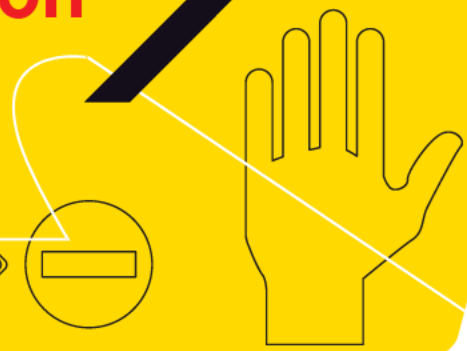
To change your doctor on the automated phone line:

1. Log in
2. Select the Option for "More Choices"
3. Select the Option to "Change Your Prescriber"
4. Follow the prompts to enter the new information

The system will tell you if you have made the change correctly. The new doctor must accept you as a patient within the iPLEDGE system before being able to give you a prescription.

Safety Information

ABOUT ISOTRETINOIN



WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT ISOTRETINOIN?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE program.
- Isotretinoin may cause serious mental health problems.

1. **Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.
Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

2. **Serious mental health problems.** Isotretinoin may cause:
   - **Depression**
   - **Psychosis** (seeing or hearing things that are not real)
   - **Suicide**
   Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See **"What is the most important information I should know about isotretinoin?"**) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE program
- Dispensed by a pharmacy that is registered with the iPLEDGE program
- Given to patients who are registered in the iPLEDGE program and agree to do everything required in the program

What Is Severe Nodular Acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- **Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment.** Isotretinoin causes severe birth defects. (See "**What is the most important information I should know about isotretinoin?**")
- **Do not take isotretinoin if you are allergic to anything in it.**

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do **not** take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
- Female patients who can get pregnant must agree to use 2 separate forms of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE system to answer questions about the program requirements and to enter your 2 chosen forms of birth control.** To access the iPLEDGE system, go to **www ipledgeprogram.com** or call **1-866-495-0654**.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this *free* visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 forms of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See **"What is the most important information I should know about isotretinoin?"**)
- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See **"What should I tell my doctor before taking isotretinoin?"**)
- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop.** Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- **Do not share isotretinoin with other people.** It can cause birth defects and other serious health problems.

What Are The Possible Side Effects Of Isotretinoin?

- **Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Isotretinoin may cause serious mental health problems.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Serious brain problems.** Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  - Bad headache
  - Blurred vision
  - Dizziness
  - Nausea or vomiting
  - Seizures (convulsions)
  - Stroke
- **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like "pink eye"), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.
- **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach). If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:
  - Severe stomach, chest, or bowel pain
  - Trouble swallowing or painful swallowing
  - New or worsening heartburn
  - Diarrhea
  - Rectal bleeding
  - Yellowing of your skin or eyes
  - Dark urine
- **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:
  - Back pain
  - Joint pain
  - A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

- **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.
- **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
- **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
- **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
- **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How Should I Store Isotretinoin?

- Store isotretinoin at room temperature. Protect from light.
- **Keep isotretinoin and all medicines out of the reach of children**.

General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for health care professionals. You can also call iPLEDGE program at **1-866-495-0654** or visit **www ipledgeprogram.com**.

For More Information About Isotretinoin And The iPLEDGE Program

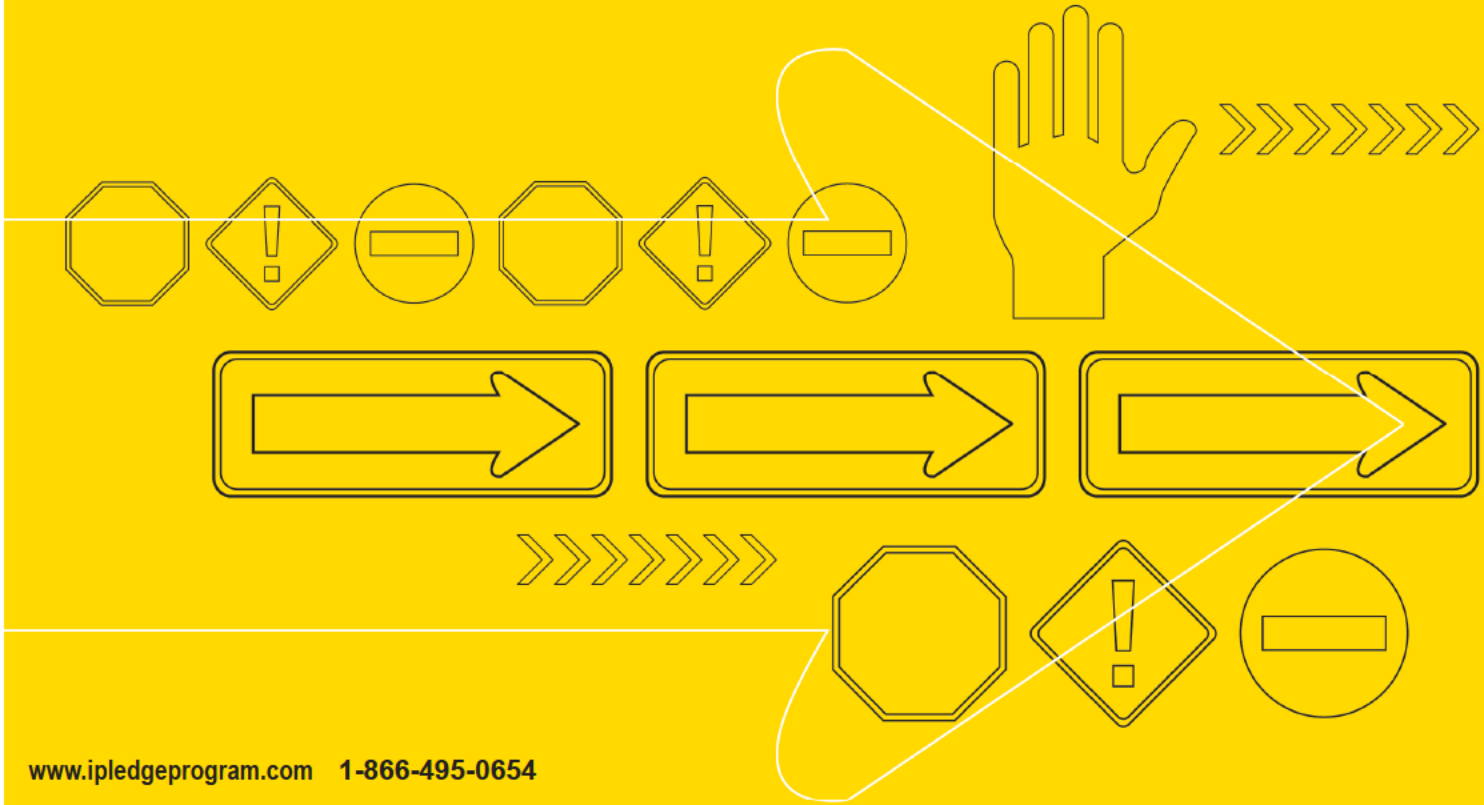
If you have questions about the iPLEDGE program, ask your doctor, visit the iPLEDGE program web site at **www.ipledgeprogram.com**, or call the automated phone line at **1-866-495-0654**.

For private birth control information, you can reach the iPLEDGE automated phone line 24 hours a day, 7 days a week at 1-866-495-0654. You can learn about different subjects, including:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Most Recent Modification: April 2012

The iPLEDGE Program

Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant

The resource to help you prepare and plan treatments during the course of isotretinoin treatment

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™
Committed to Pregnancy Prevention

The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant

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ABOUT ISOTRETINOIN

Isotretinoin (eye-soh-tret-in-OH-in) treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months.

Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby's mother takes isotretinoin. The goal of the iPLEDGE program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin.

Even if you are a male or a female patient who cannot get pregnant, the iPLEDGE program involves a set of steps that you, your doctor, and your pharmacist must follow for you to take isotretinoin. You should also learn about the side effects and the precautions and warnings.

Before starting isotretinoin, talk with your doctor about how isotretinoin can help your skin and about the side effects. Read this *iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant* and make sure you understand the requirements of the iPLEDGE program. Then decide if isotretinoin is right for you.

ISOTRETINOIN AND BIRTH DEFECTS: FOR MALE PATIENTS AND FEMALE PATIENTS WHO CANNOT GET PREGNANT

Birth Defects

There is a very high chance that babies born to female patients taking isotretinoin will be deformed, born too early, or die before they are born. This can happen even if a female patient takes isotretinoin for only a short time. It may also happen if a pregnant female receives a blood transfusion from someone taking isotretinoin.

Do male patients taking isotretinoin need to worry about birth defects?

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin. Approximately 3 to 5 babies in 100 (3% to 5%) are born with some kind of birth defect from other causes, not from isotretinoin.

If you are worried about isotretinoin birth defects from sperm, you can use a male latex condom to help prevent pregnancy. Use a condom each and every time you have intercourse (sex) while you are taking isotretinoin and for 1 month after you stop taking it.

Can isotretinoin affect a male patient's ability to father healthy children?

Studies on isotretinoin did not show effects on sperm count, how sperm look, or how well they swim and move.

Do Not Donate Blood

Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant female gets blood from you. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone

You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

See the *Safety Information* section on page 8 for more detailed information about other serious side effects, precautions, and warnings for isotretinoin.

THE iPLEDGE WEB SITE AND PHONE SYSTEM

The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant and your educational kit are resources for the information you need about isotretinoin and the iPLEDGE program. The iPLEDGE program also has a web site and an automated phone system.

- Web site: **www.ipledgeprogram.com**
- Phone system: **1-866-495-0654**

The information on the phone system is available in English and Spanish. You can get general information about isotretinoin and the iPLEDGE program right away. When you start taking isotretinoin, your doctor will give you a patient ID number and ID cardcards, and other program materials. You use these to log in to the system. (*see page 5*)

After you have been registered in iPLEDGE by your doctor, you will receive your iPLEDGE password in the mail in 5 to 10 business days. Follow the instructions that come with the password to access the iPLEDGE system.

KEY INFORMATION FOR PATIENTS

The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant explains the information about the iPLEDGE program before, during, and after your isotretinoin treatment. Here is a general overview:

- Learn about the iPLEDGE program and the isotretinoin side effects and risks in pregnancy.
- Plan for treatment and appointments.
- Sign the Patient Information/Informed Consent (for all patients) form.
- Keep monthly appointments.
- Do not donate blood during your treatment or 1 month after your last dose.
- Do not share isotretinoin.

You can use the checklist on the next page as a quick reminder of the program information during your isotretinoin treatment.

THE iPLEDGE PROGRAM CHECKLIST

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient.

Male patients and female patients who cannot get pregnant

The prescription window is 30 days and starts on the date the prescriber enters as the date of your office visit. This date is counted as DAY 1.

To determine the end date of your 30-day prescription window, you should add 29 days to the date of your office visit.

After 11:59 p m. Eastern Time on the last day of the 30-day prescription window, you can no longer fill and pick up your prescription, and must start the process over to get a new 30-day prescription window.

Before Treatment

PLANNING

- ☐ **Plan** your course of treatment (about 4 to 5 months).
- ☐ **Talk** with your doctor about isotretinoin and the iPLEDGE program.
- ☐ **Sign** the Patient Information/Informed Consent (for all patients) form.
- ☐ **Get** your patient ID card containing your patient ID number from your doctor. (*see page 5*)
- ☐ **Receive** your password in the mail.

PRESCRIPTION

- ☐ **Get** your prescription for a maximum of up to a 30-day supply.
- ☐ **Fill and Pick up** your prescription within the 30-day prescription window counting your office visit as DAY 1. (*see page 6*)

During Treatment

- ☐ **Keep** your appointments every month to get your prescription.
- ☐ **Fill and Pick up** your prescription within the 30-day prescription window counting the office visit as DAY 1. If you do not fill and pick up your prescription within the 30-day prescription window, you will be required to start the process over again by visiting your doctor.
- ☐ **Do not donate blood.**

After Treatment

Do not donate blood for 1 month after your last dose.

THE iPLEDGE PROGRAM CHECKLIST INFORMATION

Plan Your Course Of Treatment

The most isotretinoin you can get at any one time is a maximum of up to a 30-day supply. You will need to see your doctor each month to get a new prescription.

Get Your Patient ID Number And ID Cards

Your doctor will give you your patient ID cards, containing your patient ID number, when you start the iPLEDGE program. The ID cards are included in the back of this booklet. Tear out one card and keep it in a safe place. You can use the other cards in the booklet if you lose your card. Write your number down as soon as you receive it, and keep it where you will be able to find it.

You need your ID number and card:

- When you take your prescription to be filled and dispensed at the pharmacy
- When you log in to the iPLEDGE program system, either the web site, **www ipledgeprogram.com**, or phone line, **1-866-495-0654**

About The iPLEDGE System

The first time you login to iPLEDGE (either the web site or phone line) you will be asked to select a personal password and select a Date of Personal Significance. The selection of a personal password is a security feature that ensures that only you will know your password. A Date of Personal Significance is collected by the system to be used in verifying your identity should you require assistance from the iPLEDGE Call Center while using iPLEDGE.

Both your password and your Date of Personal Significance should be something that you will find easy to remember.

You can access the system to:

- Find a pharmacy where you can fill and pick up your prescription
- Change to a new doctor
- Get information about isotretinoin
- View information about your current status
- View FAQ's (Frequently Asked Questions)

If you lose your Patient ID Cards, and cannot remember your Patient ID number, contact your doctor.

Informed Consents

You must sign the Patient Information/Informed Consent (for all patients) form to be in the iPLEDGE program.

Signing the informed consent means you understand that there are risks associated with taking isotretinoin.

Fill And Pick Up Your Prescription

Fill and pick up your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

The web site, **www.ipledgeprogram.com**, has a list of registered pharmacies. Log in and choose "Find a Participating Pharmacy" in the left navigation.

Your pharmacist will contact the iPLEDGE system before filling your prescription. The system tells your pharmacist if you can get isotretinoin. It will not tell the pharmacist any personal information about you.

You can only get isotretinoin if:

- Your doctor entered your patient information in the iPLEDGE system
- You can fill and pick up the prescription within the 30-day prescription window, counting the office visit as DAY 1. Please see your doctor if you did not pick up your prescription within the 30-day prescription window.

The system will automatically compute the "Do Not Dispense To Patient After" date for your pharmacist.

To figure out the last date you can fill and pick up your prescription, add 29 days to the date of your office visit. For example:

Day 1 Day of the office visit	Day 2 – Day 29	Day 30 – Last day to fill and pick up prescription
(Friday, March 1)	(Saturday, March 2 thru Friday, March 29)	(Saturday, March 30)

The 30-day prescription window expires at 11:59 p m. Eastern Time on Day 30 of the prescription window. Your pharmacist will not be able to fill your prescription after this time. If your 30-day prescription window expires before you fill and pick up your prescription, you can start a new 30-day prescription window right away, but you must repeat the program requirements to get another prescription.

Additional information about your status, can be found by selecting "My Program Status" on the website from the Patient home page (after you log in).

Note: Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.

After Your Last Dose

It is very important that:

- You do NOT give blood for 1 month after your last dose
- You do not share any leftover isotretinoin with anyone

Changing To A New Doctor

You can change your doctor (Primary Prescriber) in the iPLEDGE system. Once you make the change, you will not be able to get any more prescriptions from your original doctor.

You can change your doctor through the iPLEDGE web site, **www.ipledgeprogram.com**, or phone line, **1-866-495-0654**. You need your patient ID number and password to log in to the system.

To change your doctor on the iPLEDGE web site:

1. Log in
2. Choose "Change Primary Prescriber" from the menu
3. You need to enter the following information about your new doctor:
   - First and last name
   - City
   - Phone number

To change your doctor on the automated phone line:

1. Log in
2. Select the option for "More Choices"
3. Select "Change Your Prescriber"
4. Follow the prompts to enter the new information

The system will tell you if you have made the change correctly. The new doctor must accept you as a patient within the iPLEDGE system before being able to give you a prescription.

Safety Information

ABOUT ISOTRETINOIN

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT ISOTRETINOIN?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE program.
- Isotretinoin may cause serious mental health problems.

1. **Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.
Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

2. **Serious mental health problems.** Isotretinoin may cause:
   - **Depression**
   - **Psychosis** (seeing or hearing things that are not real)
   - **Suicide**
   Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See **"What is the most important information I should know about isotretinoin?"**) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE program
- Dispensed by a pharmacy that is registered with the iPLEDGE program
- Given to patients who are registered in the iPLEDGE program and agree to do everything required in the program

What Is Severe Nodular Acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- **Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment.** Isotretinoin causes severe birth defects. (See "**What is the most important information I should know about isotretinoin?**")
- **Do not take isotretinoin if you are allergic to anything in it.**

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do **not** take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
- Female patients who can get pregnant must agree to use 2 separate forms of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE system to answer questions about the program requirements and to enter your 2 chosen forms of birth control.** To access the iPLEDGE system, go to **www ipledgeprogram.com** or call **1-866-495-0654**.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this *free* visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 forms of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See **"What is the most important information I should know about isotretinoin?"**)
- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See **"What should I tell my doctor before taking isotretinoin?"**)
- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop.** Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- **Do not share isotretinoin with other people.** It can cause birth defects and other serious health problems.

What Are The Possible Side Effects Of Isotretinoin?

- **Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Isotretinoin may cause serious mental health problems.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Serious brain problems.** Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  - Bad headache
  - Blurred vision
  - Dizziness
  - Nausea or vomiting
  - Seizures (convulsions)
  - Stroke
- **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like "pink eye"), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.
- **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach). If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:
  - Severe stomach, chest, or bowel pain
  - Trouble swallowing or painful swallowing
  - New or worsening heartburn
  - Diarrhea
  - Rectal bleeding
  - Yellowing of your skin or eyes
  - Dark urine
- **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:
  - Back pain
  - Joint pain
  - A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

- **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.
- **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
- **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
- **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
- **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How Should I Store Isotretinoin?

- Store isotretinoin at room temperature. Protect from light.
- **Keep isotretinoin and all medicines out of the reach of children.**

General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for health care professionals. You can also call iPLEDGE program at **1-866-495-0654** or visit **www ipledgeprogram.com**.

NOTES:

NOTES:

For More Information About Isotretinoin And The iPLEDGE Program

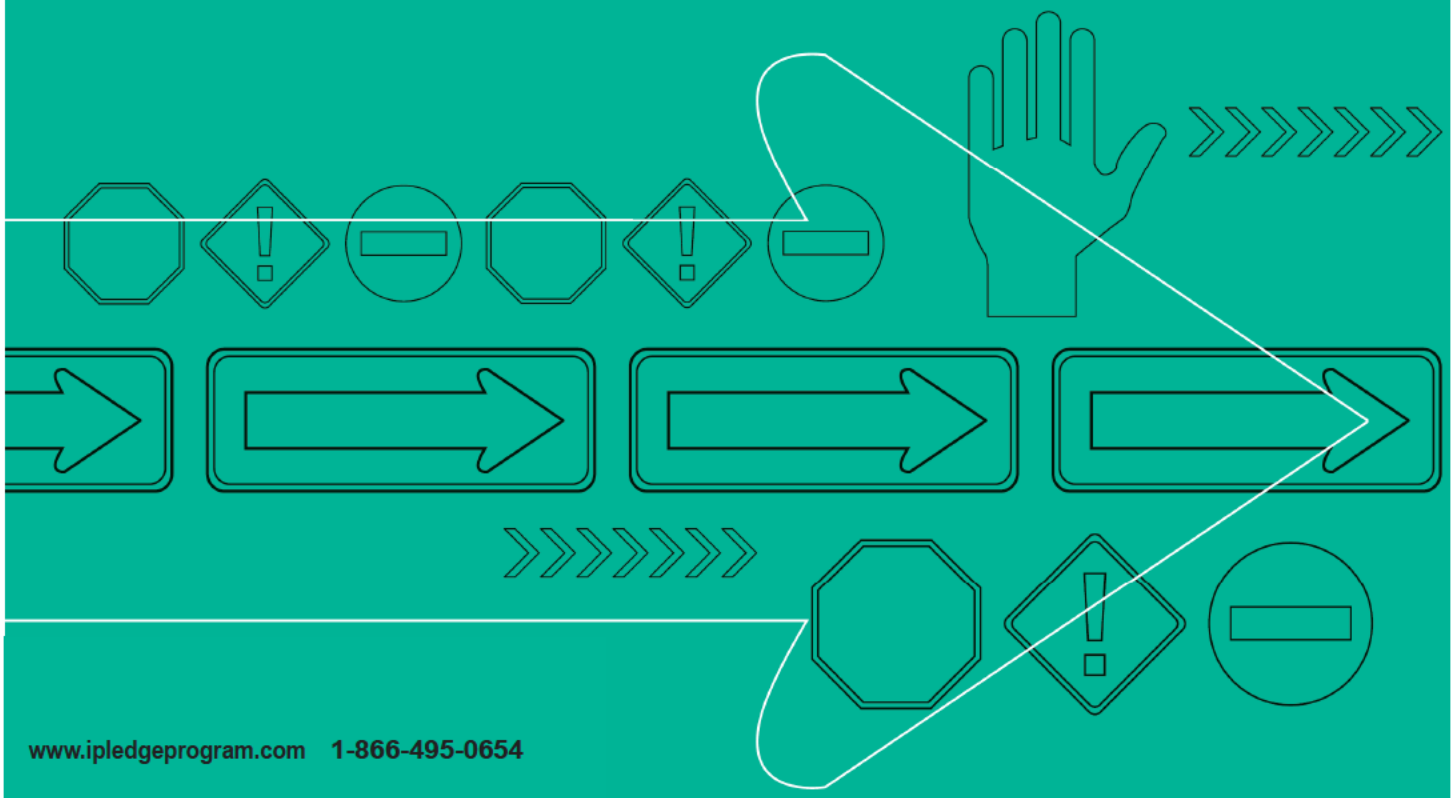
If you have questions about the iPLEDGE program, ask your doctor, visit the iPLEDGE program web site at **www.ipledgeprogram.com**, or call **1-866-495-0654**.

For private birth control information, you can reach the iPLEDGE automated phone line 24 hours a day, 7 days a week at **1-866-495-0654**. You can learn about different subjects, including:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

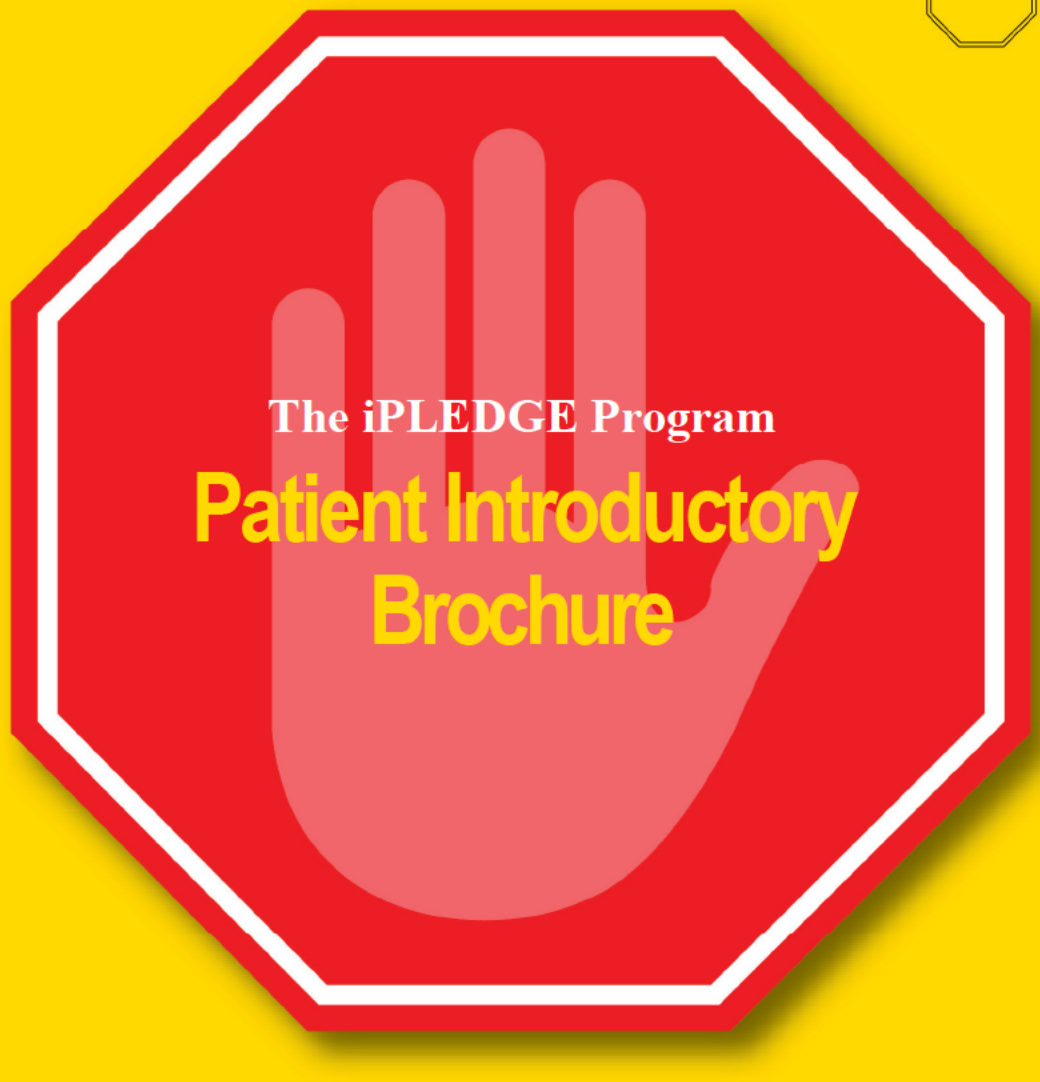
Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Most Recent Modification: April 2012



The iPLEDGE Program

Patient Introductory Brochure

The important information you need to know about isotretinoin and the iPLEDGE program before starting treatment

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Reference ID: 3122588

Are you thinking about taking isotretinoin (eye-soh-tret-in-OH-in) for acne? Read this brochure to learn more about isotretinoin and the iPLEDGE program.

Reference ID: 3122588

Isotretinoin treats a type of severe acne called nodular acne. It is used after other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months.

There is a very high chance of birth defects if an unborn baby's mother takes isotretinoin. The goal of the iPLEDGE program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin. The iPLEDGE program requires birth control for female patients who can get pregnant for at least 1 month before, during, and 1 month after stopping treatment and pregnancy tests before, during, and after treatment.

Before starting isotretinoin, you should know about its other serious side effects. Talk with your doctor about how bad your acne is and how isotretinoin can help your skin.

Decide if isotretinoin is right for you. Your doctor will ask you to read and sign forms that say you understand the serious risks of isotretinoin. It is important for you to know how to take isotretinoin correctly and what to expect.

WHAT IS THE iPLEDGE PROGRAM?

The iPLEDGE program is a set of steps all patients, doctors, and pharmacists must follow. The main goal is preventing pregnancy and birth defects, but both male patients and female patients must follow the iPLEDGE program.

To get isotretinoin, all patients must:

- Sign the Patient Information/Informed Consent form(s)
- Be able to keep appointments
- Agree to follow the iPLEDGE program steps

WHAT DO MALE PATIENTS NEED TO KNOW ABOUT THE iPLEDGE PROGRAM?

- Talk with your doctor about the iPLEDGE program and the possible side effects of taking isotretinoin.
- Keep your appointments. You must be able to see your doctor for your prescriptions. Treatment usually lasts 4 to 5 months.
- Each prescription is for up to a maximum 1-month supply.

WHAT DO ALL FEMALE PATIENTS NEED TO KNOW ABOUT THE iPLEDGE PROGRAM?

Are you a female patient who can get pregnant? This includes all female patients who have menstrual periods. It includes young female patients who have not started having menstrual periods. Even a female patient who has had her tubes tied can still get pregnant.

If you are able to get pregnant, you need to know how to keep from becoming pregnant. Your doctor has information to help you learn about effective birth control for iPLEDGE.

You would not have to follow the birth control requirements of iPLEDGE if:

- You have stopped having periods for 12 months in a row (menopause) and your doctor says you are in menopause
- You had both of your ovaries or uterus taken out by surgery
- Your ovaries do not work and you cannot get pregnant (confirmed by your doctor)
- You commit to not having any sexual contact with a male at any time for at least 1 month before, during, and 1 month after your last dose

Reference ID: 3122588

WHAT DO FEMALE PATIENTS WHO CANNOT GET PREGNANT NEED TO KNOW ABOUT THE iPLEDGE PROGRAM?

- Talk with your doctor about the iPLEDGE program and the possible side effects of taking isotretinoin.
- Keep your appointments. You must be able to see your doctor for your prescriptions. Treatment usually lasts 4 to 5 months.
- Each prescription is for up to a maximum 1-month supply.

WHAT DO FEMALE PATIENTS WHO CAN GET PREGNANT NEED TO DO FOR THE iPLEDGE PROGRAM?

Plan For Your Isotretinoin Treatment

- Talk with your doctor about the iPLEDGE program and the risks of isotretinoin for unborn babies.
- Keep your appointments. You must be able to see your doctor for your prescriptions and to get monthly pregnancy tests. Treatment usually lasts 4 to 5 months.
- Each prescription is for up to a maximum 1-month supply.

Choose 2 Effective Forms Of Birth Control

- Not all birth control is acceptable for the iPLEDGE program. Not all forms of birth control can be used together.
- Learn what birth control will work for the iPLEDGE program. Choose 2 forms that you really will use together.
- Even if you are already using birth control, get this information from your dermatologist, gynecologist, family doctor, or a birth control expert. The iPLEDGE program will pay for a visit for you to learn about birth control.

Reference ID: 3122588

Use The 2 Effective Forms Of Birth Control Together

- You must use both forms together all the time for at least 1 month before you start taking isotretinoin.
    - There is a 30 day mandatory waiting period during which you must be using both chosen forms of birth control before you are eligible to begin treatment with isotretinoin
- You must use both forms together while you are taking isotretinoin
- You must use both forms together for 1 month after isotretinoin treatment.

Get Blood Or Urine Tests For Pregnancy

You must have a negative pregnancy test:

- To enter the iPLEDGE program
- Before you start isotretinoin
- Performed in an approved lab each month before you can fill and pick up your prescription
- Right after you finish your last isotretinoin dose
- 1 month after you finish your last isotretinoin dose

Each Month Before You Can Fill and Pick Up Your Prescription

- Your doctor must enter your pregnancy test results in the iPLEDGE system
- You must access the iPLEDGE system to answer different questions about the iPLEDGE program and confirm the 2 forms of birth control that you are using.

Talk with your doctor about the iPLEDGE program. This information does not replace talking with your doctor about acne or your treatment. If you have any questions, write them down. Ask your doctor before starting isotretinoin. Be sure you understand the answers to all your questions.

REVIEW: THE KEY INFORMATION FOR THE iPLEDGE PROGRAM – FEMALE PATIENTS WHO CAN GET PREGNANT

Before You Start Treatment

- Learn about isotretinoin and the iPLEDGE program.
- Plan for office visits.
- Get birth control information. Choose 2 iPLEDGE program acceptable forms of birth control.
- Start using both forms of birth control together all the time for at least 1 month before starting isotretinoin.
- Have 2 negative pregnancy tests.
  - The first to get started in the iPLEDGE program, which may be performed in the doctor's office.
  - The second before you actually start isotretinoin, performed in an approved lab.
- Sign the Patient Information/Informed Consent form(s).
- Get a prescription from your doctor.
- Before you fill and pick up the prescription, access the system to answer questions about the iPLEDGE program and preventing pregnancy. You can answer your questions after your doctor has entered your pregnancy test result in the iPLEDGE system.
- Fill and Pick up your prescription for up to a maximum of a 1-month supply.
- Fill and Pick up your prescription within the 7-day prescription window, counting the date of the pregnancy test as DAY 1.

Each Month During Treatment

- Use 2 forms of birth control together all the time.
- Get a prescription for up to a maximum of a 1-month supply.
- Have a negative pregnancy test, performed in an approved lab.
- Answer questions about the iPLEDGE program and preventing pregnancy. You can answer your questions after your doctor has entered your pregnancy test result in the iPLEDGE system.
- Fill and Pick up your prescription for up to a maximum of a 1-month supply and within the 7-day prescription window counting the date of the pregnancy test as DAY 1.
- Do not donate blood.

After Your Last Dose

- Have a pregnancy test after your last dose.
- Use 2 forms of birth control together all the time for 30 more days.
- Have a last pregnancy test 1 month after your last dose, performed in an approved lab.
- Do not donate blood for 30 days after taking your last dose.

Reference ID: 3122588

REVIEW: THE KEY INFORMATION FOR THE iPLEDGE PROGRAM – MALE PATIENTS AND FEMALE PATIENTS WHO CANNOT GET PREGNANT

Before You Start Treatment

- Learn about isotretinoin and the iPLEDGE program.
- Plan for office visits.
- Sign the Patient Information/Informed Consent form.
- Get a prescription from your doctor.
- Fill and Pick up your prescription for up to a maximum of a 1-month supply.
- Fill and Pick up your prescription within the 30-day prescription window counting the date of the office visit as DAY 1.

Each Month During Treatment

- Get a prescription for up to a maximum of a 1-month supply.
- Fill and Pick up your prescription for up to a maximum of a 1-month supply and within the 30-day prescription window counting the office visit as DAY 1.
- Do not donate blood.

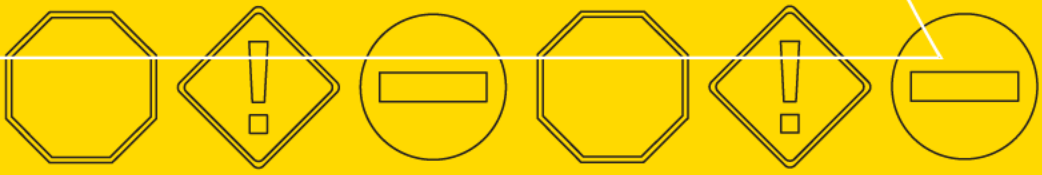
After Your Last Dose

- Do not donate blood for 30 days after taking your last dose.

Reference ID: 3122588

Safety Information

ABOUT ISOTRETINOIN



WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT ISOTRETINOIN?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE program.
- Isotretinoin may cause serious mental health problems.

1. **Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.
Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

2. **Serious mental health problems.** Isotretinoin may cause:
   - **Depression**
   - **Psychosis** (seeing or hearing things that are not real)
   - **Suicide**
   Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Reference ID: 3122588

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See **"What is the most important information I should know about isotretinoin?"**) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE program
- Dispensed by a pharmacy that is registered with the iPLEDGE program
- Given to patients who are registered in the iPLEDGE program and agree to do everything required in the program

What Is Severe Nodular Acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- **Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment.** Isotretinoin causes severe birth defects. (See "**What is the most important information I should know about isotretinoin?**")
- **Do not take isotretinoin if you are allergic to anything in it.**

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do **not** take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
- Female patients who can get pregnant must agree to use 2 separate forms of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE system to answer questions about the program requirements and to enter your 2 chosen forms of birth control.** To access the iPLEDGE system, go to **www.ipledgeprogram.com** or call **1-866-495-0654.**

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this *free* visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 forms of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See **"What is the most important information I should know about isotretinoin?"**)
- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See **"What should I tell my doctor before taking isotretinoin?"**)
- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop.** Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- **Do not share isotretinoin with other people.** It can cause birth defects and other serious health problems.

What Are The Possible Side Effects Of Isotretinoin?

- **Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Isotretinoin may cause serious mental health problems.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Serious brain problems.** Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  - Bad headache
  - Blurred vision
  - Dizziness
  - Nausea or vomiting
  - Seizures (convulsions)
  - Stroke
- **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like "pink eye"), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.
- **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach). If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:
  - Severe stomach, chest, or bowel pain
  - Trouble swallowing or painful swallowing
  - New or worsening heartburn
  - Diarrhea
  - Rectal bleeding
  - Yellowing of your skin or eyes
  - Dark urine
- **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:
  - Back pain
  - Joint pain
  - A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

- **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.
- **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
- **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
- **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
- **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How Should I Store Isotretinoin?

- Store isotretinoin at room temperature. Protect from light.
- **Keep isotretinoin and all medicines out of the reach of children.**

General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

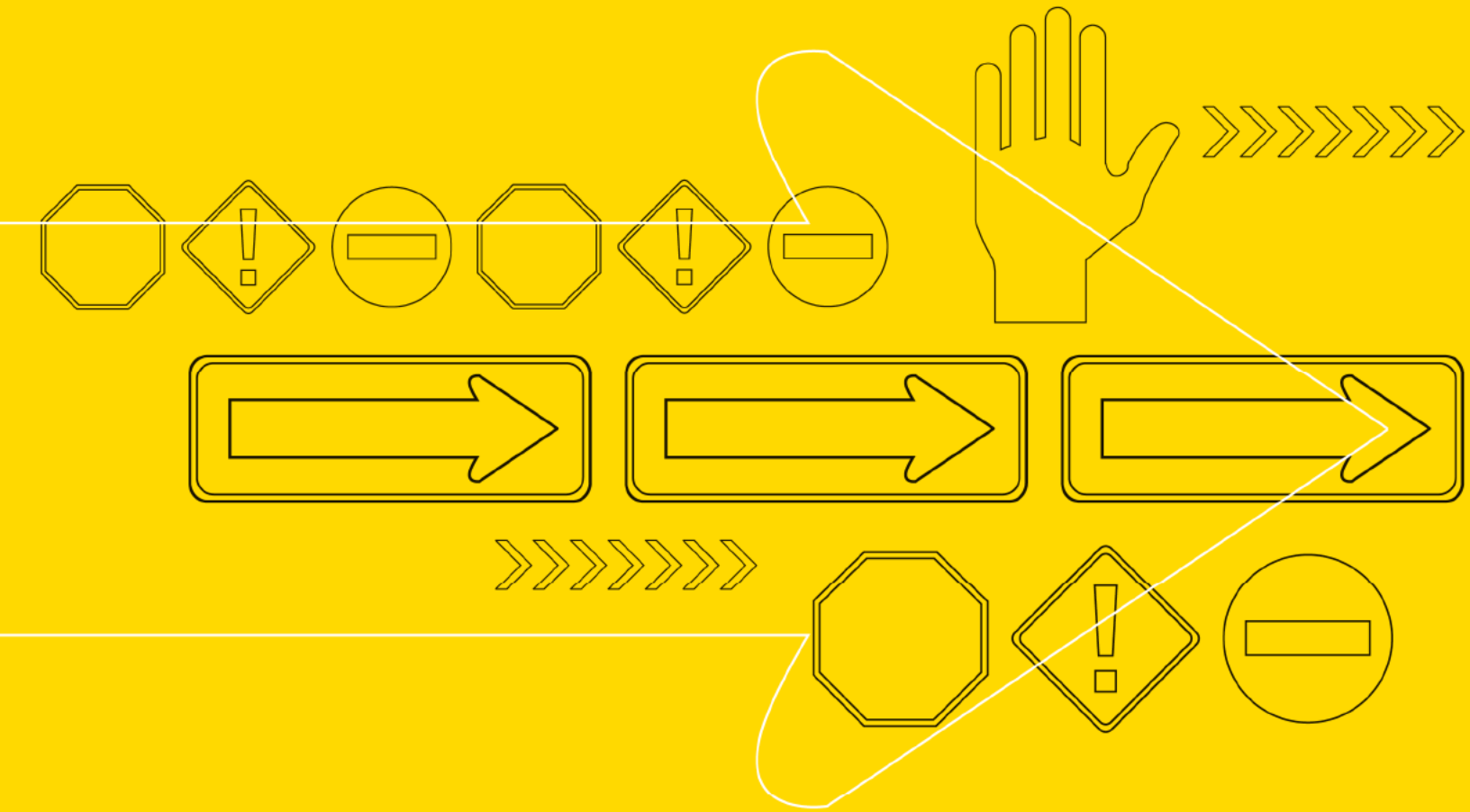
This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for health care professionals. You can also call iPLEDGE program at **1-866-495-0654** or visit **www.ipledgeprogram.com**.

NOTES:

NOTES:

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Reference ID: 3122588

Most Recent Modification: April 2012

The iPLEDGE Program

Isotretinoin Educational Kit For Male Patients And Female Patients Who Cannot Get Pregnant

The tools you need to help you prepare and plan treatments during the course of isotretinoin treatment

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

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CONTENTS

- Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant
- Patient Information/Informed Consent (for all patients)
- Patient Identification Card
- Patient Flowchart

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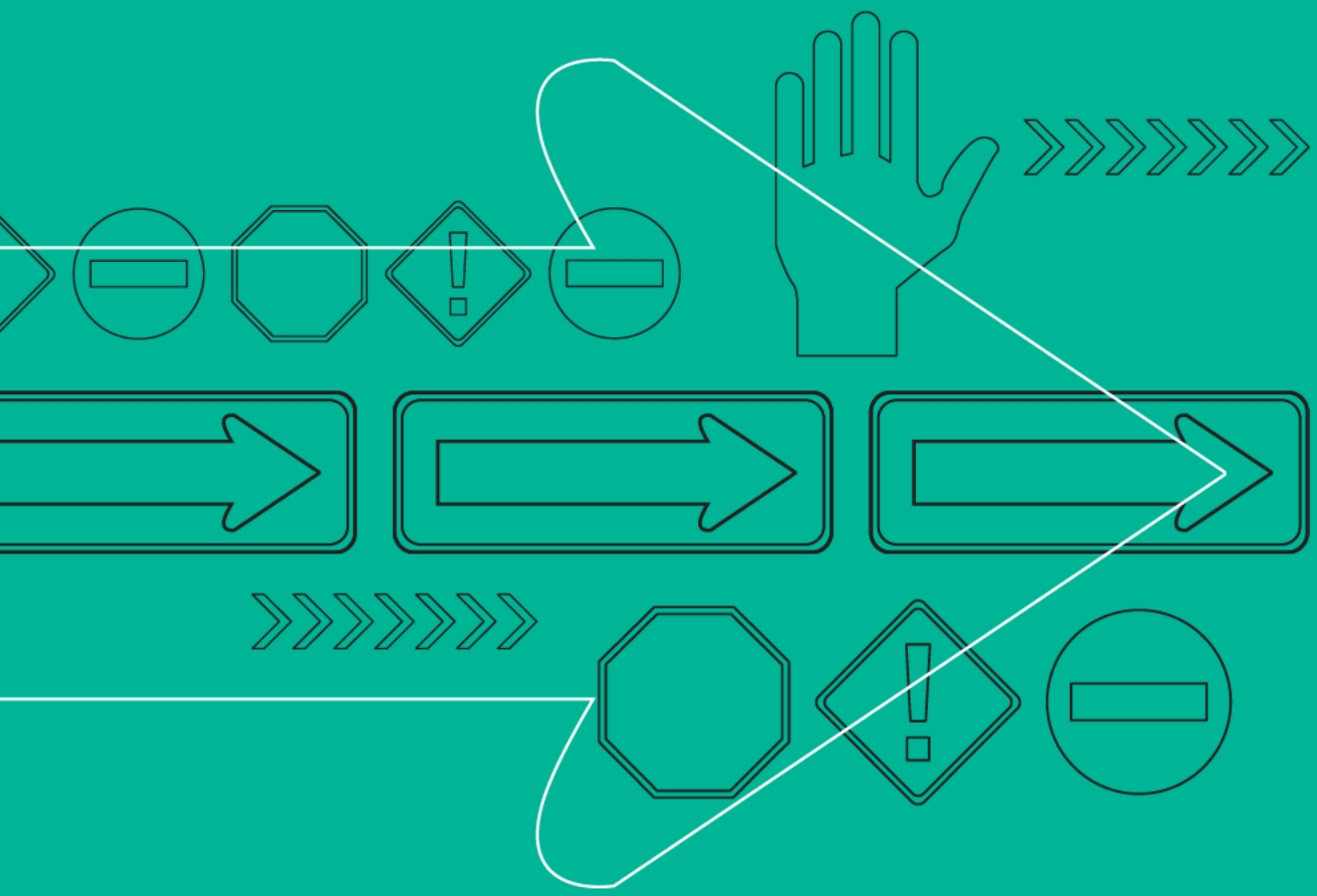
Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant



The guide to help you prepare and plan treatments during the course of isotretinoin treatment

Reference ID: 3122588

Most Recent Modification: April 2012

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Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant

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iPLEDGE™
Committed to Pregnancy Prevention

The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant

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ABOUT ISOTRETINOIN

Isotretinoin (eye-soh-tret-in-OH-in) treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months.

Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby's mother takes isotretinoin. The goal of the iPLEDGE program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin.

Even if you are a male or a female patient who cannot get pregnant, the iPLEDGE program involves a set of steps that you, your doctor, and your pharmacist must follow for you to take isotretinoin. You should also learn about the side effects and the precautions and warnings.

Before starting isotretinoin, talk with your doctor about how isotretinoin can help your skin and about the side effects. Read this *iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant* and make sure you understand the requirements of the iPLEDGE program. Then decide if isotretinoin is right for you.

ISOTRETINOIN AND BIRTH DEFECTS: FOR MALE PATIENTS AND FEMALE PATIENTS WHO CANNOT GET PREGNANT

Birth Defects

There is a very high chance that babies born to female patients taking isotretinoin will be deformed, born too early, or die before they are born. This can happen even if a female patient takes isotretinoin for only a short time. It may also happen if a pregnant female receives a blood transfusion from someone taking isotretinoin.

Do male patients taking isotretinoin need to worry about birth defects?

Unlike in female patients, there is no pattern of birth defects in babies whose fathers were taking isotretinoin. Approximately 3 to 5 babies in 100 (3% to 5%) are born with some kind of birth defect from other causes, not from isotretinoin.

If you are worried about isotretinoin birth defects from sperm, you can use a male latex condom to help prevent pregnancy. Use a condom each and every time you have intercourse (sex) while you are taking isotretinoin and for 1 month after you stop taking it.

Can isotretinoin affect a male patient's ability to father healthy children?

Studies on isotretinoin did not show effects on sperm count, how sperm look, or how well they swim and move.

Do Not Donate Blood

Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant female gets blood from you. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone

You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

See the *Safety Information* section on page 8 for more detailed information about other serious side effects, precautions, and warnings for isotretinoin.

THE iPLEDGE WEB SITE AND PHONE SYSTEM

The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant and your educational kit are resources for the information you need about isotretinoin and the iPLEDGE program. The iPLEDGE program also has a web site and an automated phone system.

- Web site: **www.ipledgeprogram.com**
- Phone system: **1-866-495-0654**

The information on the phone system is available in English and Spanish. You can get general information about isotretinoin and the iPLEDGE program right away. When you start taking isotretinoin, your doctor will give you a patient ID number and ID cardcards, and other program materials. You use these to log in to the system. (*see page 5*)

After you have been registered in iPLEDGE by your doctor, you will receive your iPLEDGE password in the mail in 5 to 10 business days. Follow the instructions that come with the password to access the iPLEDGE system.

KEY INFORMATION FOR PATIENTS

The iPLEDGE Program Guide To Isotretinoin For Male Patients And Female Patients Who Cannot Get Pregnant explains the information about the iPLEDGE program before, during, and after your isotretinoin treatment. Here is a general overview:

- Learn about the iPLEDGE program and the isotretinoin side effects and risks in pregnancy.
- Plan for treatment and appointments.
- Sign the Patient Information/Informed Consent (for all patients) form.
- Keep monthly appointments.
- Do not donate blood during your treatment or 1 month after your last dose.
- Do not share isotretinoin.

You can use the checklist on the next page as a quick reminder of the program information during your isotretinoin treatment.

THE iPLEDGE PROGRAM CHECKLIST

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient.

Male patients and female patients who cannot get pregnant

The prescription window is 30 days and starts on the date the prescriber enters as the date of your office visit. This date is counted as DAY 1.

To determine the end date of your 30-day prescription window, you should add 29 days to the date of your office visit.

After 11:59 p m. Eastern Time on the last day of the 30-day prescription window, you can no longer fill and pick up your prescription, and must start the process over to get a new 30-day prescription window.

Before Treatment

PLANNING

- ☐ **Plan** your course of treatment (about 4 to 5 months).
- ☐ **Talk** with your doctor about isotretinoin and the iPLEDGE program.
- ☐ **Sign** the Patient Information/Informed Consent (for all patients) form.
- ☐ **Get** your patient ID card containing your patient ID number from your doctor. (*see page 5*)
- ☐ **Receive** your password in the mail.

PRESCRIPTION

- ☐ **Get** your prescription for a maximum of up to a 30-day supply.
- ☐ **Fill and Pick up** your prescription within the 30-day prescription window counting your office visit as DAY 1. (*see page 6*)

During Treatment

- ☐ **Keep** your appointments every month to get your prescription.
- ☐ **Fill and Pick up** your prescription within the 30-day prescription window counting the office visit as DAY 1. If you do not fill and pick up your prescription within the 30-day prescription window, you will be required to start the process over again by visiting your doctor.
- ☐ **Do not donate blood.**

After Treatment

Do not donate blood for 1 month after your last dose.

THE iPLEDGE PROGRAM CHECKLIST INFORMATION

Plan Your Course Of Treatment

The most isotretinoin you can get at any one time is a maximum of up to a 30-day supply. You will need to see your doctor each month to get a new prescription.

Get Your Patient ID Number And ID Cards

Your doctor will give you your patient ID cards, containing your patient ID number, when you start the iPLEDGE program. The ID cards are included in the back of this booklet. Tear out one card and keep it in a safe place. You can use the other cards in the booklet if you lose your card. Write your number down as soon as you receive it, and keep it where you will be able to find it.

You need your ID number and card:

- When you take your prescription to be filled and dispensed at the pharmacy
- When you log in to the iPLEDGE program system, either the web site, **www ipledgeprogram.com**, or phone line, **1-866-495-0654**

About The iPLEDGE System

The first time you login to iPLEDGE (either the web site or phone line) you will be asked to select a personal password and select a Date of Personal Significance. The selection of a personal password is a security feature that ensures that only you will know your password. A Date of Personal Significance is collected by the system to be used in verifying your identity should you require assistance from the iPLEDGE Call Center while using iPLEDGE.

Both your password and your Date of Personal Significance should be something that you will find easy to remember.

You can access the system to:

- Find a pharmacy where you can fill and pick up your prescription
- Change to a new doctor
- Get information about isotretinoin
- View information about your current status
- View FAQ's (Frequently Asked Questions)

If you lose your Patient ID Cards, and cannot remember your Patient ID number, contact your doctor.

Informed Consents

You must sign the Patient Information/Informed Consent (for all patients) form to be in the iPLEDGE program.

Signing the informed consent means you understand that there are risks associated with taking isotretinoin.

Fill And Pick Up Your Prescription

Fill and pick up your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

The web site, **www.ipledgeprogram.com**, has a list of registered pharmacies. Log in and choose "Find a Participating Pharmacy" in the left navigation.

Your pharmacist will contact the iPLEDGE system before filling your prescription. The system tells your pharmacist if you can get isotretinoin. It will not tell the pharmacist any personal information about you.

You can only get isotretinoin if:

- Your doctor entered your patient information in the iPLEDGE system
- You can fill and pick up the prescription within the 30-day prescription window, counting the office visit as DAY 1. Please see your doctor if you did not pick up your prescription within the 30-day prescription window.

The system will automatically compute the "Do Not Dispense To Patient After" date for your pharmacist.

To figure out the last date you can fill and pick up your prescription, add 29 days to the date of your office visit. For example:

Day 1 Day of the office visit	Day 2 – Day 29	Day 30 – Last day to fill and pick up prescription
(Friday, March 1)	(Saturday, March 2 thru Friday, March 29)	(Saturday, March 30)

The 30-day prescription window expires at 11:59 p m. Eastern Time on Day 30 of the prescription window. Your pharmacist will not be able to fill your prescription after this time. If your 30-day prescription window expires before you fill and pick up your prescription, you can start a new 30-day prescription window right away, but you must repeat the program requirements to get another prescription.

Additional information about your status, can be found by selecting "My Program Status" on the website from the Patient home page (after you log in).

Note: Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.

After Your Last Dose

It is very important that:

- You do NOT give blood for 1 month after your last dose
- You do not share any leftover isotretinoin with anyone

Changing To A New Doctor

You can change your doctor (Primary Prescriber) in the iPLEDGE system. Once you make the change, you will not be able to get any more prescriptions from your original doctor.

You can change your doctor through the iPLEDGE web site, **www.ipledgeprogram.com**, or phone line, **1-866-495-0654**. You need your patient ID number and password to log in to the system.

To change your doctor on the iPLEDGE web site:

1. Log in
2. Choose "Change Primary Prescriber" from the menu
3. You need to enter the following information about your new doctor:
   - First and last name
   - City
   - Phone number

To change your doctor on the automated phone line:

1. Log in
2. Select the option for "More Choices"
3. Select "Change Your Prescriber"
4. Follow the prompts to enter the new information

The system will tell you if you have made the change correctly. The new doctor must accept you as a patient within the iPLEDGE system before being able to give you a prescription.

Safety Information

ABOUT ISOTRETINOIN

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT ISOTRETINOIN?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE program.
- Isotretinoin may cause serious mental health problems.

1. **Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.
Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

2. **Serious mental health problems.** Isotretinoin may cause:
   - **Depression**
   - **Psychosis** (seeing or hearing things that are not real)
   - **Suicide**
     Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See **"What is the most important information I should know about isotretinoin?"**) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE program
- Dispensed by a pharmacy that is registered with the iPLEDGE program
- Given to patients who are registered in the iPLEDGE program and agree to do everything required in the program

What Is Severe Nodular Acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- **Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment.** Isotretinoin causes severe birth defects. (See "**What is the most important information I should know about isotretinoin?**")
- **Do not take isotretinoin if you are allergic to anything in it.**

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do **not** take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
- Female patients who can get pregnant must agree to use 2 separate forms of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE system to answer questions about the program requirements and to enter your 2 chosen forms of birth control.** To access the iPLEDGE system, go to **www ipledgeprogram.com** or call **1-866-495-0654**.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this *free* visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 forms of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See **"What is the most important information I should know about isotretinoin?"**)
- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See **"What should I tell my doctor before taking isotretinoin?"**)
- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop.** Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- **Do not share isotretinoin with other people.** It can cause birth defects and other serious health problems.

What Are The Possible Side Effects Of Isotretinoin?

- **Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Isotretinoin may cause serious mental health problems.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Serious brain problems.** Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  - Bad headache
  - Blurred vision
  - Dizziness
  - Nausea or vomiting
  - Seizures (convulsions)
  - Stroke
- **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like "pink eye"), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.
- **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach). If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:
  - Severe stomach, chest, or bowel pain
  - Trouble swallowing or painful swallowing
  - New or worsening heartburn
  - Diarrhea
  - Rectal bleeding
  - Yellowing of your skin or eyes
  - Dark urine
- **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:
  - Back pain
  - Joint pain
  - A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

- **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.
- **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
- **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
- **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
- **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How Should I Store Isotretinoin?

- Store isotretinoin at room temperature. Protect from light.
- **Keep isotretinoin and all medicines out of the reach of children.**

General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for health care professionals. You can also call iPLEDGE program at **1-866-495-0654** or visit **www ipledgeprogram.com**.

NOTES:

NOTES:

For More Information About Isotretinoin And The iPLEDGE Program

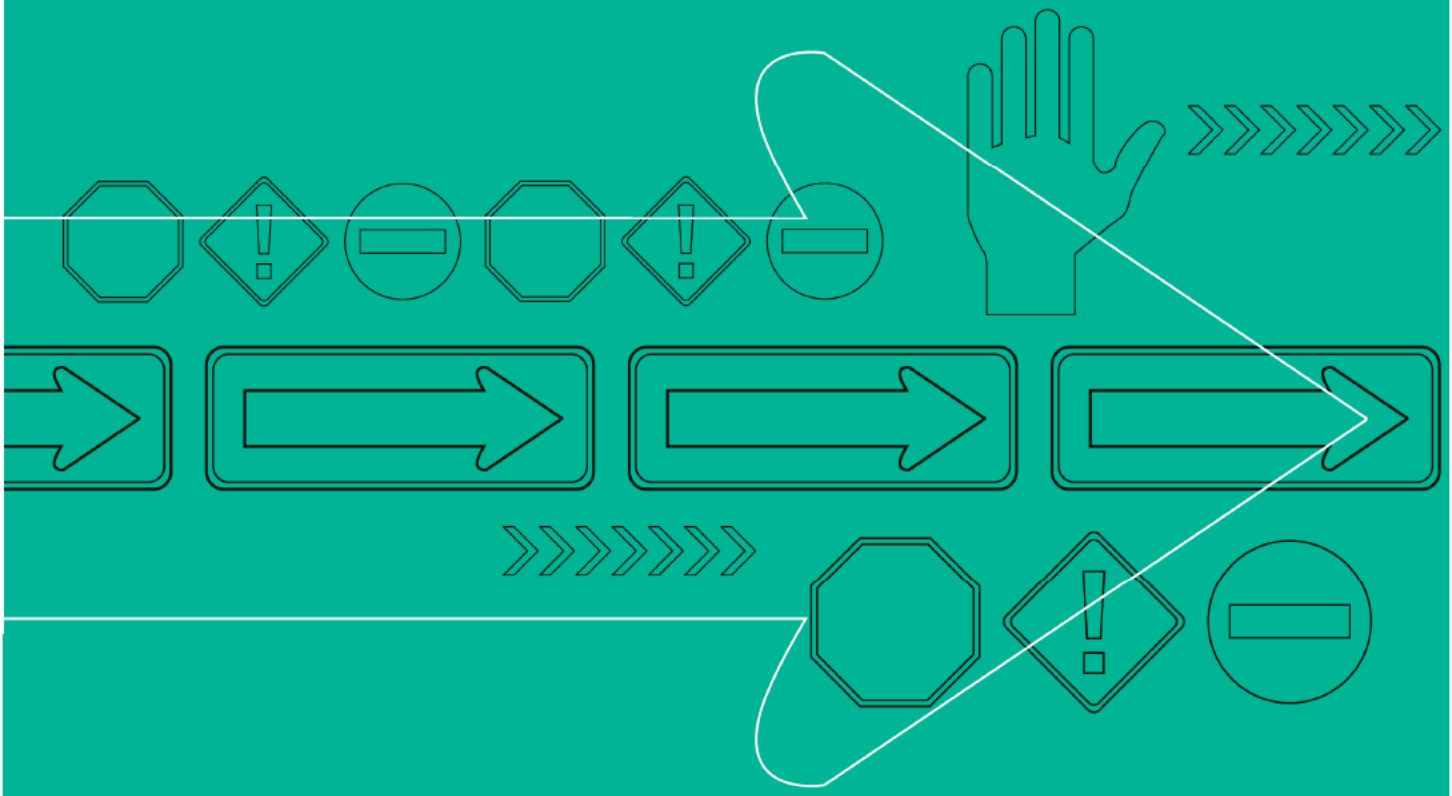
If you have questions about the iPLEDGE program, ask your doctor, visit the iPLEDGE program web site at **www.ipledgeprogram.com**, or call **1-866-495-0654**.

For private birth control information, you can reach the iPLEDGE automated phone line 24 hours a day, 7 days a week at **1-866-495-0654**. You can learn about different subjects, including:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

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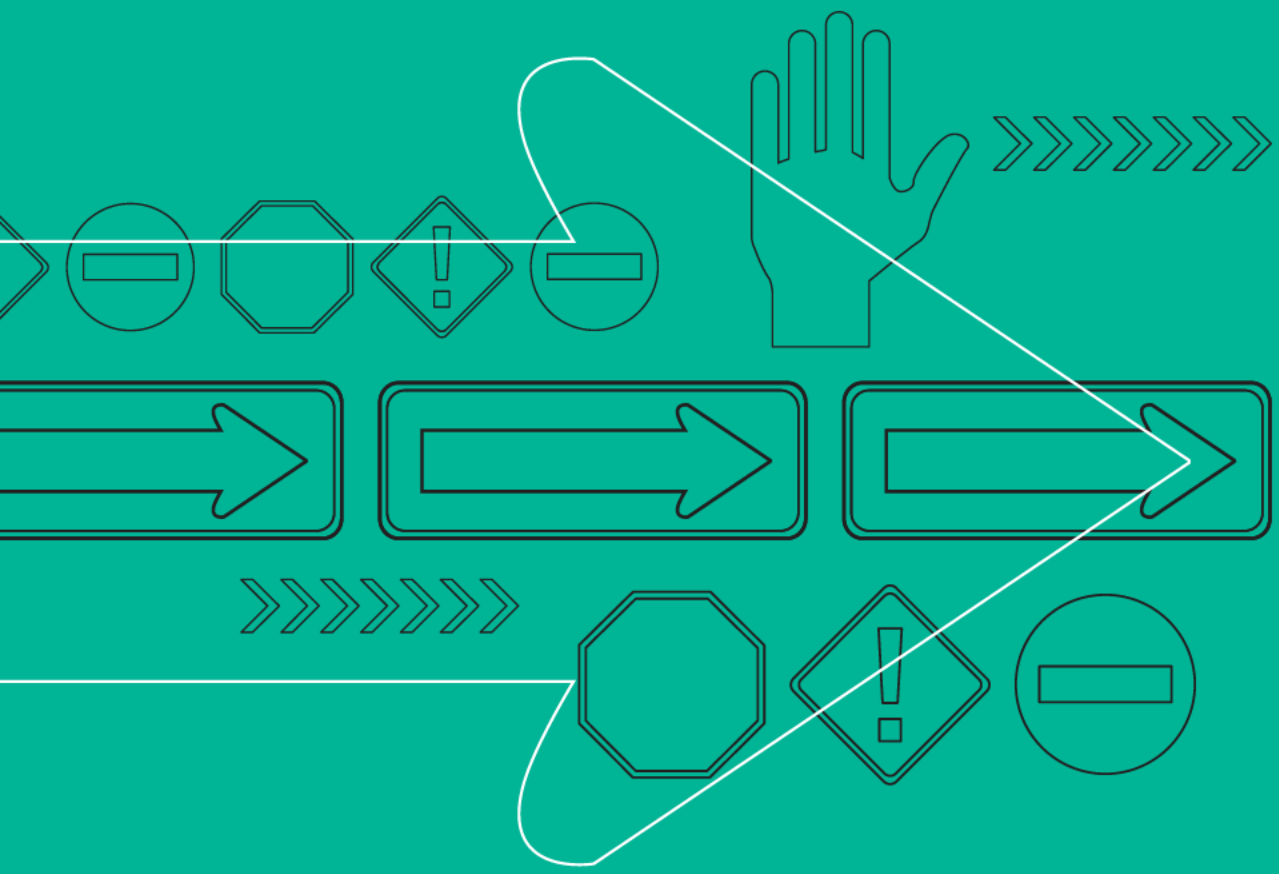
 (R-1 03/12)

Patient Information/Informed Consent



Important form you must sign before you begin taking isotretinoin

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Patient Information/Informed Consent (for all patients):

To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and agree to follow your doctor's instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, _____
(Patient's Name)

understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.

Initials: _____

2. My doctor has told me about my choices for treating my acne.

Initials: _____

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. [Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)].

Initials: _____

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, "anxious" or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives. There were reports that some of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. No one knows if isotretinoin caused these behaviors or if they would have happened even if the person did not take isotretinoin. Some people have had other signs of depression while taking isotretinoin (see #7).

Initials: _____

5. Before I start taking isotretinoin, I agree to tell my doctor if I have **ever** had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.

Initials: _____

6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or had any other serious mental problems.

Initials: _____

7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen. I:
   - Start to feel sad or have crying spells
   - Lose interest in activities I once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in my appetite or body weight
   - Have trouble concentrating
   - Withdraw from my friends or family
   - Feel like I have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting myself or taking my own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real

   Initials: _____

8. **I agree to return to see my doctor every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.**

Initials: _____

9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.

Initials: _____

10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.

Initials: _____

11. I have read *The iPLEDGE Program Patient Introductory Brochure* and other materials my provider gave me containing important safety information about isotretinoin. I understand all the information I received.

Initials: _____

12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.

Initials: _____

I now allow my doctor _____ to begin my treatment with isotretinoin.

Patient Signature: _____ Date: _____

Parent/Guardian Signature (if under age 18): _____ Date: _____

Patient Name (print) _____

Patient Address _____ Telephone _____ – _____ – _____

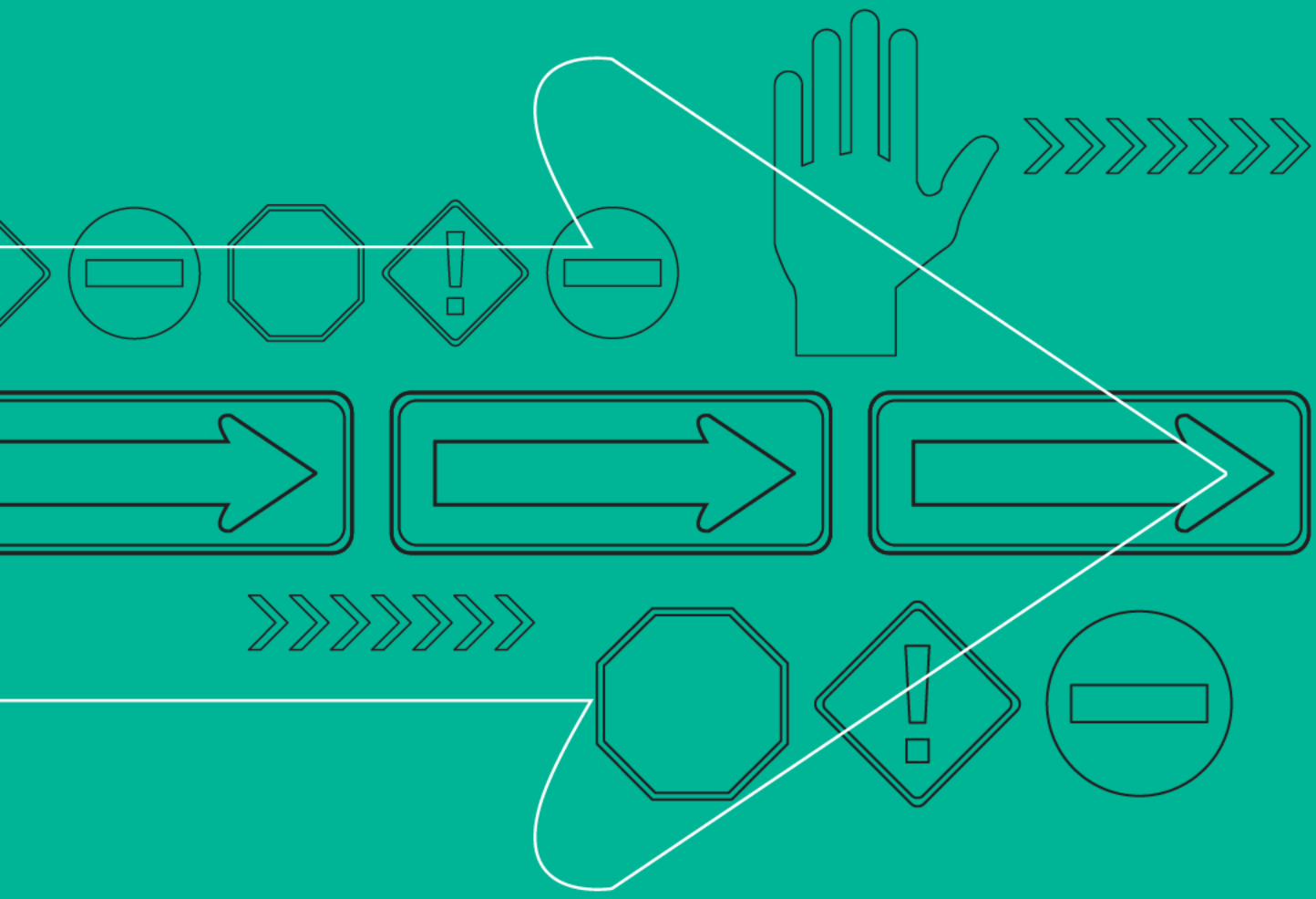
I have:

- fully explained to the patient, _____, the nature and purpose of isotretinoin treatment, including its benefits and risks
- given the patient the appropriate educational materials, *The iPLEDGE Program Patient Introductory Brochure* and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
- answered those questions to the best of my ability

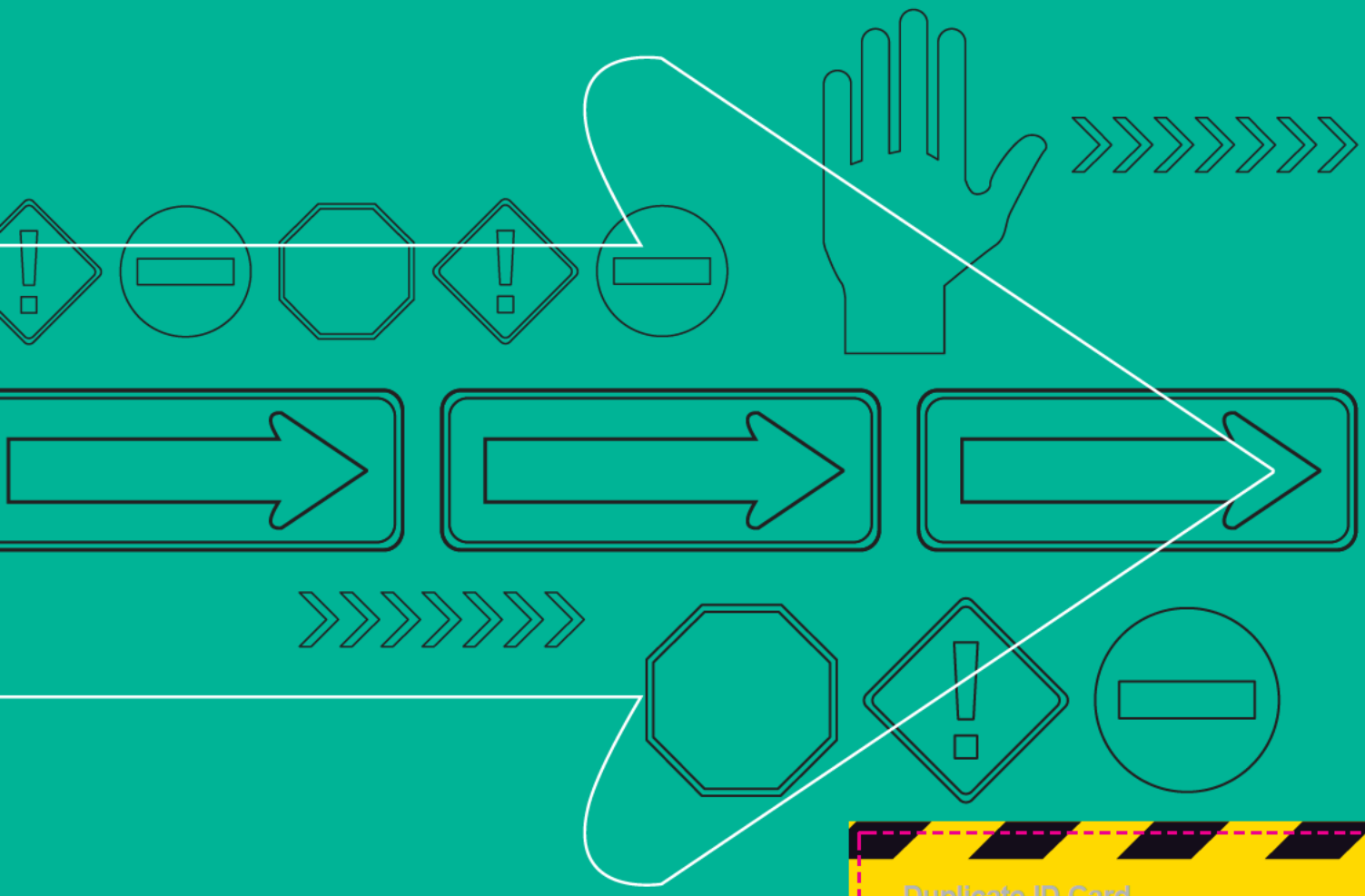
Doctor Signature: _____ Date: _____

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT'S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

Patient Identification Card



- The card you need to bring with you to doctor visits and to the pharmacy while on isotretinoin



Peel off sticker for patient's file

Duplicate ID Card

- Visit your doctor monthly
- Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
- Take this card and your prescription to the pharmacy within your prescription window
- Do not get pregnant
- Do not share your drug
- Do not donate blood

See reverse for important safety information

iPLEDGE™ Committed to Pregnancy Prevention

Duplicate ID Card

- Visit your doctor monthly
- Women who can get pregnant must:
  1. Have a monthly pregnancy test
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See reverse for important safety information

iPLEDGE™ Committed to Pregnancy Prevention

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- Take this card and your prescription to the pharmacy within your prescription window
- Do not get pregnant
- Do not share your drug
- Do not donate blood

See reverse for important safety information

iPLEDGE™ Committed to Pregnancy Prevention

Stop isotretinoin and call your doctor right away if you are pregnant.
Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

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- Have trouble concentrating
- Withdraw from your friends or family
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- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
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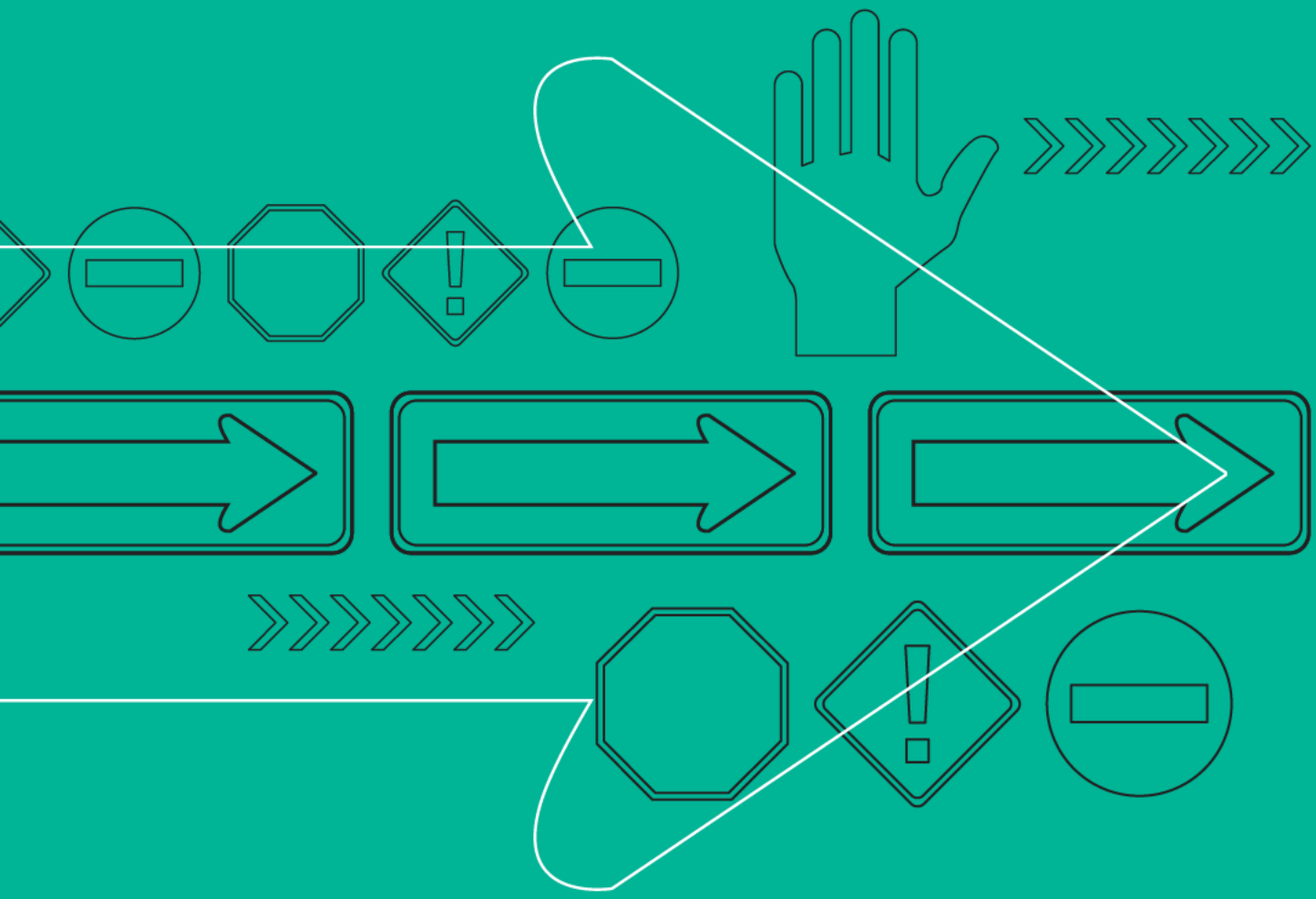
Patient Flowchart



A flowchart to assist you with the iPLEDGE program requirements

Reference ID: 3122588

REGISTERED PATIENTS

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Female patients of childbearing potential (FCBP)

BEFORE TREATMENT

- **Sign** a Patient Information/Informed Consent (for all patients) form for treatment
- **Sign** a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- **Get** a screening urine/blood pregnancy test
- **Receive** patient ID card
- **Choose** 2 effective forms of birth control
- **Start** using the 2 forms of birth control simultaneously for at least 1 month
- **Get** a second pregnancy test within the first 5 days of your menstrual period (patient with irregular cycle please check with your prescriber) in an approved lab
- **Access*** the iPLEDGE system to answer questions and to enter the 2 chosen forms of birth control. You can only answer your questions after your doctor has entered your test results into the iPLEDGE System
- **Get** a prescription for a maximum 30-day supply

EACH MONTH DURING THERAPY

- **Use** the 2 forms of birth control simultaneously
- **See** your doctor for a monthly pregnancy test in an approved lab
- **Access*** the iPLEDGE system to answer questions and confirm the 2 forms of birth control
- **Get** a prescription for a maximum 30-day supply
- **Do not** donate blood

AFTER TREATMENT

- **Get** a pregnancy test in an approved lab after the last dose
- **Continue** to use the 2 forms of birth control simultaneously for 1 month after the last dose
- **Do not** donate blood for 1 month after the last dose
- **Get** a final pregnancy test 1 month after the last dose

Male patients/Female patients not of childbearing potential (FNCBP)

BEFORE TREATMENT

- **Sign** a Patient Information/Informed Consent (for all patients) form for treatment
- **Receive** patient ID card
- **Get** a prescription for a maximum 30-day supply

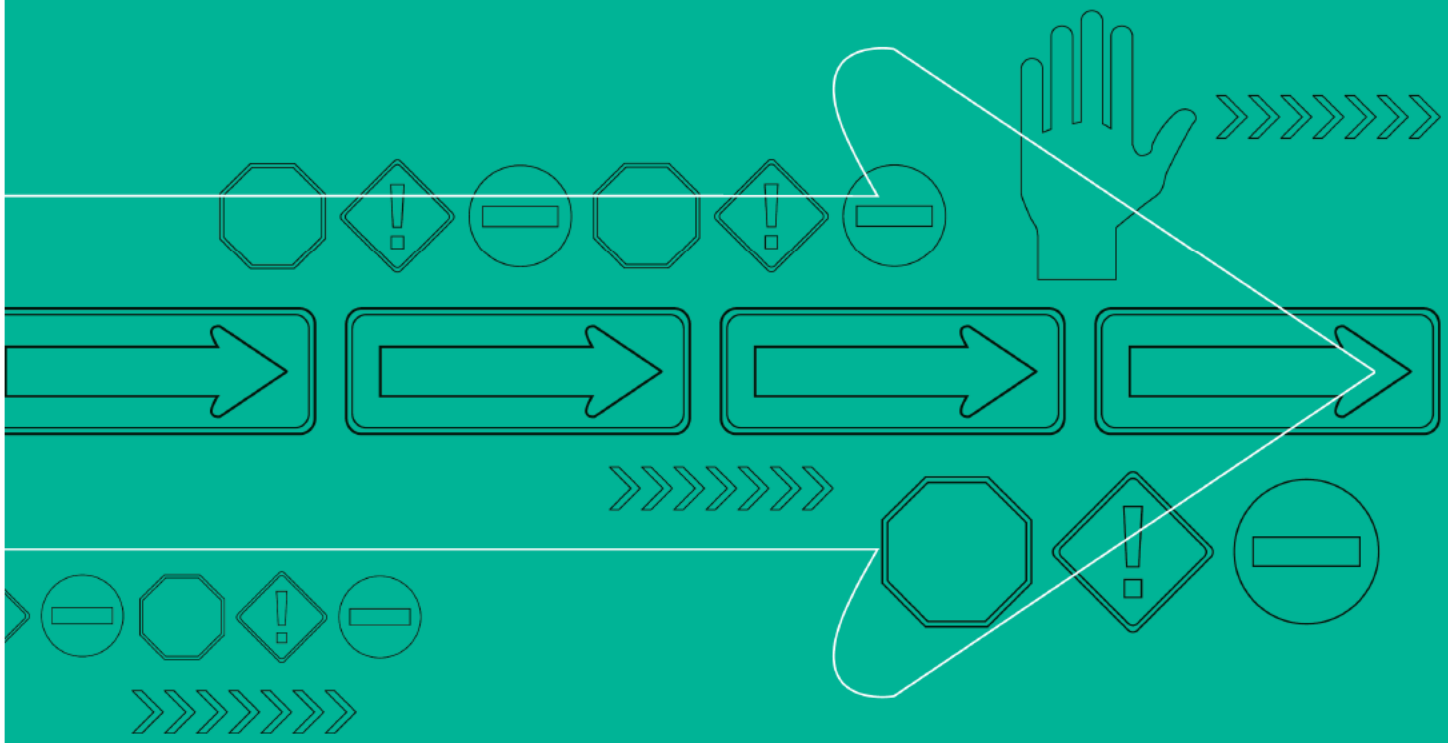
EACH MONTH DURING THERAPY

- **See** your doctor to get a prescription
- **Get** a prescription for a maximum 30-day supply
- **Do not** donate blood

AFTER TREATMENT

- **Do not** donate blood for 1 month after your last dose

*You can access the system via the web site, **www ipledgeprogram.com**, or the telephone, **1-866-495-0654**.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

 PRE_BOOK01 JUN10 (R-1 03/12)

Reference ID: 3122588

Most Recent Modification: April 2012

The iPLEDGE Program

Isotretinoin Educational Kit For Female Patients Who Can Get Pregnant

The Importance Of Avoiding Pregnancy On Isotretinoin

The tools you need to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

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CONTENTS

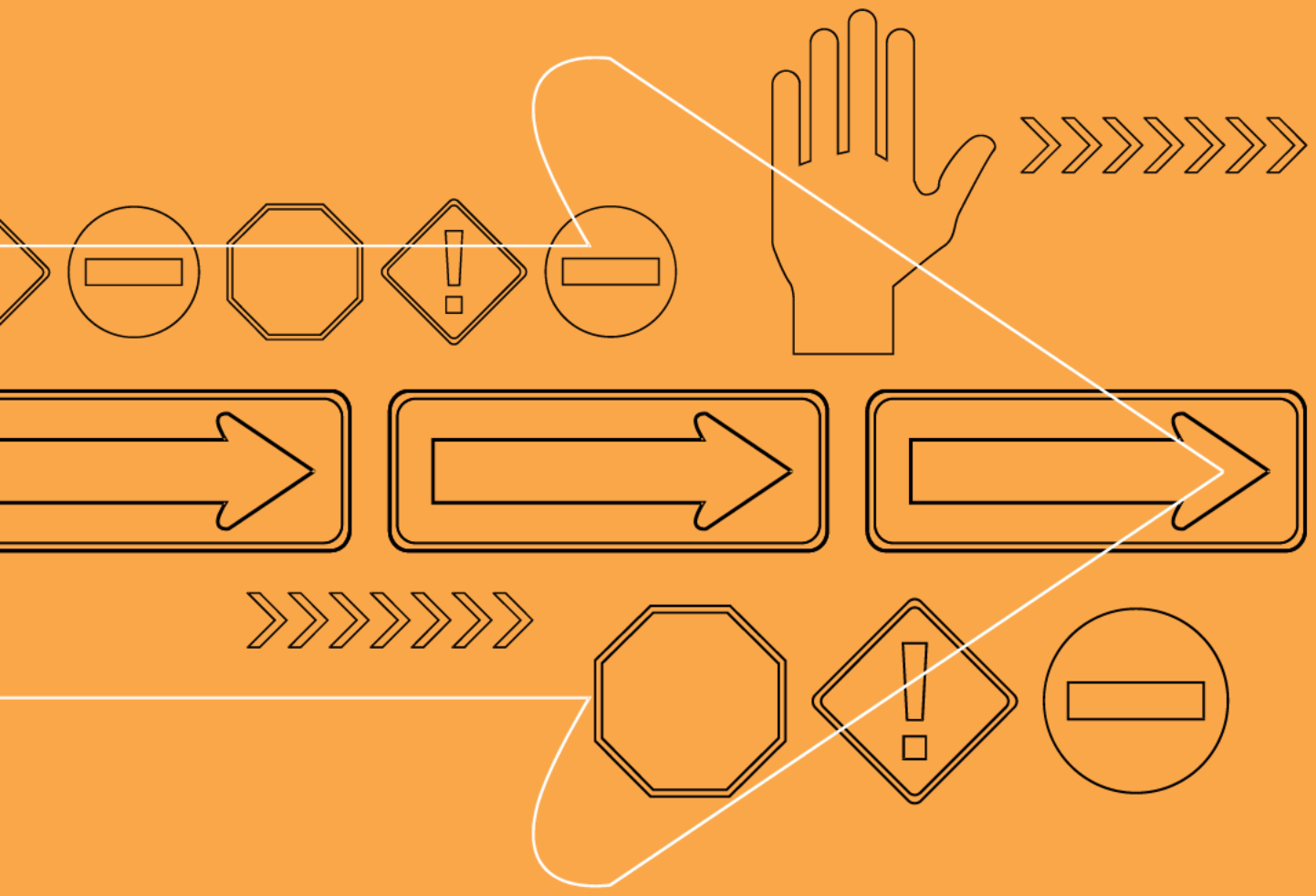
- Guide To Isotretinoin For Female Patients Who Can Get Pregnant
- Birth Control Workbook
- Contraception Referral Form And Contraception Counseling Guide
- Patient Identification Card
- Patient Information/Informed Consent (for all patients)
- Patient Information/Informed Consent About Birth Defects (for females who can get pregnant)
- Patient Flowchart

iPLEDGE™

Committed to Pregnancy Prevention

Reference ID: 3122588

Guide To Isotretinoin For Female Patients Who Can Get Pregnant



The guide to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

Reference ID: 3122588

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The iPLEDGE Program

Guide To Isotretinoin For Female Patients Who Can Get Pregnant

The Importance Of Avoiding Pregnancy On Isotretinoin

The resource to help you prepare, plan treatments, and prevent pregnancies during the course of isotretinoin treatment

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment. Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Guide To Isotretinoin For Female Patients Who Can Get Pregnant

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ABOUT ISOTRETINOIN

Isotretinoin (eye-soh-tret-in-OH-in) treats a type of severe acne called nodular acne that other treatments, including antibiotics, have not helped. It comes in a capsule you take by mouth. Treatment usually lasts 4 to 5 months.

Isotretinoin can cause serious side effects, including birth defects. There is a very high chance of birth defects if an unborn baby's mother takes isotretinoin. The goal of the iPLEDGE program is to prevent pregnancies in females taking isotretinoin and to prevent pregnant females from taking isotretinoin. The program involves a set of steps that you, your doctor, and your pharmacist must follow for you to take isotretinoin.

Before starting isotretinoin, talk with your doctor about how isotretinoin can help your skin and about the side effects. Read this *iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant* and the other materials in this educational kit. Your doctor also has an educational DVD for you to watch.

Make sure you understand the requirements of the iPLEDGE program. Then, decide if isotretinoin is right for you.

ISOTRETINOIN AND BIRTH DEFECTS: FOR FEMALE PATIENTS WHO CAN GET PREGNANT

Here are 2 key messages of the iPLEDGE program:

Do NOT take isotretinoin if you are pregnant.

Do NOT get pregnant before starting isotretinoin, while taking it, and for 1 month after your last dose.

If you get pregnant while taking isotretinoin, there is a very high chance that your baby will be deformed, born too early, or die before being born. This can happen even if you only take isotretinoin for a short time.

Prevent Pregnancy And Birth Defects

Here are some key steps you must follow in the iPLEDGE program to take isotretinoin:

Have 2 negative pregnancy tests before you start isotretinoin.

Have a negative pregnancy test before you fill and pick up each monthly prescription.

Use 2 forms of birth control together.

You must use 2 forms of birth control together correctly all the time for 1 month before you start isotretinoin, while you are taking isotretinoin, and for 1 month after your last dose. These forms of birth control must be effective in the iPLEDGE program.

Any form of birth control can fail. Using 2 forms of birth control together all the time drastically reduces the chance that you will get pregnant.

Your doctor will talk with you about birth control or refer you to a gynecologist, a family doctor, or a birth control expert for counseling.

Reasons you would not have to use 2 forms of birth control

There are 2 reasons you would not have to use 2 effective forms of birth control.

- You commit to not having any heterosexual sexual intercourse with a male for 1 month before, during, and for 1 month after your isotretinoin treatment (abstinence).
- You are unable to get pregnant because:
  - You have entered menopause, and your doctor has confirmed this.
  - You have had both of your ovaries or uterus taken out by surgery, and your doctor has confirmed this.

If you have any questions about being able to get pregnant, talk with your doctor.

Do Not Donate Blood

Isotretinoin is carried in your blood. There may be enough isotretinoin in your bloodstream to cause birth defects if a pregnant woman receives blood that you donated. You should not donate blood at any time while you are taking isotretinoin or for 1 month after your last dose.

Do Not Share Isotretinoin With Anyone

You should never share medications prescribed to you with anyone else. This is very important for isotretinoin because of the very high chance of birth defects.

See the *Safety Information* section on page 14 for more detailed information about other serious side effects, precautions, and warnings for isotretinoin.

THE iPLEDGE WEB SITE AND PHONE SYSTEM

The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant and your patient educational kit are resources for the information you need about isotretinoin and the iPLEDGE program. The iPLEDGE program also has a web site and an automated phone system.

- Web site: **www.ipledgeprogram.com**
- Phone system: **1-866-495-0654**

The information on the phone system is available in English and Spanish. You can get general information about isotretinoin and the iPLEDGE program right away. When you start taking isotretinoin, your doctor will give you a patient ID number and ID card, and other program materials. You use these to log in to the system. *(see page 9)* You will use the system to meet some of the monthly requirements of the program.

After you have been registered in iPLEDGE by your doctor, you will receive your iPLEDGE password in the mail in 5 to 10 business days. Follow the instructions that come with the password to access the iPLEDGE system.

KEY INFORMATION FOR PATIENTS

The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant explains the key information about the iPLEDGE program before, during, and after your isotretinoin treatment. Here is a general overview:

1. Learn about the iPLEDGE program and the isotretinoin side effects and risks in pregnancy.
2. Sign the Patient Information/Informed Consent forms.
3. Plan for treatment and for monthly appointments and pregnancy tests.
4. Choose 2 forms of effective birth control for the iPLEDGE program; use them all of the time.
5. Take blood or urine pregnancy tests.
6. Answer monthly educational questions to show you understand about the iPLEDGE program and about preventing pregnancy.
7. Follow requirements for pregnancy testing and follow-up after your last dose.
8. Do not donate blood during your treatment or for 1 month after your last dose.
9. Do not share isotretinoin.

This information and details of the program are described in the sections to follow. The section on page 6 reviews the forms of effective birth control in the iPLEDGE program.

You can always use the checklist on the next page as a quick reminder of the program information.

THE iPLEDGE PROGRAM CHECKLIST

All patients have a specific period of time in which they can fill and pick up their prescription. This is called the "prescription window" and its start and end dates depend on the type of patient.

Female patients who can get pregnant…

The prescription window is 7 days, and starts on the date that the urine or blood sample is taken for your pregnancy test. This date is counted as DAY 1.

To determine the end date of your 7-day prescription window, you should add 6 days to the date of the blood or urine sample being taken.

After 11:59 p m. Eastern Time on the last day of the 7-day prescription window, you can no longer fill and pick up your prescription, and must start the process over to get a new 7-day prescription window.

Before Starting Treatment

PLANNING

- ☐ **Plan** your course of treatment (about 4 to 5 months). (*see page 8*)
- ☐ **Talk** with your doctor about the iPLEDGE program.
- ☐ **Sign** the Patient Information/Informed Consent (for all patients) form.
- ☐ **Have** your first urine or blood pregnancy test, which can be performed at the doctor's office.
- ☐ **Get** your patient ID cards containing your patient ID number from your doctor. (*see page 8*)

BIRTH CONTROL (*see page 6*)

- ☐ **Read** *The iPLEDGE Program Birth Control Workbook.*
- ☐ **Talk** with your dermatologist, gynecologist, family doctor, or a birth control expert about effective birth control options.
- ☐ **Choose** 2 effective forms of birth control.
- ☐ **Start** using the 2 forms of birth control together for at least 1 month before you start isotretinoin.

YOUR FIRST PRESCRIPTION

- ☐ **Have** a second pregnancy test within the first 5 days of your menstrual period.
- ☐ **Sign** the Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form. (*see page 9*)
- ☐ **Answer** questions about the iPLEDGE program and confirm your 2 forms of birth control. (*see page 10*) **This cannot be completed until after your doctor has entered your pregnancy test result in the iPLEDGE System.**
- ☐ **Fill and Pick up** your prescription for up to a maximum of a 1-month supply. (*see page 11*)
- ☐ **Fill and Pick up** your prescription within the 7-day prescription window, counting the date of the pregnancy test as DAY 1. (*see page 12*)
  - If you are not able to fill and pick up your first prescription within the 7-day prescription window, you will be required to wait a minimum of 19 days before you can start this process again.
- ☐ **Use** 2 effective forms of birth control together all the time.
- ☐ **Keep** your appointments every month to get a prescription.
- ☐ **See** your doctor for a monthly pregnancy test.
- ☐ **Answer** different questions each month about the iPLEDGE program.

During Treatment

- ☐ **Use** 2 effective forms of birth control together all the time.
- ☐ **See** your doctor for a monthly pregnancy test.
- ☐ **Keep** your appointments every month to get a prescription.
- ☐ **Confirm** your 2 forms of birth control by entering them into the iPLEDGE System. (*see page 10*)
- ☐ **Answer** different questions each month about the iPLEDGE program. **This cannot be completed until after your doctor has entered your pregnancy test result in the iPLEDGE System.**
- ☐ **Fill and Pick up** your prescription for up to a maximum of a 30-day supply. *(see page 11)*
- ☐ **Fill and Pick up** your prescription within the 7-day prescription window counting the day of the pregnancy test as DAY 1. (*see page 12*)
  - If you do not fill and pick up your prescription within the 7-day prescription window, you will need to go back to your doctor to start this process again.
- ☐ **Do not donate** blood.

After Treatment

RIGHT AFTER YOUR LAST DOSE (*see page 13*)

- ☐ **Get** a pregnancy test after your last dose.
- ☐ **Continue** using your birth control for 1 month.
- ☐ **Do not donate** blood for 1 month after your last dose.
- ☐ **Ensure** that your doctor has entered the results of this pregnancy test into the iPLEDGE System.

1 MONTH AFTER YOUR LAST DOSE

- ☐ **Have** a final pregnancy test at 1 month after your last dose.
- ☐ **Ensure** that your doctor has entered the results of this pregnancy test into the iPLEDGE System.

EFFECTIVE FORMS OF BIRTH CONTROL

Not all forms of birth control are acceptable while you are taking isotretinoin. Choosing birth control is a very personal decision. It helps to get all the information you need and then talk with your doctor to help you decide what to do.

Read The iPLEDGE Program Birth Control Workbook

To find out what birth control is effective for the iPLEDGE program, read *The iPLEDGE Program Birth Control Workbook*. Discuss this information with someone you trust. Discuss it with your partner. Think about what forms of birth control you would really use, and then talk with your doctor or a birth control expert.

Talk With An Expert

If you want to talk to a birth control expert, your gynecologist, or family doctor about birth control, the doctor who prescribes isotretinoin for you can refer you. The makers of isotretinoin will pay for a visit for you to talk about birth control. *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide* is in this booklet.

- Make an appointment with a birth control expert, your gynecologist, or family doctor.
- Take *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide* with you. It has important information that the birth control expert, gynecologist, or family doctor needs to talk about, including the forms of effective birth control for the iPLEDGE program.
- The healthcare professional providing contraception counseling will fill out the Contraception Referral Form included in the guide after he/she talks with you and then mail or fax it back to the doctor who prescribes your isotretinoin.

Changing Your Birth Control

If you need to change forms of birth control during your isotretinoin treatment, you need to tell the doctor who prescribes your isotretinoin. You do not want to take isotretinoin if you are not protected against pregnancy all the time.

You may have to stop having sex until your new form of birth control is working. You may have to stop isotretinoin and wait until you have been on the new form for at least 1 month and have a negative pregnancy test.

Changing From Abstinence

If you have been abstinent (not having any sexual activity) and you decide to start having sexual activity, you must tell the doctor who prescribes your isotretinoin. You and your doctor must make a plan to start birth control and be sure you are not pregnant before you continue isotretinoin.

One of the most common reasons that women get pregnant is that they do not avoid sexual activity when they plan to be abstinent.

DVD: *Be Prepared, Be Protected, And Be Aware: The Risk Of Pregnancy While On Isotretinoin*

Your doctor has a DVD that shows the kinds of birth defects that may happen if a woman takes any amount of isotretinoin while she is pregnant. It also reviews the steps for preventing pregnancy.

THE iPLEDGE PROGRAM CHECKLIST INFORMATION

Plan Your Course Of Treatment

Pregnancy tests

To start isotretinoin, you need to have 2 negative pregnancy tests. They can be urine or blood tests. You will need to plan with your doctor when and where to take your pregnancy tests.

- You take the first test when you decide to take isotretinoin.
- You take the second test in an approved lab during the first 5 days of the menstrual period right before you start isotretinoin. The interval between the two tests must be at least 19 days. You must use 2 effective forms of birth control together all the time for at least 1 month before you can take this second test.

You also take a pregnancy test in an approved lab during treatment. You take a pregnancy test each month, during treatment, after your last dose, and 1 month after your last dose. You will need to plan with your doctor when to take your pregnancy test each month.

Prescriptions

The most isotretinoin you can get at any one time is up to a maximum of a 30-day supply. You will need to see your doctor each month to get a new prescription, and meet the monthly program requirements.

Get Your Patient ID Number And Cards

Your doctor will give you your patient ID number and cards when you start the iPLEDGE program. The ID cards are included in the back of this booklet. Tear out one card and keep it in a safe place. You can use the other cards in the booklet if you lose your card. It is important not to lose these cards. Write your number down as soon as you receive it and keep it where you will be able to find it.

You need your ID number and card:

- When you take your prescription to be filled at the pharmacy
- When you log in to the iPLEDGE program automated system, either the web site, **www.ipledgeprogram.com**, or automated phone line, **1-866-495-0654**

About The iPLEDGE Automated System

The first time you login to iPLEDGE (either the web site or phone line) you will be asked to select a personal password and select a Date of Personal Significance. The selection of a personal password is a security feature that ensures that only you will know your password. A Date of Personal Significance is collected by the system to be used in verifying your identity should you require assistance from the iPLEDGE Call Center while using iPLEDGE.

Both your password and your Date of Personal Significance should be something that you will find easy to remember.

You can access the system to:

- Find a pharmacy where you can fill and pick up your prescription
- Change to a new doctor
- Get information about isotretinoin
- Answer your Comprehension Questions, required before you can fill and pick up your prescription
- View information about your current status, your 7-day prescription window, and next steps required in the program
- View FAQ's (Frequently Asked Questions)

If you lose your patient ID cards, and cannot remember your patient ID number, contact your doctor.

Informed Consents

You sign 2 consent forms to be in the iPLEDGE program.

1. **Patient Information/Informed Consent (for all patients)**

Signing the Patient Information/Informed Consent (for all patients) form means you understand that there are risks with isotretinoin.

2. **Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)**

Your doctor will talk to you about the risks of isotretinoin during pregnancy. You must also get this information in writing. You must understand that a baby exposed to isotretinoin could have severe birth defects. Signing the consent form means the following:

- You understand the risks of isotretinoin for unborn babies.
- You agree to use 2 effective forms of birth control, as the iPLEDGE program requires. *The iPLEDGE Program Birth Control Workbook* has the list of effective forms.

The iPLEDGE Program Pregnancy Registry

Because isotretinoin causes such severe birth defects, it is very important for us to know about all the pregnancies that happen during treatment and within 1 month after the last dose. The confidential iPLEDGE Program Pregnancy Registry is a way to collect that information. It may help us prevent more pregnancies in the future.

Your doctor will tell you about the confidential iPLEDGE Program Pregnancy Registry. You are encouraged to contact the iPLEDGE Program Pregnancy Registry, if you get pregnant.

Answering Questions About The iPLEDGE Program And Preventing Pregnancy

The iPLEDGE Program requires you to answer comprehension questions before picking up every prescription. These questions will demonstrate your understanding of the iPLEDGE program requirements, the birth control that you have chosen and the risks associated with isotretinoin. **You will not be able to answer your questions until your doctor has entered your pregnancy test result in the iPLEDGE System.** You may not fill and pick up your prescription until you have correctly answered the questions. You may use your iPLEDGE educational kit as a resource as you answer the questions.

Your First Month Taking Isotretinoin

The first month that you answer your questions, you will be asked a series of questions about iPLEDGE information and counseling provided to you. There are no wrong answers to these questions. The answers are used to determine how often the iPLEDGE materials are shared with patients.

Birth Control Verification

You must enter the 2 forms of birth control you are using. Your doctor will also separately enter the 2 forms of birth control you told him or her you are using. This information must be in the iPLEDGE system and must match for you to fill and pick up your prescription.

Comprehension Questions

Before each prescription can be filled and picked up at the Pharmacy, you will have different questions about the iPLEDGE program and preventing pregnancy to answer. You answer the questions in the iPLEDGE program system using the web site, **www.ipledgeprogram.com**, or automated phone line, **1-866-495-0654** within the 7-day prescription window.

You can use *The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant* and *The iPLEDGE Program Birth Control Workbook* to help you with the answers.

You need your patient ID number and password to log in to the iPLEDGE system.

To answer questions on the iPLEDGE web site:

1. Log in
2. Click on the button under "Answer the Questions"
3. Enter the 2 forms of birth control you are using
4. Follow the prompts to answer the questions

To answer the questions on the iPLEDGE phone system:

1. Log in
2. Select the option to "Demonstrate Your Program Knowledge"
3. Follow the prompts to enter the 2 forms of birth control you are using
4. Follow the prompts to answer the questions

The system will let you know if you answered correctly. If you missed any questions, you will get to try other questions like the ones you missed. You must answer the questions correctly before you will be able to fill and pick up your prescription.

If you miss a question again, the system will tell you where to look in *The iPLEDGE Program Guide To Isotretinoin For Female Patients Who Can Get Pregnant* or *The iPLEDGE Program Birth Control Workbook* to find answers. You can answer the questions again later. You may also talk with your doctor about questions you missed.

Fill And Pick Up Your Prescription

Fill and pick up your isotretinoin prescriptions only at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

The web site, **www.ipledgeprogram.com**, has a list of registered and activated pharmacies. Log in and choose "Finding a Participating Pharmacy" on the Patient home page.

The pharmacist will contact the iPLEDGE system before filling the prescription. The system tells your pharmacist if you can get isotretinoin. It will not tell the pharmacist any personal information about you.

You can only fill and pick up your prescription for isotretinoin if:

- Your pregnancy test was negative
- Your doctor entered your 2 forms of birth control in the iPLEDGE system

- You answered your questions correctly. **This can only be done after your doctor has entered your pregnancy test result in the iPLEDGE System.**
- You also entered your 2 forms of birth control

You **fill** the prescription ***and*** **pick it up** within the 7-day prescription window (1 week) of the date of your pregnancy test, counting the date of the pregnancy test as DAY 1.

To figure out the last date you can pick up your prescription, add 6 to the date of your pregnancy test. For example:

Day 1 Day of the pregnancy test	Day 2–Day 6	Day 7 – Last day to fill and pick up prescription
(Friday, March 1)	(Saturday–Wednesday)	(Thursday, March 7)

The 7-day prescription window expires at 11:59 p m. Eastern Time on Day 7 of the prescription window. Your pharmacist will not be able to fill your prescription after this time. If your 7-day prescription window expires before you fill and pick up your prescription, you can start a new 7-day prescription window right away (unless it is your first prescription window), but you must repeat the program requirements to get another prescription. Additional information regarding the specific dates of your 7-day prescription window, and other information about your current status can be found by selecting "My Program Status" on the website from the Patient home page (after you log in).

Note: Isotretinoin comes in blister packs of 10 capsules. The pharmacist cannot break a blister pack.

A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com.

After Your Last Dose

It is very important that you:

- Get a pregnancy test.
- Keep using 2 effective forms of birth control together all the time for 1 month after your last dose. It takes time for isotretinoin to leave your bloodstream.
- Go back to your doctor 1 month after your last dose for your last pregnancy test, even if you think you are not pregnant. If you miss this appointment, you will receive a reminder notification.
- Do not give blood for 1 month after your last dose.
- If your doctor does not enter the results of the pregnancy test after your last dose, and does not enter the pregnancy test 1 month after your last dose, both you and your doctor will be contacted for additional information.

Changing To A New Doctor

You can change your doctor (Primary Prescriber) in the iPLEDGE system. Once you make the change, you will not be able to get any more prescriptions from your original doctor.

You can change your doctor through the iPLEDGE web site, **www.ipledgeprogram.com**, or automated phone line, **1-866-495-0654**. You need your patient ID number to log in to the system.

To change your doctor on the iPLEDGE web site:

1. Log in
2. Choose "Change Primary Prescriber" from the menu
3. You need to enter the following information about your new doctor:
   - First and last name
   - City
   - Phone number

To change your doctor on the automated phone line:

1. Log in
2. Select the Option for "More Choices"
3. Select the Option to "Change Your Prescriber"
4. Follow the prompts to enter the new information

The system will tell you if you have made the change correctly. The new doctor must accept you as a patient within the iPLEDGE system before being able to give you a prescription.

Safety Information

ABOUT ISOTRETINOIN

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT ISOTRETINOIN?

- Isotretinoin is used to treat a type of severe acne (nodular acne) that has not been helped by other treatments, including antibiotics.
- Because isotretinoin can cause birth defects, isotretinoin is only for patients who can understand and agree to carry out all of the instructions in the iPLEDGE program.
- Isotretinoin may cause serious mental health problems.

1. **Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** Female patients who are pregnant or who plan to become pregnant must not take isotretinoin.
Female patients must not get pregnant:
   - For 1 month before starting isotretinoin
   - While taking isotretinoin
   - For 1 month after stopping isotretinoin

If you get pregnant while taking isotretinoin, stop taking it right away and call your doctor. Doctors and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The iPLEDGE Program Pregnancy Registry at 1-866-495-0654

2. **Serious mental health problems.** Isotretinoin may cause:
   - **Depression**
   - **Psychosis** (seeing or hearing things that are not real)
   - **Suicide**
   Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

After stopping isotretinoin, you may also need follow-up mental health care if you had any of these symptoms.

What Is Isotretinoin?

Isotretinoin is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments, including antibiotics. Isotretinoin can cause serious side effects. (See **"What is the most important information I should know about isotretinoin?"**) Isotretinoin can only be:

- Prescribed by doctors that are registered in the iPLEDGE program
- Dispensed by a pharmacy that is registered with the iPLEDGE program
- Given to patients who are registered in the iPLEDGE program and agree to do everything required in the program

What Is Severe Nodular Acne?

Severe nodular acne is when many red, swollen, tender lumps form in the skin. These can be the size of pencil erasers or larger. If untreated, nodular acne can lead to permanent scars.

Who Should Not Take Isotretinoin?

- **Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment.** Isotretinoin causes severe birth defects. (See "**What is the most important information I should know about isotretinoin?**")
- **Do not take isotretinoin if you are allergic to anything in it.**

What Should I Tell My Doctor Before Taking Isotretinoin?

Tell your doctor if you or a family member has any of the following health conditions:

- Mental problems
- Asthma
- Liver disease
- Diabetes
- Heart disease
- Bone loss (osteoporosis) or weak bones
- An eating problem called anorexia nervosa (where people eat too little)
- Food or medicine allergies

Tell your doctor if you are pregnant or breastfeeding. Isotretinoin must not be used by women who are pregnant or breastfeeding.

Tell your doctor about all of the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Isotretinoin and certain other medicines can interact with each other, sometimes causing serious side effects. Especially tell your doctor if you take:

- **Vitamin A supplements.** Vitamin A in high doses has many of the same side effects as isotretinoin. Taking both together may increase your chance of getting side effects.
- **Tetracycline antibiotics.** Tetracycline antibiotics taken with isotretinoin can increase the chances of getting increased pressure in the brain.
- **Progestin-only birth control pills (mini-pills).** They may not work while you take isotretinoin. Ask your doctor or pharmacist if you are not sure what type you are using.
- **Dilantin (phenytoin).** This medicine taken with isotretinoin may weaken your bones.
- **Corticosteroid medicines.** These medicines taken with isotretinoin may weaken your bones.
- **St. John's Wort.** This herbal supplement may make birth control pills work less effectively.

These medicines should not be used with isotretinoin unless your doctor tells you it is okay.

Know the medicines you take. Keep a list of them to show to your doctor and pharmacist. Do not take any new medicine without talking with your doctor.

How Should I Take Isotretinoin?

You must take isotretinoin exactly as prescribed. You must also follow all the instructions of the iPLEDGE program. Before prescribing isotretinoin, your doctor will:

- Explain the iPLEDGE program to you.
- Have you sign the Patient Information/Informed Consent (for all patients). Female patients who can get pregnant must also sign another consent form.

You will not be prescribed isotretinoin if you cannot agree to or follow all the instructions of the iPLEDGE program.

- You will get no more than a 30-day supply of isotretinoin at a time. This is to make sure you are following the isotretinoin iPLEDGE program. You should talk with your doctor each month about side effects.
- The amount of isotretinoin you take has been specially chosen for you. It is based on your body weight, and may change during treatment.
- Take isotretinoin 2 times a day with a meal, unless your doctor tells you otherwise. **Swallow your isotretinoin capsules whole with a full glass of liquid. Do not chew or suck on the capsule.** Isotretinoin can hurt the tube that connects your mouth to your stomach (esophagus) if it is not swallowed whole.
- If you miss a dose, just skip that dose. Do **not** take 2 doses at the same time.
- If you take too much isotretinoin or overdose, call your doctor or poison control center right away.
- Your acne may get worse when you first start taking isotretinoin. This should last only a short while. Talk with your doctor if this is a problem for you.
- You must return to your doctor as directed to make sure you don't have signs of serious side effects. Your doctor may do blood tests to check for serious side effects from isotretinoin. Female patients who can get pregnant will get a pregnancy test each month.
- Female patients who can get pregnant must agree to use 2 separate forms of effective birth control at the same time 1 month before, while taking, and for 1 month after taking isotretinoin. **You must access the iPLEDGE system to answer questions about the program requirements and to enter your 2 chosen forms of birth control.** To access the iPLEDGE system, go to **www ipledgeprogram.com** or call **1-866-495-0654**.

You must talk about effective birth control methods with your doctor or go for a free visit to talk about birth control with another doctor or family planning expert. Your doctor can arrange this *free* visit, which will be paid for by the company that makes isotretinoin.

If you have sex at any time without using 2 forms of effective birth control, get pregnant, or miss your expected period, stop using isotretinoin and call your doctor right away.

What Should I Avoid While Taking Isotretinoin?

- **Do not get pregnant** while taking isotretinoin and for 1 month after stopping isotretinoin. (See **"What is the most important information I should know about isotretinoin?"**)
- **Do not breastfeed** while taking isotretinoin and for 1 month after stopping isotretinoin. We do not know if isotretinoin can pass through your milk and harm the baby.
- **Do not give blood** while you take isotretinoin and for 1 month after stopping isotretinoin. If someone who is pregnant gets your donated blood, her baby may be exposed to isotretinoin and may be born with birth defects.
- **Do not take other medicines or herbal products** with isotretinoin unless you talk to your doctor. (See **"What should I tell my doctor before taking isotretinoin?"**)
- **Do not drive at night until you know if isotretinoin has affected your vision.** Isotretinoin may decrease your ability to see in the dark.
- **Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using isotretinoin and for at least 6 months after you stop.** Isotretinoin can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.
- **Avoid sunlight and ultraviolet lights** as much as possible. Tanning machines use ultraviolet lights. Isotretinoin may make your skin more sensitive to light.
- **Do not share isotretinoin with other people.** It can cause birth defects and other serious health problems.

What Are The Possible Side Effects Of Isotretinoin?

- **Isotretinoin can cause birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby, and early (premature) births.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Isotretinoin may cause serious mental health problems.** (See **"What is the most important information I should know about isotretinoin?"**)
- **Serious brain problems.** Isotretinoin can increase the pressure in your brain. This can lead to permanent loss of eyesight and, in rare cases, death. Stop taking isotretinoin and call your doctor right away if you get any of these signs of increased brain pressure:
  - Bad headache
  - Blurred vision
  - Dizziness
  - Nausea or vomiting
  - Seizures (convulsions)
  - Stroke
- **Skin problems.** Skin rash can occur in patients taking isotretinoin. In some patients a rash can be serious. Stop using isotretinoin and call your doctor right away if you develop conjunctivitis (red or inflamed eyes, like "pink eye"), a rash with fever, blisters on legs, arms or face and/or sores in your mouth, throat, nose, eyes, or if your skin begins to peel.
- **Stomach area (abdomen) problems.** Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus (connection between mouth and stomach). If your organs are damaged, they may not get better even after you stop taking isotretinoin. Stop taking isotretinoin and call your doctor if you get:
  - Severe stomach, chest, or bowel pain
  - Trouble swallowing or painful swallowing
  - New or worsening heartburn
  - Diarrhea
  - Rectal bleeding
  - Yellowing of your skin or eyes
  - Dark urine
- **Bone and muscle problems.** Isotretinoin may affect bones, muscles, and ligaments and cause pain in your joints or muscles. Tell your doctor if you plan hard physical activity during treatment with isotretinoin. Tell your doctor if you get:
  - Back pain
  - Joint pain
  - A broken bone. Tell all healthcare providers that you take isotretinoin if you break a bone.

Stop isotretinoin and call your doctor right away if you have muscle weakness. Muscle weakness with or without pain can be a sign of serious muscle damage.

Isotretinoin may stop long bone growth in teenagers who are still growing.

- **Hearing problems.** Stop using isotretinoin and call your doctor if your hearing gets worse or if you have ringing in your ears. Your hearing loss may be permanent.
- **Vision problems.** Isotretinoin may affect your ability to see in the dark. This condition usually clears up after you stop taking isotretinoin, but it may be permanent. Other serious eye effects can occur. Stop taking isotretinoin and call your doctor right away if you have any problems with your vision or dryness of the eyes that is painful or constant. If you wear contact lenses, you may have trouble wearing them while taking isotretinoin and after treatment.
- **Lipid (fats and cholesterol in blood) problems.** Isotretinoin can raise the level of fats and cholesterol in your blood. This can be a serious problem. Return to your doctor for blood tests to check your lipids and to get any needed treatment. These problems usually go away when isotretinoin treatment is finished.
- **Serious allergic reactions.** Stop taking isotretinoin and get emergency care right away if you develop hives, a swollen face or mouth, or have trouble breathing. Stop taking isotretinoin and call your doctor if you get a fever, rash, or red patches or bruises on your legs.
- **Blood sugar problems.** Isotretinoin may cause blood sugar problems including diabetes. Tell your doctor if you are very thirsty or urinate a lot.
- **Decreased red and white blood cells.** Call your doctor if you have trouble breathing, faint, or feel weak.
- **The common, less serious side effects of isotretinoin** are dry skin, chapped lips, dry eyes, and dry nose that may lead to nosebleeds. Call your doctor if you get any side effect that bothers you or that does not go away.

These are not all of the possible side effects with isotretinoin. Your doctor or pharmacist can give you more detailed information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How Should I Store Isotretinoin?

- Store isotretinoin at room temperature. Protect from light.
- **Keep isotretinoin and all medicines out of the reach of children**.

General Information About Isotretinoin

Do not use isotretinoin for a condition for which it was not prescribed. Do not give isotretinoin to other people, even if they have the same symptoms that you have. It may harm them.

This safety section summarizes the most important information about isotretinoin. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about isotretinoin that is written for health care professionals. You can also call iPLEDGE program at **1-866-495-0654** or visit **www ipledgeprogram.com**.

For More Information About Isotretinoin And The iPLEDGE Program

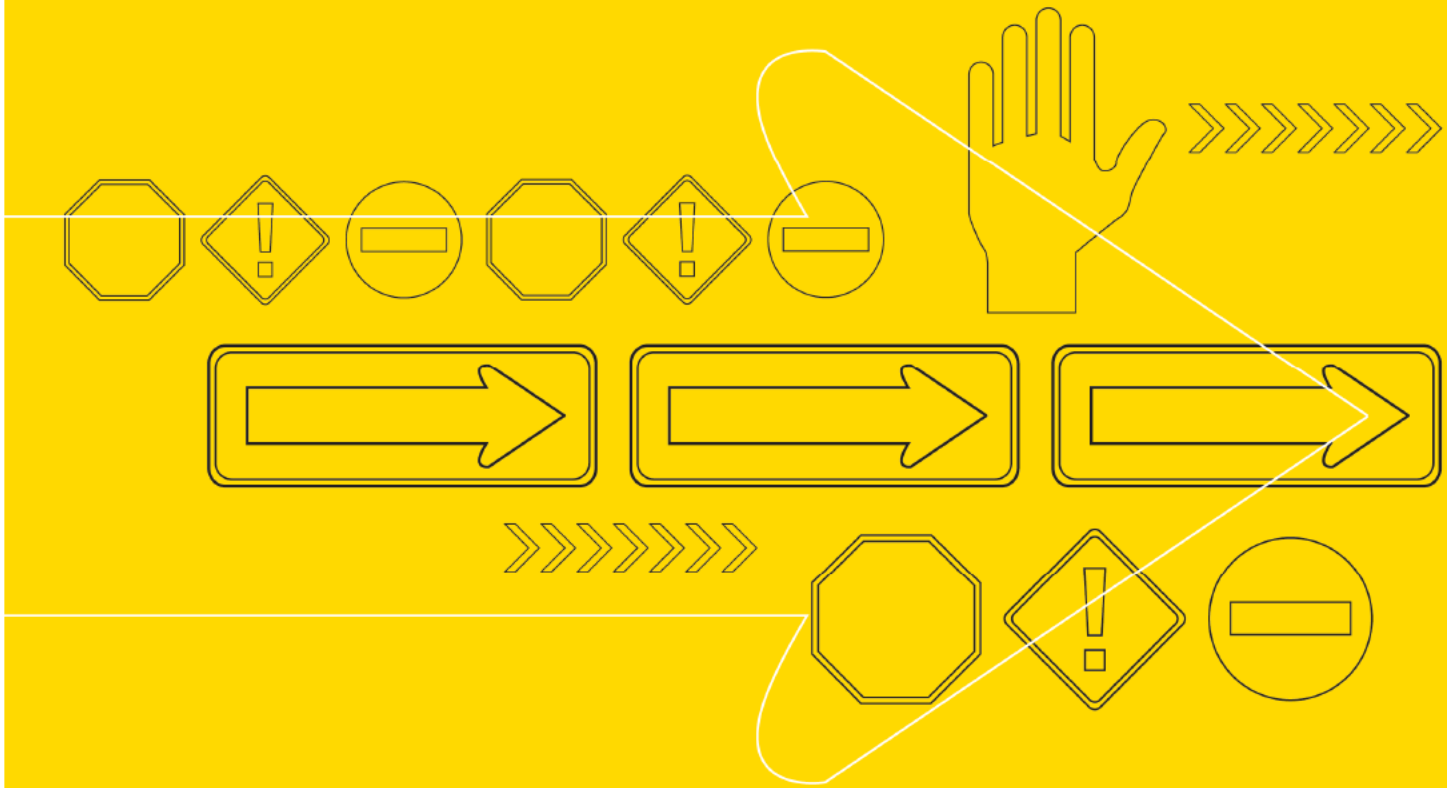
If you have questions about the iPLEDGE program, ask your doctor, visit the iPLEDGE program web site at **www.ipledgeprogram.com**, or call the automated phone line at **1-866-495-0654**.

For private birth control information, you can reach the iPLEDGE automated phone line 24 hours a day, 7 days a week at 1-866-495-0654. You can learn about different subjects, including:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

Isotretinoin Products

To get information about specific brands of isotretinoin, the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

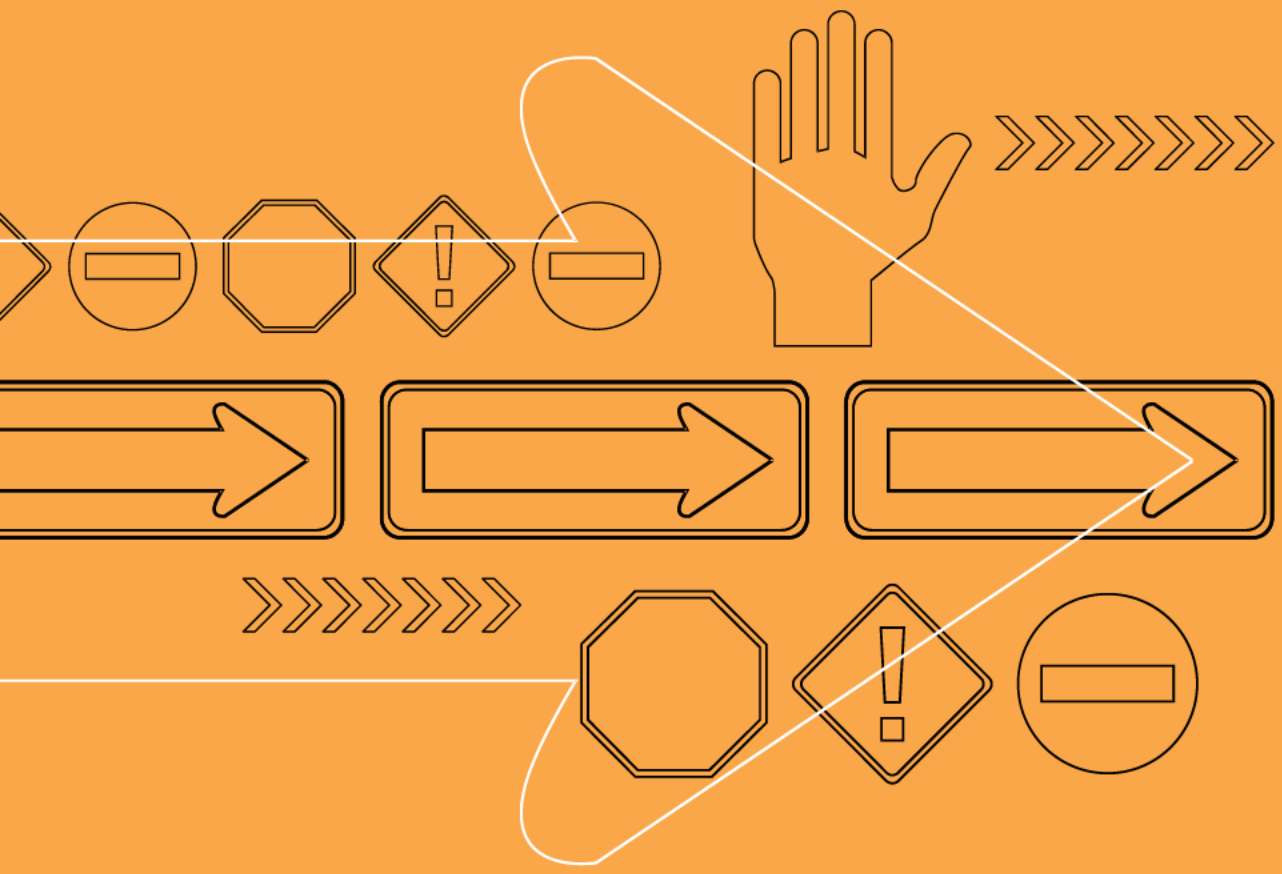
Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

 (R-1 03/12)

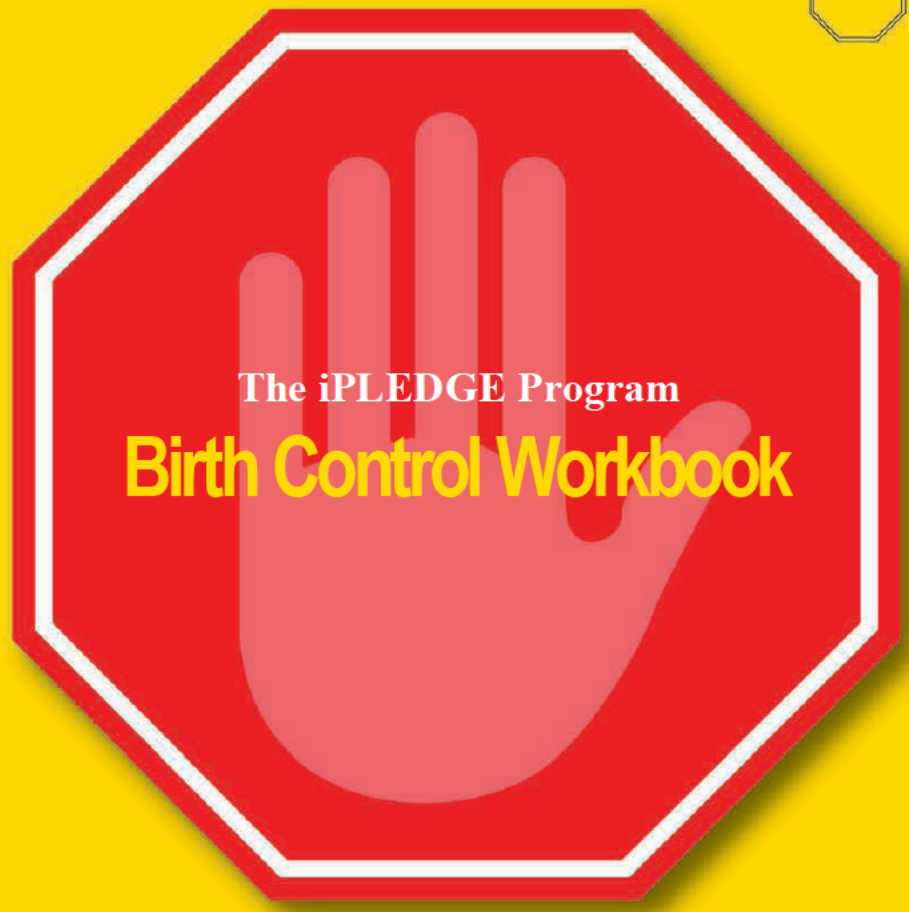
Birth Control Workbook



The guide to help you decide which forms of birth control are best for you

Reference ID: 3122588

Most Recent Modification: April 2012



The iPLEDGE Program

Birth Control Workbook

The guide to help you decide which forms of birth control are best for you during treatment with isotretinoin

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

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iPLEDGE™

Committed to Pregnancy Prevention

The iPLEDGE Program Birth Control Workbook

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PREVENTING PREGNANCIES

Not all forms of birth control are effective while you are taking isotretinoin. Choosing birth control is a very personal decision. It helps to get all the information you need and then talk with your doctor to help you decide what to do.

Read This Birth Control Workbook

To find out what birth control is effective for the iPLEDGE program, read this *iPLEDGE Program Birth Control Workbook*. Read it before you make any decisions about birth control. Read it even if you are already using birth control. Read it even if you think you will not have sex with a male for your whole isotretinoin treatment.

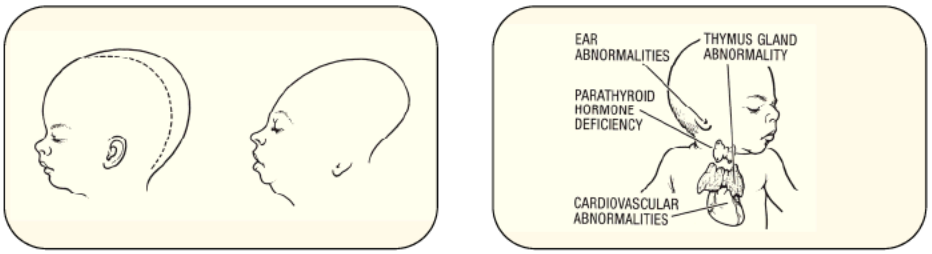
After you have read through the booklet, talk it over with someone you trust. Think about what kinds of birth control you would really use. Then talk with your doctor or a birth control expert.

Share this workbook with your partner. Talk with your partner about birth defects and isotretinoin. Explain what you both need to do to prevent pregnancy. Tell him you need to prevent pregnancy for at least 1 month before you start isotretinoin, during your treatment, and for 1 month after your last dose. This can be several months.

Write down a list of questions for your dermatologist, gynecologist, or family doctor. No question is too silly. Make sure you know how to use the birth control forms you choose.

WHY SHOULD I USE THIS WORKBOOK?

You are getting ready to start isotretinoin (eye-soh-tret-in-OH-in). It treats severe acne, but it can also cause birth defects. You must not get pregnant right before starting isotretinoin, while taking it, and for 1 month after your last dose. **There is a very high chance that your baby could be deformed, born too early, or die.** This can happen even if you take isotretinoin for only a short time.



The pictures show some of the birth defects your baby can have. Your baby's head could be deformed; the ears could be an odd shape or even missing. The eyes could be too far apart, the bridge of the nose too low, or the chin smaller than normal. The baby could have mental retardation or severe problems in the glands, heart, and brain.

You do not want to be pregnant or get pregnant right before starting isotretinoin, while taking it, and for 1 month after your last dose.

To keep from getting pregnant, you need to use 2 effective forms of birth control together correctly all the time:

- For at least 1 month before you start isotretinoin
- While you take it—treatment usually lasts 4 to 5 months
- For 1 month after your last dose—you still need protection against pregnancy

This workbook is for ALL female patients who can possibly get pregnant. This means that:

- You are physically able to get pregnant
- You have a uterus and ovaries
- You have menstrual periods

Even if you are not having sex, you still need to follow the requirements of the iPLEDGE program.

Female Patients Who Cannot Get Pregnant

Female patients who cannot get pregnant are not required to be on birth control. This applies to you if:

- You have entered menopause, and your doctor has confirmed this.
- You have had your ovaries or uterus taken out by surgery, and your doctor has confirmed this.

If you have any questions about being able to get pregnant, talk with your doctor.

HOW SHOULD I USE THIS WORKBOOK?

Use this workbook as a guide to help you decide which 2 effective birth control forms are best for you during your treatment. You will want to pick a birth control form that works for you and gives you the best protection against pregnancy (primary form). Since all forms of birth control can fail, you must also pick a second form (another primary form or a secondary form) that you use every time you have sex.

This workbook also provides information about abstinence, emergency birth control, and issues around conception and pregnancy.

THE iPLEDGE PROGRAM AND BIRTH CONTROL

Referral for birth control counseling

Before beginning treatment, you or the doctor may choose a referral to a birth control expert. The makers of isotretinoin will pay for 1 visit for birth control counseling. The patient educational kit contains *The iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide*. The referral form is in the booklet; the guide outlines the birth control requirements and the effective forms of birth control of the iPLEDGE program for the birth control expert. The referral form should be taken with you to the birth control counselor.

Why Do I Have To Use 2 Forms Of Birth Control Together?

- Any single birth control form can fail.
- Using 2 forms of birth control together all the time drastically reduces the chance that you will get pregnant.
- Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control!

Can I Use Any 2 Forms Of Birth Control?

No, you must choose from the iPLEDGE program list of effective birth control forms.

The 2 types of birth control you use for the iPLEDGE program are called **primary forms** and **secondary forms**.

- **Primary forms** do not fail very often. Be sure to choose a primary form that gives you the lowest chance of failure. This depends on such things as how well you remember to take medicine every day, whether you have had children or your partner has had a vasectomy, or you have medical problems.
- **Secondary forms** include **barrier forms** and **other forms** of birth control. The most important thing about a secondary form is using it every time you have sex.
  - **Barrier forms** keep sperm from entering the uterus. Barrier forms include the diaphragm and the cervical cap, both of which must be used with a cream that kills sperm, called a spermicide. The Male Latex Condom is also a Barrier form, and it can be used with or without spermicide.
  - **Other forms** (vaginal sponge) contain spermicide.

Preventing Pregnancy By Abstinence (Not Having Sex)

Abstinence means that you ***will not have sex*** or sexual contact with any male 24 hours a day, 7 days a week. This can be hard to do, especially if you are used to having sex.

It is easier not to have sex when it is a lifestyle choice, such as religious practice. One of the most common causes of unplanned pregnancy is not being able to avoid sex (failing to maintain abstinence).

If you cannot commit completely to not having sex (abstinence) while taking isotretinoin, you must use 2 separate, effective forms of birth control at the same time. The only exceptions are if you have had surgery to remove your uterus (a hysterectomy) or both of your ovaries (bilateral oophorectomy), or if your doctor has medically confirmed that you are post-menopausal. Isotretinoin is not recommended if you do not follow the birth control requirements of the iPLEDGE program.

Concerns About Birth Control Pills

Many female patients use birth control pills. But birth control pills can fail, and you can get pregnant. They fail because you forget to take them.

- If you take them every day, they are very effective birth control.
- If you miss pills and do not take them every day, your chance of getting pregnant is much higher with birth control pills than with other primary birth control forms, such as hormonal shots or an intrauterine device (IUD).

If you are taking birth control pills, do you remember to take them every day? If not you need to consider another primary form of birth control as you read this workbook.

The iPLEDGE Program Effective Birth Control Forms

Effective forms of contraception include both primary and secondary forms of contraception:

Primary forms	Secondary forms
• Tubal sterilization (tying your tubes) • Partner's vasectomy • Intrauterine device • Hormonal (combination birth control pills, skin patches, shots, under-the-skin implants, or vaginal ring)	*Barrier forms (always used with spermicide)* • Diaphragm • Cervical cap *Barrier form (used with or without spermicide)* • Male latex condom *Others:* • Vaginal sponge (contains spermicide)

You cannot use 2 hormonal forms together. Progesterone-only "mini-pills" are not effective for the iPLEDGE program.

Female condoms are not an effective secondary form for the iPLEDGE program.

Birth Control Forms That Are NOT Acceptable

You cannot use the following forms of birth control while you are taking isotretinoin. They do not give enough protection even when used with a second form of birth control.

- Birth control pills without estrogen (progesterone-only mini-pills)
  - Ortho Micronor® Tablets*
- IUD Progesterone T
- Female condoms
  - *A thin, loose-fitting, and flexible plastic tube that you put inside your vagina. It covers your cervix to block sperm.*
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
  - *This means not having sex during certain times of the month when you might be more likely to get pregnant. It does not work.*
- Withdrawal
  - *Your partner can leak enough sperm to get you pregnant even if he does not ejaculate inside you.*
- Cervical shield‡
  - *A silicone disc that sticks to your cervix to keep sperm out.*

Tell your doctor what type of birth control you are using. You will need to change to effective forms if your birth control is listed above. You must use 2 effective forms together all the time for at least 1 month and have a negative pregnancy test.

*Ortho Micronor is a registered trademark of Ortho-McNeil Pharmaceutical, Inc

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception See page 28

Ask yourself:

1. Which of the following is NOT one of the effective primary or secondary forms of birth control while taking isotretinoin?

   A) Partner's vasectomy or tubal sterilization (tying your tubes)

   B) Natural family planning

   C) LNg20 IUD

   D) Cervical cap with spermicide

2. Which of the following are effective forms of birth control for someone on isotretinoin?

   A) The hormonal skin patch and a male latex condom

   B) Cervical cap and a male latex condom

   C) Copper T380A IUD and withdrawal

   D) Birth control pills and a diaphragm with spermicide

Answer key: page 38

WHY DO I NEED HELP CHOOSING BIRTH CONTROL?

Not every birth control form is good for everyone. Some female patients should not use certain birth control, such as hormones or an IUD. If you are not good at remembering to take medicines, you should not choose birth control pills. Your dermatologist, gynecologist, or family doctor will help you choose the right forms for you. They will also give you exact instructions on how to use them.

Choose forms that you will actually use all the time. Some female patients have found it hard to use 2 forms of birth control together all the time. **This workbook will help you sort through these questions.** It will help you choose the 2 birth control forms that will be best for you. Here are some questions to think about.

Ask yourself:

- Have you ever used birth control? Did you think you will need to use birth control someday?
- What birth control are you using now? Do you like it and want to continue using it? Is it on the list of effective birth control for the iPLEDGE program?
- Are you currently having sex?
- Are you ever pressured into sex or think you may be forced to have sex?
- If you are taking birth control pills, do you ever forget to take them? Do you ever take them out of order? Do you always take medications the way you are told?
- Are there any forms of birth control you have heard about and would like to try?
- Can you rely on your partner's cooperation when using birth control, such as getting him to use a male latex condom each time you have sex?
- Are you worried about protecting yourself from STDs (sexually transmitted diseases) or HIV (AIDS)?
- Is the cost of birth control a problem for you?
- Do you mind having to stop sex play to use a male latex condom or diaphragm?
- Do you worry about certain forms of birth control?
- Do you ever want to be pregnant?

What If I Cannot Use 2 Forms Of Birth Control Together All The Time?

Talk with your dermatologist, gynecologist, or family doctor. If you plan to have sex during your treatment and feel you cannot be 100% successful in using 2 forms of birth control each time, you should not take isotretinoin.

What If My Birth Control Fails?

The section on "Emergency Birth Control (Emergency Contraception)" is on page 31 of this workbook. It tells you what emergency birth control is and where to get it quickly.

MAKING A CHOICE ABOUT BIRTH CONTROL

General Advice

Stay with your current primary form of birth control if:

- You are currently using an effective primary form AND you use it perfectly. For example, you do not miss birth control pills or hormone shots.
- You are satisfied with it.

Talk with your dermatologist, gynecologist, or family doctor about changing birth control before you start isotretinoin treatment if you:

- Do not use your current form of birth control perfectly. For example, you forget to change hormonal skin patches every week.
- Are not satisfied with the birth control you are using now. Changing birth control in the middle of your isotretinoin treatment is difficult.

You need to tell the doctor who prescribes your isotretinoin if you decide to change forms of birth control during treatment. You may have to stop having sex until your new form of birth control is working. You may have to stop isotretinoin and wait until you have been using the new form with a second form for at least 1 month and have a negative pregnancy test.

Planning Ahead With Your Partner

You want your partner to support you as you go through isotretinoin treatment. It is a great idea to talk with him about the iPLEDGE program before you start. Do not surprise him later.

1. Talk to him about why you decided to take isotretinoin at this time.
2. You will want him to agree with and support your decision to have this treatment.
3. Make sure he knows all the facts about isotretinoin and birth defects. Show him the patient information. Your partner needs to understand all the facts about isotretinoin. He needs to be aware of what good it can do, as well as its risks.
4. Make sure he knows you have to use 2 forms of birth control together correctly all the time for at least 1 month before beginning isotretinoin treatment, during treatment for several months, and 1 month after the last dose of isotretinoin.
5. Make sure he is willing to go along with the iPLEDGE program for several months.

You could ask your partner:

1. To help you make a list of questions to ask your doctor
2. To come with you to a doctor's office visit
3. To help you choose the 2 forms of birth control you will be using

Ask yourself:

1. Your doctor tells you that you need to have a pregnancy test before you can fill and pick up a prescription. You would:
   - A) Refuse the test because you know you are not pregnant
   - B) Ask your doctor to explain why you need the test
   - C) Go to another doctor to get isotretinoin

2. I need to use 2 separate, effective forms of birth control at the same time while on isotretinoin because:
   - A) There is a high chance for multiple births from taking isotretinoin
   - B) There is a very high chance that my baby will be deformed if I get pregnant
   - C) I may find it hard to not have sex during treatment and 1 month after my last dose

3. You already take birth control pills. If you want to start isotretinoin, you:
   - A) Review this *iPLEDGE Program Birth Control Workbook*, and then get counseling before you choose a second form
   - B) Do not worry about a second form now, because you are not having sex with anyone

Answer key: page 38

PRIMARY FORMS OF BIRTH CONTROL

This section of the workbook provides information about the different forms of primary birth control. It only gives you the most important information you need for the iPLEDGE program. It does not cover all the side effects or other information about these forms. If you want more information, ask your dermatologist, gynecologist, or family doctor. They have more information written for healthcare professionals and for patients.

None of the primary forms protect against sexually transmitted diseases (STDs) or HIV (AIDS).

Hormonal Birth Control Forms

Hormonal birth control forms include combination birth control pills, the skin patch, shots, under-the-skin implants, and the vaginal ring. They are prescription medicines that prevent pregnancy.

Hormonal Combination Birth Control Pills

Hormonal combination birth control pills are birth control pills you take by mouth every day as prescribed.

Progesterone-only birth control pills (mini-pills), such as Ortho Micronor® Tablets, are not acceptable for the iPLEDGE program because they are not effective enough. If you are using these, you will have to choose another primary form of birth control.

Who should not take birth control pills?

You should not use birth control pills if you:

- Smoke
- Had blood clots or breast cancer
- Have a history of heart disease, liver problems, high blood pressure, or diabetes
- Are pregnant or nursing

Why is it important how I take birth control pills?

Birth control pills provide very good protection only if you take them every day and do not miss any pills. If you miss pills, your chance of pregnancy is much greater. Your chance of getting pregnant is higher if you miss pills at the beginning of your cycle or start your pills too late in your cycle. Less than half of all females take their birth control pills as prescribed.

- The most important thing about using birth control pills as your primary form of birth control is taking them every day to keep the chance of pregnancy as low as possible. If you have not used them perfectly, you may need to choose another primary form of birth control, such as the hormonal shot, an IUD, or a hormonal skin patch.
- Isotretinoin may make birth control pills less effective. That means you could be more likely to get pregnant while you are taking isotretinoin, particularly if you miss a pill.

Are you taking birth control pills now?

If you are, is this going to be your primary form of birth control? Before you decide, ask yourself:

- Do you ever have pills left at the end of the month?
- How often do you miss more than 1 pill per cycle? Do you do it more than 2 cycles in a year?
- Have you ever taken birth control pills out of order?

If you answered yes to any of these questions, you probably need to choose another primary form of birth control.

If you are not taking birth control pills now, why do you think you want to try them? Ask yourself:

- Have you ever had to remember to take a pill every single day?
- Why do you think you can remember this task?

If you do not remember to take your pill every day without fail or have never taken pills every day before, you should probably not use birth control pills during isotretinoin treatment.

Advantages

- You may be able to get pregnant within 3 months after stopping birth control pills.
- Breast cysts may occur less frequently
- May provide some protection against the development of uterine and ovarian cancer

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Disadvantages

- Birth control pills do not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- Common side effects include breakthrough bleeding, nausea and vomiting, and headaches.
- If you skip pills, your chance of pregnancy is very high.
- Isotretinoin, antibiotics, and St. John's Wort may make birth control pills less effective.

What should I do if I miss birth control pills when I am on isotretinoin?

If you miss any birth control pills, do not have sex for the rest of your cycle. You could get pregnant.

- If you miss 1 pill, take it as soon as you remember. Continue taking your other pills at the regular time. Call your doctor as soon as you realize it.
- If the whole day goes by before you realize you missed a pill, it is OK to take 2 pills together.
- **If you miss more than 2 days, you should call your doctor as soon as you realize it.** You are at a greater chance for pregnancy if you start a cycle late or miss taking pills during the first week of each cycle.

Ask yourself:

1. If your 2 birth control forms are birth control pills and the diaphragm with spermicide, and you forgot to take 2 pills in a row, you should:
   - A) Not worry because you are using a diaphragm with spermicide, too
   - B) Not have sex and call your doctor because you do not have enough protection to keep from getting pregnant
   - C) Take birth control pills 2 at a time until you catch up

2. You are talking to your doctor about having your second pregnancy test, so you can start isotretinoin. You have been on birth control pills for 1 month, and it is the second day of your period. Three days ago, you and your partner forgot to use a male latex condom when you had sex. You should:
   - A) Have the pregnancy test anyway because it will tell you if you are pregnant
   - B) Not worry because you have your period
   - C) Tell the doctor you and your partner forgot to use a male latex condom once
   - D) Not worry because you forgot before and never got pregnant

Answer key: page 38

Hormonal Skin Patch

The hormonal skin patch is a thin, plastic patch that you put on your skin. It releases female hormones into your body to protect against pregnancy.

Who should not use the hormonal skin patch?

You should not use the patch if you:

- Smoke
- Had blood clots or breast cancer
- Have a history of heart disease, liver problems, high blood pressure, or diabetes
- Are pregnant or nursing

How do I use the hormonal skin patch?

You put a new patch on each week for 3 weeks. The fourth week is patch free, usually the time that you have a menstrual period. You place the hormonal skin patch where you can check it easily—on the upper outer arm, stomach, or upper body—but NOT on your breasts.

Are you using the hormonal skin patch now?

If you are, is this going to be your primary form of birth control? Before you decide, ask yourself:

- Do you have trouble remembering to change the patch each week? Has the patch ever come loose or fallen off and you did not immediately put on another one?
- Have you gained weight so that you weigh close to or more than 200 pounds?

If you answered yes to any of these questions, talk with your dermatologist, gynecologist, family doctor, or birth control counselor. Another primary form of birth control may be better for you.

- If you are not using the hormonal skin patch, why do you think you would change to it?

Advantages

- It is not necessary to remember to take a daily pill.
- Many patients have more regular, lighter and shorter periods.

Disadvantages

- The patch does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- If it becomes loose or falls off for more than 24 hours, you can get pregnant.
- If you leave the same patch on more than 1 week, you can get pregnant.
- Common side effects include breakthrough bleeding, nausea and vomiting, headaches and breast tenderness.
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective.
- Possible increased risk of blood clots. Please discuss this with your doctor.

Hormonal Vaginal Ring

The hormonal vaginal ring is a small flexible ring that you put into your vagina once a month. It releases female hormones into your body and works like birth control pills.

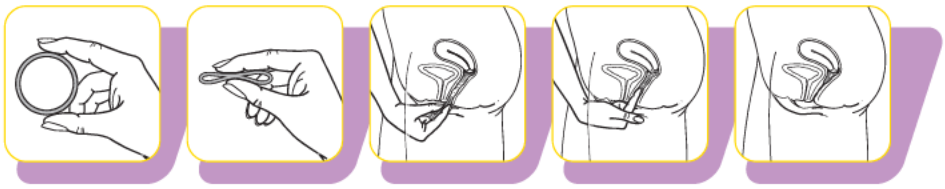
Who should not use the hormonal vaginal ring?

You should not use the hormonal vaginal ring if you:

- Smoke
- Had blood clots or breast cancer
- Have a history of heart disease, liver problems, high blood pressure, or diabetes
- Are pregnant or nursing

How do I use the hormonal vaginal ring?

You put a new ring in your vagina once every 4 weeks on the same day of the week. You leave it there for 3 weeks and then take it out. During the one-week break, you usually have a menstrual period. **If the ring slips out of the vagina during the 3-week period, you must replace it within 3 hours.**



Are you using the hormonal vaginal ring now?

If you are, is this going to be your primary form of birth control?
Before you decide, ask yourself:

- Do you have trouble remembering to remove the ring after 3 weeks?
- Has the ring ever slipped out and you did not notice?
- Do you have trouble inserting the ring?

If you answered yes to any of these questions, talk with your dermatologist, gynecologist, family doctor, or birth control counselor. Another primary form of birth control may be better for you.

- If you are not using a hormonal vaginal ring, why do you think you would change to it?

Advantages

- It is not necessary to remember to take a daily pill.
- It does not need to be fitted by a doctor.
- Many female patients have more regular, lighter, and shorter menstrual periods.
- Your ability to have children returns quickly after stopping the ring.

Disadvantages

- The ring does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- You cannot use it with a diaphragm or cervical cap.
- Some medicines for a vaginal yeast infection increase the level of hormones released into the blood.
- You may have trouble inserting the ring.
- Pregnancy can happen if:
  - The unopened package containing the ring is put into direct sunlight or exposed to very high temperatures
  - The ring slips out of the vagina and you do not replace it within 3 hours
  - The ring does not stay in the vagina for 3 weeks
  - You leave the ring in the vagina for more than 3 weeks
- Common side effects include breakthrough bleeding, nausea and vomiting, and headaches.
- Isotretinoin, antibiotics, and St. John's Wort may make hormonal forms less effective.

Hormonal Shots—Single Hormone

Single hormonal shots use a progestin (a female hormone) to prevent pregnancy. They keep you from releasing eggs, keep eggs from growing in the uterus, and make it harder for sperm to get to an egg.

Who should not take single hormonal shots?

You should not take single hormonal shots if you have any unexplained vaginal bleeding, have or had breast cancer, have liver problems or are pregnant.

How do I take single hormonal shots?

Your dermatologist, gynecologist, or family doctor can give you a shot in your arm, belly, or buttocks once every 12 weeks.

Are you taking single hormonal shots now?

- If yes, is this going to be your primary form of birth control? How often do you miss shots?
- If you are not getting single hormonal shots, why do you think you would change to them?

Advantages

- A single shot works for 12 weeks at a time.
- There is no daily pill to take.
- You can use it if you cannot take the hormone estrogen.

Disadvantages

- Single hormonal shots do not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- They may cause thinning or loss of bone and should not be used for more than 2 years.
- They may cause irregular bleeding.
- If you are planning to get pregnant AFTER you finish your isotretinoin treatment, it may take up to 18 months to get pregnant after you stop getting single hormonal shots.

How soon does the single hormonal shot start to work?

If you get the shot within the first 5 days of your menstrual flow, the protection against pregnancy begins right away.

Hormonal Intrauterine Device (LNg20 IUD)

The hormonal IUD LNg20 is a small piece of plastic your doctor puts into your uterus. The LNg20 IUD has a progestin (female hormone) that keeps you from releasing eggs and slows down sperm.

The Progesterone T IUD is different from the LNg20. The Progesterone T IUD **is not an acceptable primary form of birth control for the iPLEDGE program**. If you are using it, you will have to choose another primary form of birth control.

Who should not use a hormonal IUD?

Some of the reasons women should not use the hormonal IUD include pregnancy; serious pelvic infection; having more than 1 sexual partner; problems with your immune system; leukemia; AIDS; IV drug abuse; cancer of the uterus, cervix, or breast; unexplained bleeding from the vagina; liver disease; and fibroids in the uterus.

How do I use a hormonal IUD?

Your gynecologist or family doctor can put in an IUD for you. It may cause cramping at first. The hormonal IUD can stay in place for up to 5 years. You must check for the IUD strings in the first few months after insertion and after each menstrual period.

Do you have a hormonal IUD now?

If you do, is this going to be your primary form of birth control? First, ask yourself these questions:

- Is the IUD in place? Can you feel the string?
- When did you last have it checked by your clinician? It needs to be checked within 3 months after you had it inserted.
- If you are not using a hormonal IUD, why do you think you would change to it?

Advantages

- It is a good choice for long-term birth control (5 years), and you may get pregnant fairly quickly when it is taken out.
- It is a good choice if you are not at risk for STDs (sexually transmitted diseases) and have not had a lot of pelvic infections.

Disadvantages

- An IUD does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- Side effects may include cramps and heavy and longer menstrual periods for the first few months after it is placed, and increased chance of infection.
- Your body may push out the IUD. This can happen without your knowing it. This occurs mostly during a woman's menstrual period.
- You must check for the strings after each menstrual period to make sure the IUD is in place. If you cannot feel the strings or if you can feel the IUD itself, call your gynecologist.

Ask yourself:

1. You have an IUD inserted as your choice for a primary form of birth control. Which of the following can you use as a second form?

   A) Male latex condoms with or without spermicide

   B) Hormonal shots

   C) Cervical cap without spermicide

   D) Diaphragm with spermicide

   E) Mini-pills (e.g., progesterone-only birth control pills)

   F) All of the above

Answer key: page 38

Hormonal Implants (Under-The-Skin)

Implantable birth control is a plastic rod(s), the size of a matchstick that is put under the skin in the upper arm by a healthcare provider in the office. It is effective for up to three years.

Who should not use

You should not use implantable birth control if you:

- Are pregnant
- Have or have had a current or past history of clots
- Have or have had liver disease
- Have or have had breast cancer
- Are allergic to anything in the implant

How do I use

The implant is put under the skin by a healthcare provider in the office. It generally cannot be seen once under the skin and once in, is effective for up to 3 years. It can be removed at any time by a procedure done by the healthcare provider in the office.

Advantages

- The rod works for up to 3 years
- There is no daily pill to take
- You can use it if you cannot take the hormone estrogen
- Your ability to have children may return quickly after removing the implant

Disadvantages

- Implant does not protect against STDs (sexually transmitted diseases) or HIV (AIDS)
- May cause irregular and unpredictable bleeding
- Other side effects can include headache, acne, cramping and emotional changes

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- There can be side effects related to putting in the implant such as swelling, redness, pain, bruising, scarring, or infection
- There can be side effects related to removing the rod including a broken rod, or scar tissue making removal more difficult
- Rarely, it can be difficult or impossible to remove which may result in having to go to the operating room
- If you get pregnant, the chance of an ectopic pregnancy (a pregnancy not in your womb) is higher
- Ovarian cysts can occur
- May be less effective in women who are overweight or have liver problems – discuss this with your doctor
- Isotretinoin, antibiotics, and St. John's Wort may make the implant less effective

How soon does the implant work?

Discuss this with your healthcare provider.

Please make sure you can feel the implant rod under your skin after placement. If you cannot feel it, please do not start isotretinoin or have sexual intercourse until you talk to your healthcare provider.

Non-hormonal Intrauterine Device (Copper T IUD)

The Copper T IUD is a thin piece of plastic covered with the metal copper. It prevents pregnancy by slowing sperm down and keeping sperm from getting to the egg.

Who should not use the Copper T IUD?

Some of the reasons you should not use the Copper T IUD include pregnancy; serious pelvic infection; having more than 1 sexual partner; cancer of the uterus, cervix, or breast; unexplained bleeding from the vagina; liver disease; and fibroids in the uterus. You cannot use this IUD if you are allergic to copper or have Wilson's disease.

How do I use the Copper T IUD?

Your gynecologist or family doctor can put in an IUD for you. It may cause cramping at first. The Copper T IUD can stay in place for up to 10 years. You must check for the IUD strings in the first few months after insertion and after each menstrual period.

Advantages

- You can use it if you cannot take hormones.
- It is a good choice for long-term birth control (10 years).
- You may get pregnant fairly quickly when it is taken out.
- It is a good choice if you are not at risk for STDs (sexually transmitted diseases) and have not had a lot of pelvic infections.

Disadvantages

- An IUD does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- Side effects may include cramps, heavy and longer menstrual periods.
- Your body may push out the IUD. This can happen without you knowing it. This occurs mostly during your menstrual period.
- You must check for the string to make sure it is in place. If you cannot feel the strings or if you can feel the IUD itself, call your gynecologist.

Tubal Sterilization (Tying Your Tubes)

Tubal sterilization (tying your tubes) is an operation that closes the tubes from the ovaries to the uterus so that the sperm cannot get through to the egg. Female sterilization may be accomplished using a variety of techniques. They are all considered to be very effective, virtually permanent methods of pregnancy prevention and, with the exception of hysteroscopic tubal sterilization, are immediately effective. Hysteroscopic tubal sterilizations are not effective immediately and require that a test be done in three months to confirm that the tubes are blocked. For the purposes of the iPLEDGE program, hysteroscopic tubal sterilization is not considered an effective primary method of birth control unless the confirmation test has been performed.

Who should not have a tubal sterilization?

- You should not have a tubal sterilization if you ever want to get pregnant, at any time now or in the future.
- If you have already had a tubal sterilization, this is your primary form of birth control while taking isotretinoin. You must also choose either a secondary form of birth control or another primary form.
- If you are thinking about tubal sterilization, here is some information

Advantages

- It is very effective birth control.
- It works immediately after the surgery, with the exception of hysteroscopic tubal sterilization which requires that a test be done in three months to confirm that the tubes are blocked.

Disadvantages

- Tubal sterilization does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- If you want to have a child later, it is very difficult to re-open the tubes.
- It is surgery. You would need to have an operation.
- It increases the chance of ectopic pregnancy (pregnancy in the tubes) if sperm manage to get through the blocked tubes.

Partner's Vasectomy

A vasectomy is an operation that closes off the tubes that carry a man's sperm. The man's fluid should not have sperm in it after a vasectomy. If a man has sex before his doctor says his fluid has no sperm, the woman could get pregnant.

- If you have *only 1* partner *and* he has had a vasectomy, this can be your primary form of birth control while taking isotretinoin. You must also choose a second form of birth control. It is strongly recommended that you choose another primary form to give you very effective protection against getting pregnant.

If your partner is thinking about a vasectomy, here is some information about this very effective, but permanent, means of birth control.

Advantages

- It is very effective birth control.

Disadvantages

- A vasectomy does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- If a male wants a child later, it is very difficult to open the tubes again.
- A vasectomy requires minor surgery.

Ask yourself:

- Is this my only sexual partner?

If you said no or if you are not sure, you cannot choose vasectomy as your primary form of birth control.

SECONDARY FORMS OF BIRTH CONTROL

Secondary forms of birth control do not adequately protect against pregnancy if they are the only form used. However, they greatly increase your protection against getting pregnant if you use them along with a primary form every time you have sex. Effective secondary forms of birth control forms include barrier forms (male latex condoms, diaphragms, and cervical caps) and other forms (vaginal sponge). The diaphragm and cervical cap must always be used with a spermicide, and the male latex condom can be used with or without spermicide. The vaginal sponge contains spermicide. If a secondary form is your second form of birth control, you must use it every time you have sex with a male. The female condom is not an effective secondary form for the iPLEDGE program.

Always use a spermicide with diaphragms and cervical caps.

Ask your doctor, gynecologist, or family doctor to show you how to use secondary forms. Be sure you know how to use them correctly.

Make sure you know exactly how to use these forms of birth control. Know what mistakes people make with secondary forms. These mistakes can get you pregnant.

Spermicides

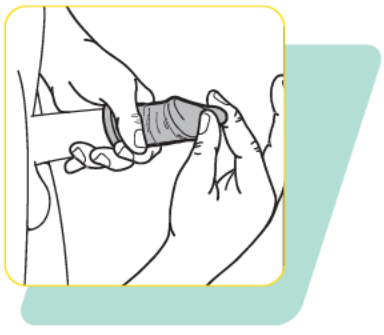
Spermicides come in several forms—creams, jellies, foams, and suppositories. You use spermicide 10 to 30 minutes before you have sex—each and every time—whenever the male comes in or near the female patient's vagina. Your dermatologist, gynecologist, family doctor, or birth control counselor can tell you how to use spermicides with your secondary barrier form.

Some people are allergic to spermicides. If you cannot use a spermicide, you must use 2 primary forms of birth control together, or a primary form with a male latex condom as your second form.

Male Latex Condom With or Without Spermicide

What is a male latex condom?

The male latex condom, also called a "rubber," is a thin cover put on the male's penis that traps sperm. You can use them with or without a spermicide .



How does my partner use it?

The male latex condom is unrolled on a male's erect penis as soon as he gets an erection. Waiting too long lets sperm leak out!

You can use a male latex condom with or without spermicide.

A male latex condom is good for 1 time only. Do not let your partner try to use it more than once. Oils like petroleum jelly or baby oil can ruin a male latex condom. Safe lubricants include anything made with a water-based gel such as KY Jelly®.

Make sure the male latex condom stays on during sex. If it tears or comes off, call your doctor about emergency birth control.

Choosing a male latex condom as your secondary form

If you choose male latex condoms as a secondary form, your partner must be willing to use a male latex condom each and every time you have sex. Ask yourself:

- Does your sexual partner use a latex condom? Does he have a problem with using a latex condom each time you have sex?
- Does anyone ever force you to have sex if you do not want to?
- Have you and your partner ever forgotten to use latex condoms even when you had meant to?
- Have you ever had sex after drinking when you had not planned to?

  Alcohol and drugs can affect your judgment and decisions about having sex.

Male latex condoms may not be the best secondary form for you to choose if:

- Your partner does not want to use them
- You do not like to interrupt sex to let your partner put on a male latex condom
- You have had sex when you did not plan to and did not use birth control

You may want to choose a form you can control or one that you can insert before having sex.

Advantages

- Male latex condoms *do* protect against STDs (sexually transmitted diseases) and HIV (AIDS).
- Male latex condoms are easy to buy, and no doctor's appointment or pelvic exam is needed.
- It is easy to tell when it breaks or slips.

Disadvantages

- Males and females can have a latex allergy.
- Male latex condoms can break or slip during sex.
- Many males do not like or want to use them. Your partner has to be committed to using male latex condoms. You are not in control of this birth control form.
- You must remember to use them every time.
- You must interrupt sex play to put on a male latex condom.

How soon does a male latex condom work?

It works as soon as the male puts it on his erect penis.

Ask yourself:

- Will your partner actually use the latex condom?
- Did you talk with him about it?
- Did he agree?

1. Your partner says he is tired of using latex condoms and asks if he can skip it once in a while. Hormonal shots are your primary form of birth control. You should:

   A) Agree to let him just use a condom every other time you have sex

   B) Tell him to use latex condoms until you get a diaphragm to use

   C) Tell him that you will not have sex with him unless he uses a latex condom

   D) Not worry because you have not gotten pregnant yet

Answer key: page 38

Diaphragm And Spermicide

What is a diaphragm?

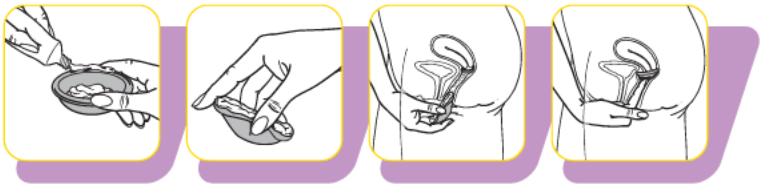
The diaphragm is a shallow latex cup edged with a flexible ring. It covers your cervix and keeps sperm from getting into your uterus. Your gynecologist or family doctor can fit you with one.

Who should not use the diaphragm?

You should not use a diaphragm if you have an allergy to latex or silicone, difficulty putting the diaphragm in, weak vaginal muscles, a history of bladder infections or toxic shock, or had a recent abortion.

How do I use a diaphragm?

You bend the flexible ring and insert the diaphragm into your vagina. The back rim rests below and behind the cervix. The front rim is tucked behind your pubic bone. Before you insert it, you put spermicide in the center of the cup and around the ring.



You can put your diaphragm into the vagina up to 6 hours before sex. You have to leave it in place for at least 6 hours after you have sex. You must put spermicide in the vagina if you have sex again during this time. You should not leave it in for more than 24 hours at a time.

Choosing a diaphragm as your secondary form

Studies have shown that female patients under 30 and female patients who have sex 3 or more times a week have a higher pregnancy rate using diaphragms. If you are in one of these 2 groups, talk with your dermatologist, gynecologist, family doctor, or birth control counselor about whether the diaphragm is right for you.

Have you ever used a diaphragm? What do you like or dislike about the diaphragm?

- Do you find it easy to put it in?
- Have you been using spermicide with the diaphragm?
- Do you find it easy to remember to use it?
- Have you had your diaphragm checked by your gynecologist in the last 2 years to see if it still fits? You must have your diaphragm checked every 2 years, after a gain or loss of 10 pounds, OR after childbirth or an abortion.

If you answered yes to these questions, the diaphragm may be a good secondary form for you.

If you answered no to any of these questions, you should think about another secondary form.

Advantages

- You can easily carry a diaphragm with you and control its use.
- It is immediately effective.
- There are no hormones.
- You do not have to interrupt sex play—it can be inserted before sex.
- You can use it during your menstrual period.

Disadvantages

- A diaphragm does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- Some female patients have an allergy to latex.
- Some female patients find it hard to insert.
- You must put spermicide in your vagina if you have sex again.
- It can get pushed out of place during sex.
- It requires a prescription and pelvic exam. A diaphragm lasts about 1 to 2 years.
- You must check it for holes and tears and clean it after sex.

How soon does a diaphragm work?

It works as soon as spermicide is applied and you put it in correctly.

Cervical Cap And Spermicide

What is the cervical cap?

The cervical cap is a small latex or rubber cup. You use it with spermicide. It covers your cervix so that sperm cannot get in your uterus. It must fit perfectly to work. Your gynecologist or family doctor can fit you for one.

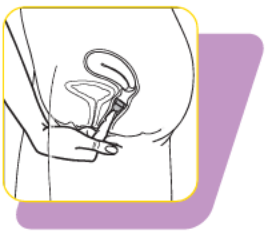
Who should not use a cervical cap?

You should not use a cervical cap if you have an allergy to latex or rubber, a history of pelvic infections, abnormal Pap tests, or Toxic Shock Syndrome (TSS).

How do I use a cervical cap?

The cap is filled one-third full with spermicide. You squeeze it as you put it in your vagina. You press it onto the cervix to cover it completely. You can put the cap in the vagina right before sex, but it stays better if you put it in place 30 minutes before sex. You have to leave it in place for at least 6 hours after you have sex. You can leave in place up to 48 hours.

The cervical cap is made of latex. Never use it with an oil-based lubricant like petroleum jelly. This will destroy the cap.



What is the difference between a diaphragm and a cervical cap?

The cervical cap is a little harder to learn how to use. With a cervical cap, there is no need to insert extra spermicide if you have sex again. You can also leave the cap in place for a longer time—48 hours instead of 24 hours. You cannot use the cervical cap if there is any vaginal bleeding, such as during your menstrual period.

Choosing the cervical cap as your secondary form

Studies have shown that female patients under 30 and female patients who have sex 3 or more times a week have a higher pregnancy rate using the cervical cap. If you are in one of these 2 groups, talk with your gynecologist or family doctor about whether the cervical cap is right for you.

Have you ever used a cervical cap? What do you like or dislike about it?

- Do you find it easy to put in?
- Have you been using spermicide with the cervical cap?
- Do you find it easy to remember to put it in?

If you answered yes to these questions, the cervical cap may be a good secondary form for you.

If you answered no to any of these questions, talk with your gynecologist or family doctor before choosing this secondary form.

Advantages

- You can easily carry a cervical cap with you and control its use.
- It is immediately effective.
- It has no hormones.
- There is no interruption of sex play—it can be inserted in advance.

Disadvantages

- A cervical cap does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- Some female patients have an allergy to latex.
- Some female patients find it harder to insert than a diaphragm.
- You cannot use it during your menstrual period.
- You need a prescription and a pelvic examination to fit a cervical cap.
- A cap lasts about 1 year.
- You must check it for holes and tears and clean it after sex.

Vaginal Sponge

What is the vaginal sponge?

The vaginal sponge is a soft foam disc or pillow containing 1 gram of the spermicide nonoxynol-9. Inserting the sponge puts spermicide in your vagina and keeps it there during sex. You insert it in the vagina so it sits over your cervix. It has a string loop attached for easy removal.

Who should not use a vaginal sponge?

Female patients who are allergic to the spermicide nonoxynol-9 should not use the vaginal sponge.

How do I use the vaginal sponge?

First, wash your hands. Wet the sponge thoroughly with clean tap water. Squeeze the sponge gently several times until it is foamy. This releases the spermicide. Pinch the sides of the sponge together. Be sure the string loop is on the underside of the sponge. Squat or sit down, bend your wrist, and push the sponge gently up into your vagina as far as it will go. Check the position of the sponge to make sure the sponge covers your cervix.

How do I take the sponge out?

Wait at least 6 hours after your last sexual activity before taking the sponge out. You can leave it in place for up to 30 hours. You do not need more spermicide if you have sex more than once during that time. To take the sponge out, you need to catch the string loop and gently pull on it.

Choosing the vaginal sponge as your secondary form

Have you ever used a vaginal sponge? What do you like or dislike about it?

- Do you find it easy to put in? Easy to take out?
- Do you find it easy to remember to put it in?

If you answered yes to these questions, the vaginal sponge may be a good secondary form for you.

If you answered no to any of these questions, talk with your gynecologist or family doctor before choosing this secondary form.

Advantages

- You can easily carry a vaginal sponge with you and control its use.
- It is immediately effective.
- It has no hormones.
- There is no interruption of sex play—it can be inserted in advance and is effective for up to 30 hours.
- No fitting is needed; you can buy it over the counter.
- It is comfortable and easy to use.

Disadvantages

- The vaginal sponge does not protect against STDs (sexually transmitted diseases) or HIV (AIDS).
- It is not as effective in female patients who have had children.

EMERGENCY BIRTH CONTROL (Emergency Contraception)

Emergency birth control is also called "after sex" or "morning after" birth control. It can prevent pregnancy after sex without adequate protection. Emergency birth control prevents release of the egg, joining of the sperm and the egg, or implanting of the egg in the uterus. Emergency birth control is only for a female patient who is sure she is not already pregnant.

There are 2 forms of emergency birth control:

1. Emergency Contraceptive Pills (ECPs)—used within 3 days. ECP is several high-dose birth control pills. You must take the first dose of ECP within 3 days of having sex without enough protection. The sooner you take ECP, the more likely it is to work. It is best if ECP begins within 12 hours after you have sex without adequate protection. The pills can give you severe nausea. Ask your doctor for something to help with the nausea if you need this treatment.
2. Putting in an IUD—used within 5 days. You need to have the IUD inserted within 5 days of having sex without adequate protection.

   This form is not good for female patients who have not had a child or are at risk for STDs (sexually transmitted diseases). This includes those with new sex partners, more than 1 partner, or whose partners have other partners, and those who were raped.

When would I need emergency birth control?

Call your doctor or gynecologist about emergency birth control if you had sex without adequate protection, such as:

- You forgot to take 2 or more birth control pills and had sex.
- You had sex without using a second form of birth control.
- You were late for your birth control hormonal shot and had sex.
- Your partner's condom broke or slipped off.
- Your diaphragm or cervical cap slipped out of place or ripped during sex.

Emergency birth control is meant only for emergencies. It does NOT take the place of your usual 2 forms of birth control. Emergency birth control is not to be used instead of regular birth control.

Where can I get emergency birth control?

You can get emergency birth control from:

- Private doctors or nurse practitioners
- Planned Parenthood
- Women's health centers
- Many hospital emergency rooms (unless they are owned by organizations opposing birth control)
- Available over-the-counter at pharmacies for patients that are 18 years old or older

Whom should I call if I cannot find emergency birth control?

Call the private toll-free Emergency Contraception Hotline at 1-888-NOT-2-LATE (1-888-668-2528). They will ask for your city or ZIP code to help you find emergency birth control near you.

Ask yourself:

1. The right way to use emergency birth control is:
   - A) As a second form of birth control
   - B) If you find a tear in your cervical cap after sex
   - C) If you missed several birth control pills and then have sex
   - D) Only after a positive pregnancy test

Answer key: page 38.

REASONS FEMALE PATIENTS GET PREGNANT

There are many reasons female patients get pregnant when they do not want to. You can avoid most of these.

- They did not avoid sex with a male when they were not using birth control.
- They used a birth control form that did not work very well.
- They did not use birth control all the time and every time they had sex.
- They did not use their birth control the right way.
- They had sex with a male partner when they were not expecting to.
- Their birth control form failed.

For most of the reasons, you can make a choice not to make the same mistake. It is very important that you are careful about birth control. Use your birth control as the iPLEDGE program requires. Do not make mistakes that can lead to unexpected pregnancy.

SEPARATING THE MYTHS FROM THE FACTS

Myths are ideas that many people believe are true, but they are not true. You need to know the facts about sex, birth control, and pregnancy to protect yourself.

MYTH—WHAT YOU HEAR	FACT—WHAT IS TRUE
You cannot get pregnant the first time you have sex.	You can get pregnant **any** time you have sex.
You cannot get pregnant if you "do it" standing up.	You can get pregnant in any position.
You will not get pregnant if you do not have an orgasm (come).	You can get pregnant any time you have sex regardless of whether or not you have an orgasm.
Douching keeps you from getting pregnant.	Douching does **not** prevent pregnancy.
You do not have to use something every time.	You should use birth control every time you have sex.
You will not get pregnant if it is the "safe time" of the month.	There is no safe time, even for female patients who are regular with their menstrual periods. Your body can change and you could get pregnant.
You will not get pregnant if he pulls out before he comes.	Even if he pulls out, he may leak sperm before he comes and you can get pregnant.
It is safe for me to have sex any time, unless I feel PMS changes or pain near my ovaries.	You can get pregnant any time you have sex, not just when you think you are ovulating (releasing an egg).
You cannot get pregnant if you have not had a menstrual period yet.	Your ovaries release an egg (ovulation) before your first menstrual period. You can get pregnant even the very first time this happens, if you have been having sex.
You cannot get pregnant if you have sex underwater.	You can get pregnant **anywhere** you have sex.

MYTH—WHAT YOU HEAR	FACT—WHAT IS TRUE
My partner says he is sterile (has no sperm) because he had mumps. He never got anyone else pregnant, so I will not get pregnant.	Mumps rarely causes sterility (no sperm). You can get pregnant if you have sex with a man who has had mumps.
You cannot get pregnant if you miss only 1 birth control pill.	Birth control pills work best when you take them as prescribed. You can get pregnant if you miss even one pill, especially at the beginning of your pill cycle
Sexually active means you have to move during sex. If I do not move, I cannot get pregnant.	You can get pregnant any time you have sex, whether you move or lie still.
I am going through menopause and only get my menstrual period every couple of months.	You can get pregnant until you have missed your menstrual period for 1 year—12 months in a row.

You may have heard or read about something that is not listed here that you think might keep you from getting pregnant. Be sure to ask your dermatologist, gynecologist, or family doctor about any form that you cannot find in this book that you think, or have heard, will keep you from getting pregnant. You can only use the effective forms of birth control for the iPLEDGE program.

SEX, ALCOHOL, AND DRUGS

You have seen this message many times before. Alcohol and drugs can make you unable to use good judgment. While you are taking isotretinoin and for 1 month after your last dose, you need to be able to remember to use 2 effective forms of birth control together each and every time you have sex with a male.

Do not let drugs or alcohol keep you from using your secondary form when you have sex. Use it the right way. You need to be in control of yourself so:

- You use your secondary form, OR you get your partner to use a male latex condom
- You use a vaginal sponge, or a diaphragm or a cervical cap with spermicide
- You use a male latex condom with or without spermicide

RECOGNIZING PREGNANCY

If you think you might be pregnant, stop isotretinoin and call your doctor right away. Here are some signs that you might be pregnant:

- You miss your menstrual period.
- You have nausea first thing in the morning.
- Your breasts feel really tender, like at the beginning of a menstrual period.
- The area around your nipples may look darker.
- You feel really tired and want to sleep.
- You feel you have to go to the bathroom a lot.
- You may have spotting of blood at the time of your menstrual period, but no real bleeding.

Ectopic (Tubal) Pregnancy

Sometimes a baby starts to grow outside the uterus. This is a serious problem. Call your doctor right away, if you have these signs:

- Sudden pain or severe cramping in your lower abdomen
- Bleeding or spotting with abdominal pain after you miss a menstrual period
- Fainting or dizziness lasting more than a few seconds

Pregnancy Testing

If you have any questions about whether you might be pregnant, talk with your doctor.

NOTES:

NOTES:

Birth Control Information

You can get information about birth control 24 hours a day, 7 days a week on the telephone. Call the toll-free number **1-866-495-0654** to learn about these subjects:

1. Isotretinoin and Birth Defects
2. Sex, Pregnancy, and Birth Control
3. Different Methods of Birth Control
4. Emergency Contraception
5. Pregnancy and Pregnancy Testing

This telephone line is for education only. It does not take the place of talking with your doctor. He or she is the best source of information for you.

Answer Key To Birth Control Questions

Page 8:
- 1. B
- 2. A and D

Page 11:
- 1. B
- 2. B and C
- 3. A

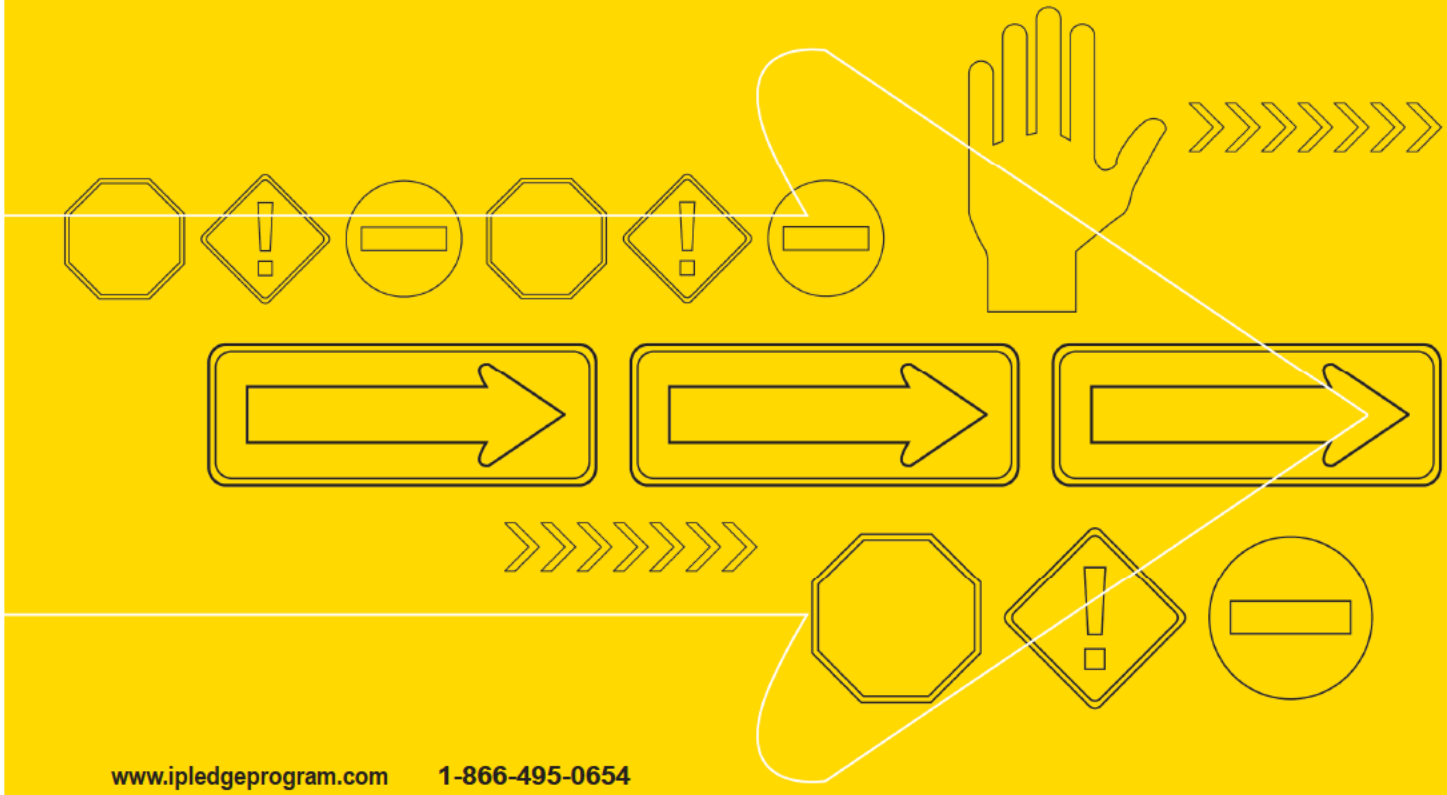
Page 14:
- 1. B
- 2. C

Page 20:
- 1. A and D

Page 26:
- 1. B and C

Page 32:
- 1. B and C

Reference ID: 3122588



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

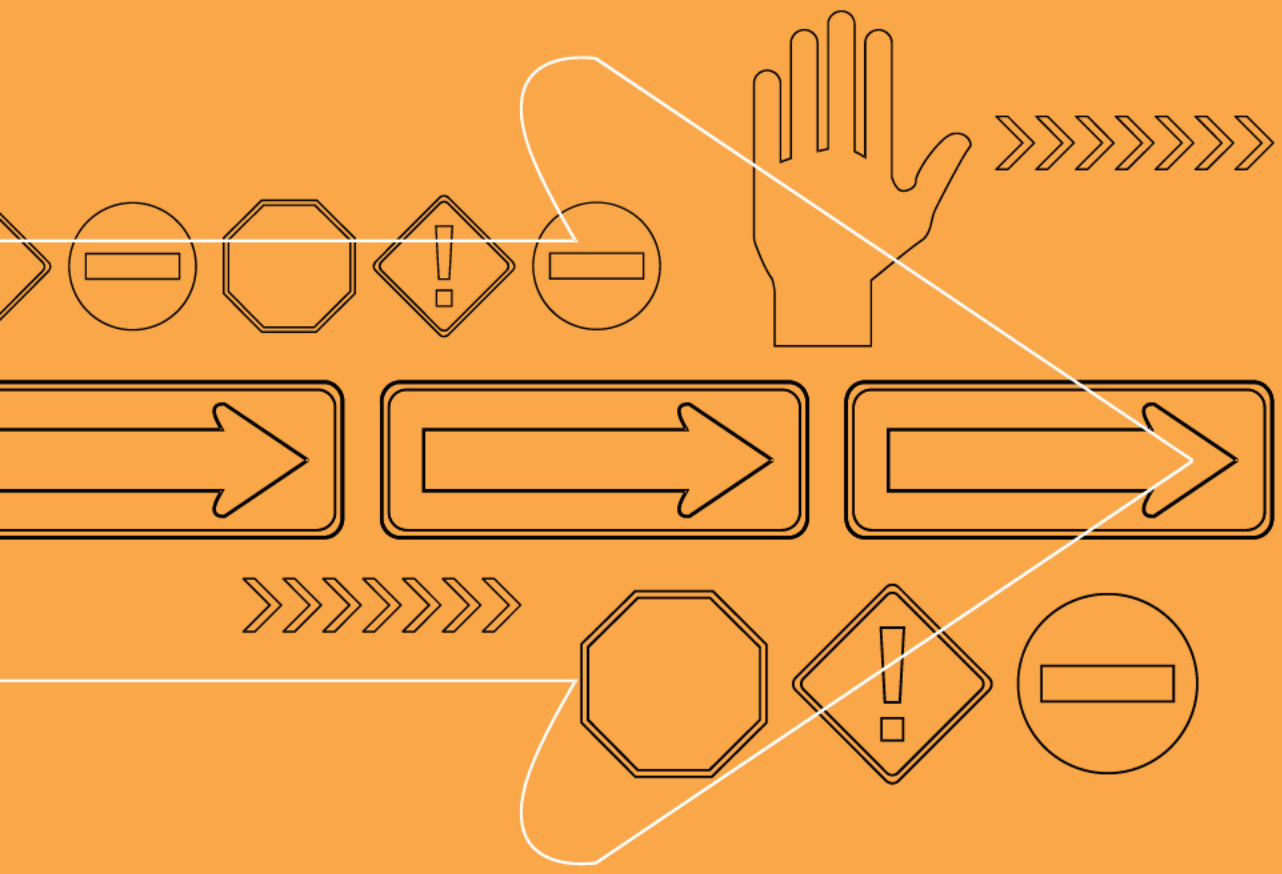
Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Contraception Referral Form And Contraception Counseling Guide



- Referral form for contraception counseling and guide for counselors on effective forms of contraception

Reference ID: 3122588

Most Recent Modification: April 2012

The iPLEDGE Program

Contraception Referral Form And Contraception Counseling Guide

Referral form for contraception counseling and guide for counselors to effective forms of contraception

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

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Contraception Referral Form And Contraception Counseling Guide

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Counseling goals 5

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Emergency contraception 9

Abstinence 9

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About This Referral Form

The Isotretinoin Contraception Referral Form, brought in to you by this patient, has been filled out in part by the prescriber. Please fill out the rest of the form at the conclusion of your counseling session and fax or mail the copy back to the prescriber, keeping a copy for your own records.

On the back of the referral form is a reimbursement form for contraceptive counseling services. The iPLEDGE program provides reimbursement for 1 contraception counseling session for patients who have been prescribed isotretinoin. Please complete the form and fax it to 1-866-495-0660.

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iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

ISOTRETINOIN CONTRACEPTION REFERRAL FORM

Prescriber: Complete for Patients Being Referred for Contraception Counseling

Patient_____, iPLEDGE program ID#_____ is considering treatment with isotretinoin. I am referring her for counseling to help her choose her 2 forms of contraception before she receives her first prescription.

Please complete the Record of Contraception Counseling below and return this form to my office, via fax or mail.

She had a negative (serum/urine) pregnancy test on _____

Please review this *Contraception Counseling Guide* for details on the iPLEDGE program contraception requirements.

Isotretinoin Prescriber's Name_____

Address _____

Telephone _____-_____-_____ Fax _____-_____-_____

Isotretinoin Prescriber's Signature _____

Date _____

RECORD OF CONTRACEPTION COUNSELING

Contraception Counselor: Complete Form and Fax or Mail Back to Isotretinoin Prescriber

I have provided the following for your patient _____

- ❑ Comprehensive contraception counseling
- ❑ Information about emergency contraception

The patient has:

- ❑ Not yet decided upon the forms of contraception she will use
- ❑ Chosen 2 forms of contraception
- ❑ Decided to abstain from any sexual contact with a male and is not planning to use 2 forms of contraception. I informed her that abstinence without using contraception is not recommended for the iPLEDGE program for sexually active women.

Primary Form _____

Secondary or Second Primary Form_____

I have prescribed the selected contraception.

❑ Yes ❑ No (Please comment below)

I believe that this patient is fully committed to complying with the contraceptive requirements of the iPLEDGE program.

❑ Yes ❑ No (Please comment below)

_____

Name_____

Address _____

Telephone _____

Specialty (circle one): OB-GYN Fam Prac IM RN LPN Other_____

Contraception Counselor's Signature _____

Date _____

Prescriber Copy-White **Contraception Counselor Copy-Yellow** **Patient Copy-Pink**

Please see accompanying complete product information, including boxed CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

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FAXABLE REIMBURSEMENT FORM

The Following Restrictions Apply:

Only consulting clinicians who provide initial pregnancy prevention counseling are eligible for reimbursement for such counseling. Other services provided during this visit are not eligible for reimbursement. The physician prescribing isotretinoin, or any other person working under the direct supervision of said physician, is not eligible for this reimbursement provision. The reimbursement fee is up to $150.00, which has been determined to be an average, usual, and customary reimbursement for service of this type. Information will be used only for reimbursement; the isotretinoin manufacturers will not use it for any other purpose.

Reimbursement For Pregnancy Prevention Counseling

To receive reimbursement for providing pregnancy prevention counseling to an isotretinoin patient, please answer the following questions, and sign, date, and send the completed form via fax to: 1-866-495-0660.

Contraception Counselor Name _____

Payee Name (if different than Contraceptive Counselor) _____

Office Telephone Number _____-_____-_____ Tax ID Number_____

Payee Address _____

City_____ State _____ ZIP _____

Name of Referring Physician _____

Office Telephone Number _____-_____-_____

City_____ State _____ ZIP _____

Patient's Name _____

Patient's iPLEDGE Program ID Number _____

- ☐ I have provided pregnancy prevention counseling to this patient. I have mailed or faxed the record of pregnancy prevention counseling (on reverse side) to the isotretinoin prescriber.
- ☐ I am not the prescribing physician of isotretinoin to the patient referenced above, nor am I employed by said prescribing physician.
- ☐ I have not, and will not, bill or submit for reimbursement either directly or indirectly, under Medicaid, Medicare, or similar federal or state healthcare programs, or under any private insurance, HMO, or other healthcare benefit program for the pregnancy prevention counseling services described above.
- ☐ I attest that all of the above information is accurate and understand that I must check each box above to receive reimbursement.
- ☐ I have included a signed W-9 Form, or already have a W-9 form on file for payment from iPLEDGE. A blank W-9 form and instructions for completion can be found at www.irs.gov

Signature _____ Date _____

CONTRACEPTION COUNSELING FOR ISOTRETINOIN PATIENTS

Isotretinoin is used to treat severe recalcitrant nodular acne; however, it is also a known human teratogen. Over one third of all babies exposed to isotretinoin *in utero* and carried to term have major birth defects.[1,2] The public health goal for isotretinoin is to eliminate fetal exposure by ensuring that no female starts isotretinoin therapy if pregnant and no female on isotretinoin therapy becomes pregnant. The US Food and Drug Administration has approved the iPLEDGE program, an enhanced pregnancy risk management program for isotretinoin, to help achieve that end.

The contraception that a patient selects can have a dramatic effect on her chance of becoming pregnant. A patient using isotretinoin needs to select forms with low failure rates that she and/or her partner will use correctly each time they have intercourse.

Your Role

This patient is being referred to you because she has asked for counseling to help her comply with the contraception requirements of the iPLEDGE program.

The patient must select and commit to using 2 forms of effective contraception simultaneously, at least 1 of which must be a primary form, unless the patient commits to continuous abstinence from heterosexual contact, or the patient has undergone a hysterectomy or bilateral oophorectomy, or has been medically confirmed to be post-menopausal. She must use 2 forms of effective contraception for at least 1 month prior to initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

It is strongly recommended that a patient use a primary form of contraception and is committed to using a second form as well, even if she says she will be abstinent for the entire required period. Isotretinoin is not recommended for sexually active female patients of childbearing potential whom you believe will not be able to maintain abstinence or will not use contraception, as the program requires.

Please read this *iPLEDGE Program Contraception Referral Form And Contraception Counseling Guide* completely before you begin your counseling session. It provides a pregnancy risk management context through which contraception choices for female patients taking isotretinoin can be viewed. It does not contain detailed information on the various forms of contraception.

The iPLEDGE Program Birth Control Workbook, which is for patients, contains more information on effective primary and secondary forms of contraception. It is not complete information on any of the forms, and the patient is encouraged to ask questions about specific forms or issues. The workbook has questions on such issues as medication adherence and lifestyle choices for the patient to think about in choosing contraception. Please review her responses with her.

COUNSELING GOALS

Ensure That The Patient:

- Understands the risk of having a child with significant birth defects from exposure to isotretinoin.
- Understands the need for using 2 forms of contraception together consistently and correctly and knows when to contact her prescriber for emergency contraception.
- Chooses the forms of contraception that will work best for her, that will provide her with the lowest practical failure rate, and that she and her partner will actually use. Adherence impacts the failure rate of hormonal combination oral contraceptives more strongly than other primary forms. (Please see "Hormonal Combination Oral Contraceptives As A Primary Form" on page 6.)
- Commits fully to not becoming pregnant and to using 2 forms of contraception simultaneously, consistently, and correctly. In previous isotretinoin risk management programs, patients understood the need for 2 forms of contraception; however, they did not comply, despite adequate information about the risk to the fetus. If, after counseling, the patient recognizes she will not be able to commit fully, encourage her to not take isotretinoin or do not prescribe.
- Is able and willing to maintain abstinence, if that is her choice after counseling. If a patient who has ever been sexually active chooses abstinence, and you believe that she will not be able to maintain abstinence and will not use contraception, encourage her to not take isotretinoin.

Counseling younger teens

For younger teens, it is important to stress the following aspects of contraception for the iPLEDGE program during counseling:

- The birth control forms that are effective as primary and secondary forms.
- Why it is important to use 2 forms of birth control. Younger teens may need more emphasis on this point to fully understand it and comply.
- Emergency contraception. Younger teens may need more explanation from you about the need to take immediate action if they had unprotected sex.

CONTRACEPTION REQUIREMENTS

Using 2 Forms Of Contraception Provides More Protection

Use of 2 forms of contraception (at least one of which is a primary form) simultaneously substantially reduces the chances that a female will become pregnant over the risk of pregnancy with either form alone.

In addition, it is not known if hormonal contraceptives are less effective when used with isotretinoin.[3] Because of this possibility and the fact that all contraceptive forms are less than 100% effective, the iPLEDGE program requires the additional protection of a second form of contraception.

Selecting An Effective Primary Form Of Contraception

Table 1 on the next page lists, by typical use failure rate, the primary forms of contraception acceptable in the iPLEDGE program. The single most important decision in contraception for the iPLEDGE program is selecting a primary form with a very low failure rate that the patient can and will use as perfectly as possible. Other important factors to consider in selecting a primary form include side effects, contraindications, and willingness and ability to use it perfectly. All of these factors influence compliance and the chance of unwanted pregnancy.

Hormonal Combination Oral Contraceptives As A Primary Form

If the patient is currently taking or planning to take oral contraceptives, review that section in *The iPLEDGE Program Birth Control Workbook* with her. Her answers to questions on consistency and medication adherence will provide insight into potential issues with iPLEDGE program adherence.

Other contraception not requiring daily choices may be a better choice for a patient who does not take oral contraceptives perfectly. For example, if such a patient chooses an IUD, she reduces her chances of becoming pregnant by up to approximately 90%.[3] It is critical that such a patient choose a form other than oral contraceptive agents.

Table 1: Primary Forms Of Contraception By Typical Use Failure Rate

	Percentage of Women Experiencing an Unintended Pregnancy Within the First Year of Use[a]	
Form	**Perfect Use**	**Typical Use**
Hormonal Implantable	0.05%	0.05%
Partner's Vasectomy	0.10%	0.15%
Hormonal IUD (LNg20)	0.20%	0.20%
Tubal Sterilization	0.50%	0.50%
Non-hormonal IUD (Copper T380A)[b]	0.60%	0.80%
Hormonal Injectable (single)	0.30%	3.00%
Hormonal Transdermal Patch	0.30%	8.00%
Hormonal Vaginal Ring	0.30%	8.00%
Hormonal Combination Oral Contraceptives[b]	0.30%	8.00%

a Adapted from Trussell J Contraceptive efficacy In: Hatcher RA, Trussell J, Stewart F, et al, eds *Contraceptive Technology*. Nineteenth Revised Edition, New York, NY: Ardent Media 2007

b The IUD Progesterone T and progestin-only "mini-pills" are not acceptable primary forms for the iPLEDGE program (See "Unacceptable Forms Of Contraception" on page 8)

Selecting An Effective Secondary Form Of Contraception

Table 2 lists the acceptable secondary forms of contraception in the iPLEDGE program. There are 2 forms of secondary contraception: barrier and other. Barrier forms include the diaphragm and cervical cap (both of which must be used with spermicide) and the male latex condom (which can be used with or without spermicide). The other form is the vaginal sponge, which contains spermicide. The most important issue for a secondary form is whether it will be used each time the patient has intercourse (i.e., will it be in place when the first form fails). Failure rate with perfect use is of secondary importance.

Help the patient select a secondary form that she and/or her partner can fully commit to using correctly each time they have intercourse. If it is apparent that more than 1 of the forms would be equally suited, select the form with the lower or lowest perfect use failure rate, as this will reduce the overall likelihood of becoming pregnant.

Table 2: Secondary Forms Of Contraception Listed By Typical Use Failure Rate		
	Percentage of Women Experiencing an Unintended Pregnancy Within the First Year of Use[a]	
Form	**Perfect Use**	**Typical Use**
Barrier Forms		
Male Latex Condom[b]	2%	15%
Diaphragm[*]	6%	16%
Cervical Cap[d,*]	9%	20%
Other Forms		
Vaginal Sponge[c]	9%	16%

a Adapted from Trussell J Contraceptive efficacy In: Hatcher RA, Trussell J, Stewart F, et al, eds *Contraceptive Technology* 19th Revised Edition, New York, NY: Ardent Media, 2007

b Female condoms are not acceptable for the iPLEDGE program (See "Unacceptable Forms Of Contraception" below) Failure rate for Male Latex Condom is for use without spermicide

c Failure rate for nulliparous women; rate is approximately double for parous women

d Adapted from Trussell J Contraceptive efficacy In: Hatcher RA, Trussell J, Stewart F, et al,eds *Contraceptive Technology*. 17th Edition, New York, NY: Irvington Publishers 1998

* Failure rates for Diaphragm and Cervical Cap include the use of spermicide

UNACCEPTABLE FORMS OF CONTRACEPTION

The following forms of contraception are not acceptable for the iPLEDGE program:

- Progesterone-only "mini-pills," e.g.:
  - Ortho Micronor® Tablets*
- IUD Progesterone T

Typical use and perfect use failure rates (2.0%, 1.5%) are unacceptably high compared with other available IUDs.

- Female condoms
- Natural family planning (rhythm method) or breastfeeding
- Fertility awareness
- Withdrawal
- Cervical shield, a silicone disc with a one-way air valve that creates suction to adhere to the cervix‡

Patients currently using these forms of contraception must switch to effective forms of contraception. They must use 2 effective forms together (at least one of which must be a primary form) consistently and correctly for at least 1 month and have a negative pregnancy test before beginning isotretinoin.

* Ortho Micronor is a registered trademark of Ortho-McNeil Pharmaceutical, Inc

‡ A cervical shield should not be confused with a cervical cap, which is an effective secondary form of contraception

EMERGENCY CONTRACEPTION

Review this section in *The iPLEDGE Program Birth Control Workbook* with the patient. She should know when to call her prescriber for possible emergency contraception. She should also realize that emergency contraception should not be used on a regular basis as a replacement for the other contraceptive forms she selected.

ABSTINENCE

For this program, all female patients of childbearing potential must fully commit to pregnancy prevention. Abstinence without appropriate contraception is not recommended for patients in the iPLEDGE program who are or have been sexually active. Abstinence may be appropriate when it is a lifestyle choice, such as religious practice, and not just a social circumstance, such as not having a current partner. If, after counseling, a sexually active patient chooses abstinence without contraception, she must understand that isotretinoin is not recommended for any female patient of childbearing potential who cannot or will not follow the contraceptive requirements of the iPLEDGE program.

REFERENCES

1 Lammer EJ, Chen DT, Hoar RM, et al Retinoic acid embryopthy *N Engl J Med* 1985;313:837-841
2 Gideon K, Avner M, Shear N Generic isotretinoin: a new risk for unborn children *CMAJ* 2004;170:1567-1568
3 Isotretinoin Prescribing Information, 2005

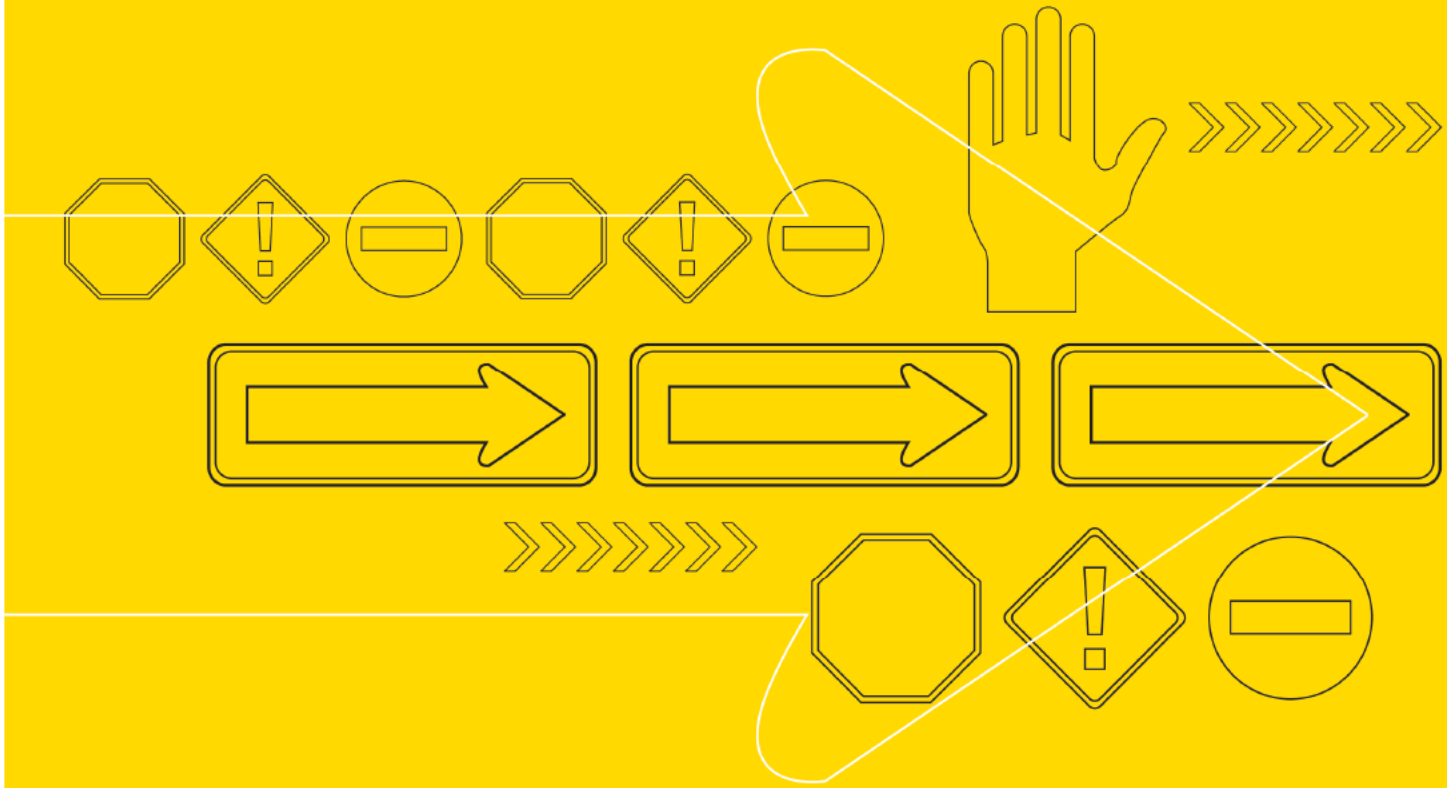
Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**

Reporting a Pregnancy

If you become aware of a pregnancy in a patient taking isotretinoin, please report the pregnancy to the iPLEDGE program by calling **1-866-495-0654** and choosing the option to "Report a Pregnancy."

Please also remind any patient who is pregnant to contact the doctor who prescribed her isotretinoin.

Please see accompanying complete product information, including boxed **CONTRAINDICATIONS AND WARNINGS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS,** and **ADVERSE REACTIONS.**



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Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amount, even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

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Fill isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

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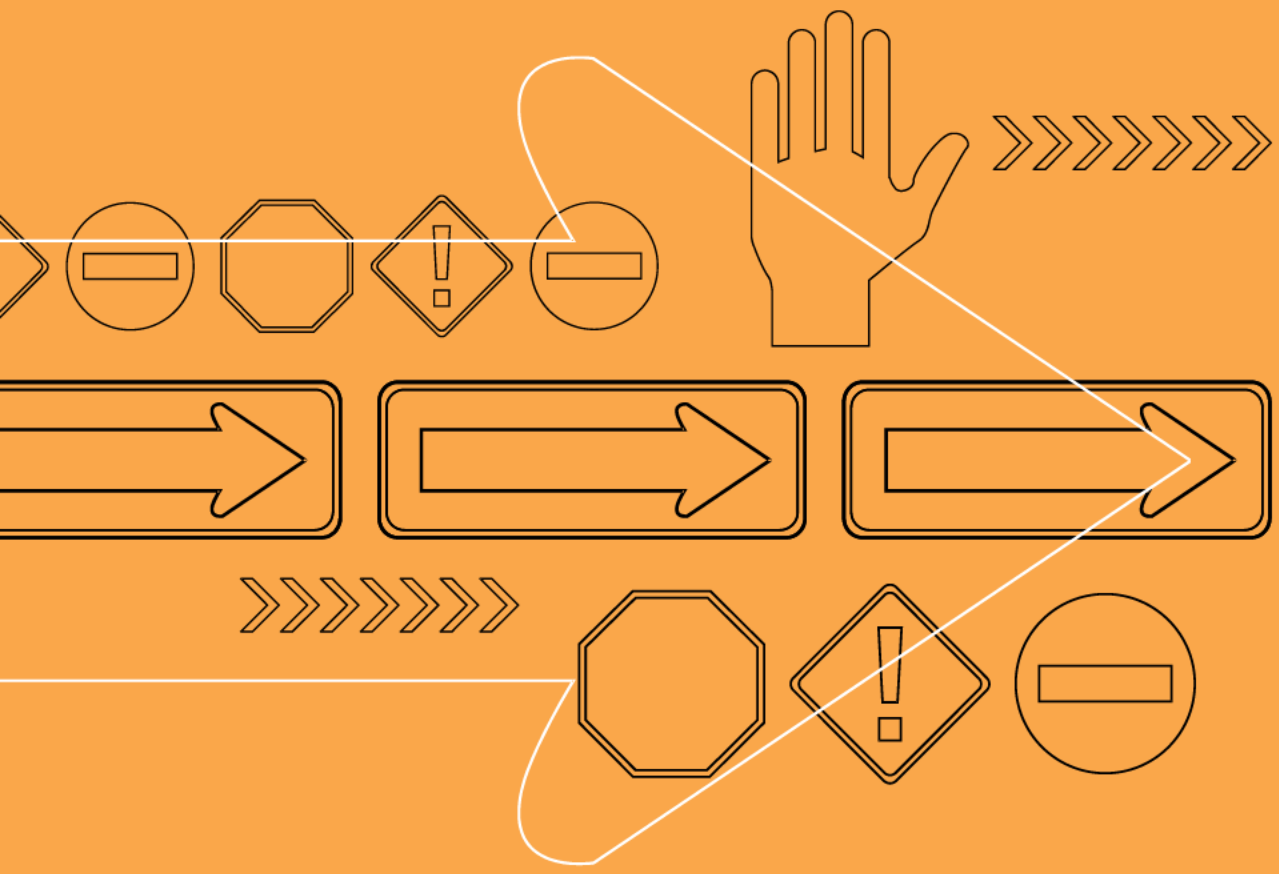
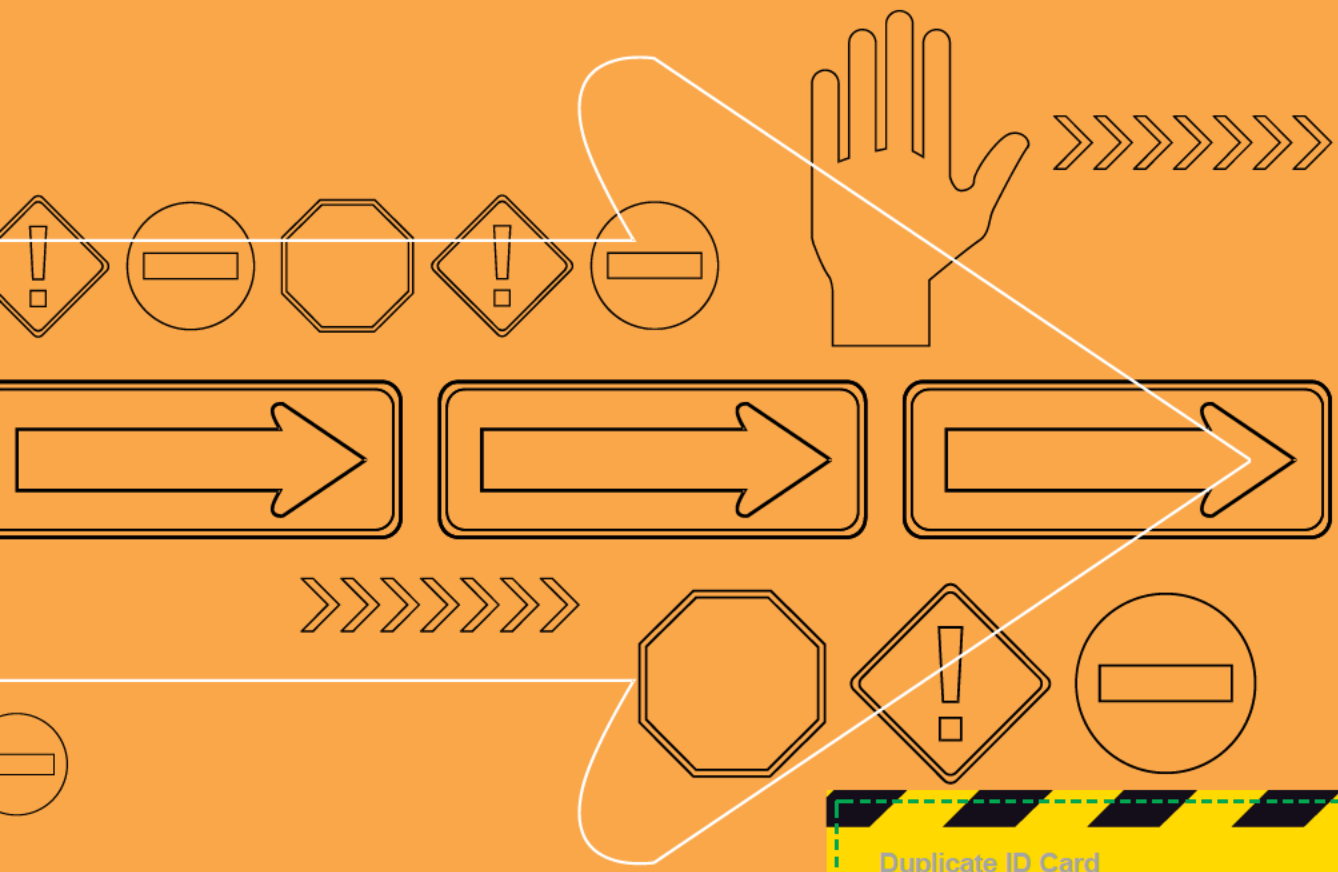
Patient Identification Card



- The card you need to take with you to doctor visits and to the pharmacy while on isotretinoin



Peel off sticker for patient's file

Duplicate ID Card

- Visit your doctor monthly
- Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
- Take this card and your prescription to the pharmacy within your 7-day window
- Do not get pregnant
- Do not share your drug
- Do not donate blood

See reverse for important safety information

iPLEDGE™ Committed to Pregnancy Prevention

Duplicate ID Card

- Visit your doctor monthly
- Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
- Take this card and your prescription to the pharmacy within your 7-day window
- Do not get pregnant
- Do not share your drug
- Do not donate blood

See reverse for important safety information

iPLEDGE™ Committed to Pregnancy Prevention

- Visit your doctor monthly
- Women who can get pregnant must:
  1. Have a monthly pregnancy test
  2. Complete monthly questions by web at www.ipledgeprogram.com or by calling 1-866-495-0654
- Take this card and your prescription to the pharmacy within your 7-day window
- Do not get pregnant
- Do not share your drug
- Do not donate blood

See reverse for important safety information

iPLEDGE™ Committed to Pregnancy Prevention

Stop isotretinoin and call your doctor right away if you are pregnant.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

Stop isotretinoin and call your doctor right away if you are pregnant.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

- Start to feel sad or have crying spells
- Lose interest in activities you once enjoyed
- Sleep too much or have trouble sleeping
- Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

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Stop isotretinoin and call your doctor right away if you are pregnant.

Stop isotretinoin and call your doctor right away if you or a family member notices that you have any of the following signs and symptoms of depression or psychosis:

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- Have a change in your appetite or body weight
- Have trouble concentrating
- Withdraw from your friends or family
- Feel like you have no energy
- Have feelings of worthlessness or guilt
- Start having thoughts about hurting yourself or taking your own life (suicidal thoughts)
- Start acting on dangerous impulses
- Start seeing or hearing things that are not real

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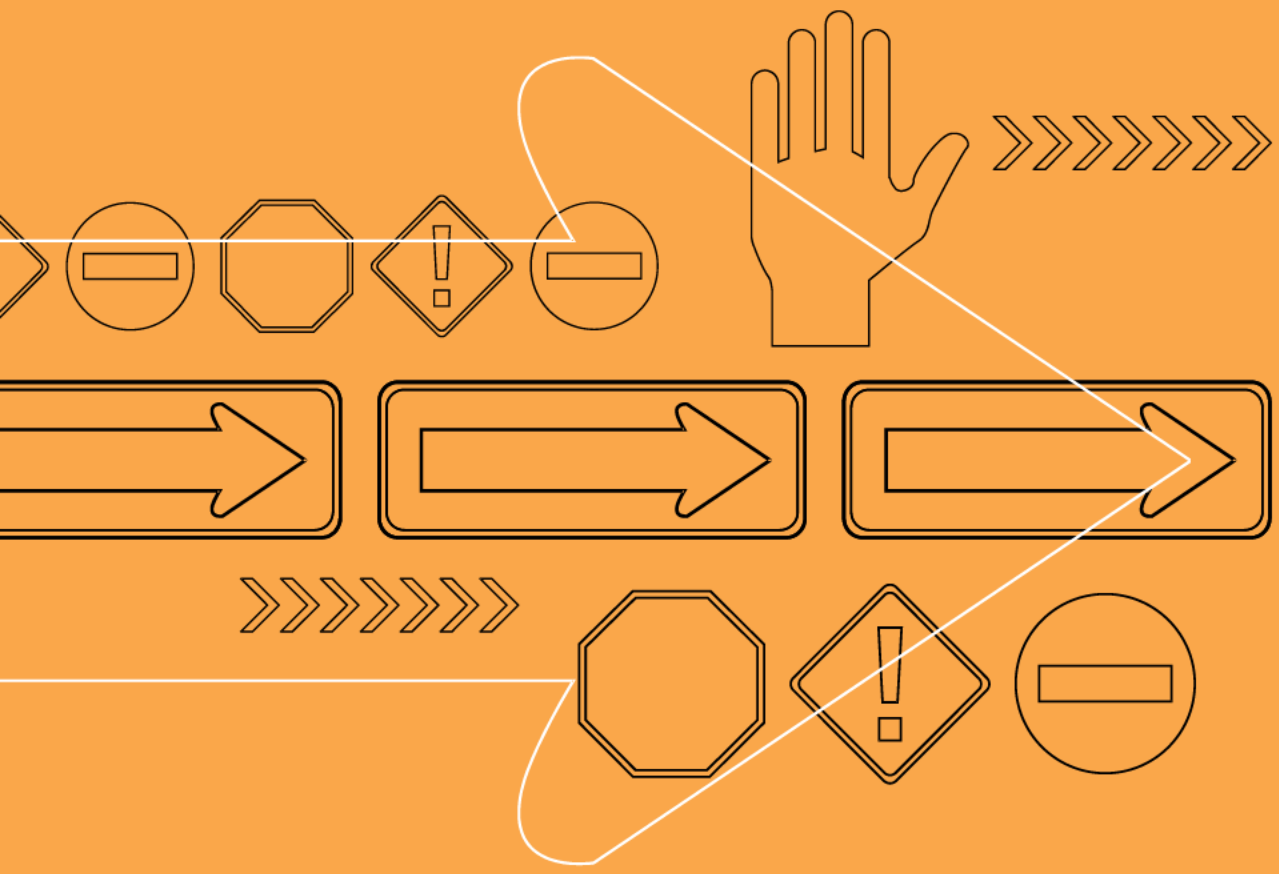


Important forms you must sign before you begin taking isotretinoin

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Patient Information/Informed Consent (for all patients):

To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and agree to follow your doctor's instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, _____
(Patient's Name)

understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.

Initials: _____

2. My doctor has told me about my choices for treating my acne.

Initials: _____

3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. [Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)].

Initials: _____

4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, "anxious" or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives. There were reports that some of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. No one knows if isotretinoin caused these behaviors or if they would have happened even if the person did not take isotretinoin. Some people have had other signs of depression while taking isotretinoin (see #7).

Initials: _____

5. Before I start taking isotretinoin, I agree to tell my doctor if I have **ever** had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.

Initials: _____

6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or had any other serious mental problems.

Initials: _____

7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen. I:
   - Start to feel sad or have crying spells
   - Lose interest in activities I once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in my appetite or body weight
   - Have trouble concentrating
   - Withdraw from my friends or family
   - Feel like I have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting myself or taking my own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real

   Initials: _____

8. **I agree to return to see my doctor every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.**

Initials: _____

9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.

Initials: _____

10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.

Initials: _____

11. I have read *The iPLEDGE Program Patient Introductory Brochure* and other materials my provider gave me containing important safety information about isotretinoin. I understand all the information I received.

Initials: _____

12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.

Initials: _____

I now allow my doctor _____ to begin my treatment with isotretinoin.

Patient Signature: _____ Date: _____

Parent/Guardian Signature (if under age 18): _____ Date: _____

Patient Name (print) _____

Patient Address _____ Telephone _____ – _____ – _____

I have:

- fully explained to the patient, _____, the nature and purpose of isotretinoin treatment, including its benefits and risks
- given the patient the appropriate educational materials, *The iPLEDGE Program Patient Introductory Brochure* and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
- answered those questions to the best of my ability

Doctor Signature: _____ Date: _____

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT'S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

To be completed by the patient (and her parent or guardian* if patient is under age 18) and signed by her doctor.

Read each item below and initial in the space provided to show that you understand each item and agree to follow your doctor's instructions. **Do not sign this consent and do not take isotretinoin if there is anything that you do not understand.**

*A parent or guardian of a minor patient (under age 18) must also read and initial each item before signing the consent.

_____
(Patient's Name)

1. I understand that there is a very high chance that my unborn baby could have severe birth defects if I am pregnant or become pregnant while taking isotretinoin. This can happen with any amount and even if taken for short periods of time. This is why I must not be pregnant while taking isotretinoin.
   Initial: _____
2. I understand that I must not get pregnant 1 month before, during the entire time of my treatment, and for 1 month after the end of my treatment with isotretinoin.
   Initial: _____
3. I understand that I must avoid sexual intercourse completely, or I must use 2 separate, effective forms of birth control (contraception) **at the same time.** The only exceptions are if I have had surgery to remove the uterus (a hysterectomy) or both of my ovaries (bilateral oophorectomy), or my doctor has medically confirmed that I am post-menopausal.
   Initial: _____
4. I understand that hormonal birth control products are among the most effective forms of birth control. Combination birth control pills and other hormonal products include skin patches, shots, under-the-skin implants, vaginal rings, and intrauterine devices (IUDs). Any form of birth control can fail. That is why I must use 2 different birth control methods at the same time, starting 1 month before, during, and for 1 month after stopping therapy every time I have sexual intercourse, even if 1 of the methods I choose is hormonal birth control.
   Initial: _____
5. I understand that the following are effective forms of birth control:

Primary forms	Secondary forms
• tubal sterilization (tying your tubes) • partner's vasectomy • intrauterine device • hormonal (combination birth control pills, skin patches, shots, under-the-skin implants, or vaginal ring)	*Barrier forms* • male latex condom with or without spermicide • diaphragm with spermicide • cervical cap with spermicide *Others:* • vaginal sponge (contains spermicide)

   A diaphragm and cervical cap must each be used with spermicide, a special cream that kills sperm

   I understand that at least 1 of my 2 forms of birth control must be a primary method.
   Initial: _____
6. I will talk with my doctor about any medicines including herbal products I plan to take during my isotretinoin treatment because hormonal birth control methods may not work if I am taking certain medicines or herbal products.
   Initial: _____
7. I may receive a free birth control counseling session from a doctor or other family planning expert. My isotretinoin doctor can give me an isotretinoin Patient Referral Form for this free consultation.
   Initial: _____
8. I must begin using the birth control methods I have chosen as described above at least 1 month before I start taking isotretinoin.
   Initial: _____
9. I cannot get my first prescription for isotretinoin unless my doctor has told me that I have 2 negative pregnancy test results. The first pregnancy test should be done when my doctor decides to prescribe isotretinoin. The second pregnancy test must be done in a lab during the first 5 days of my menstrual period right before starting isotretinoin therapy treatment, or as instructed by my doctor. I will then have 1 pregnancy test; in a lab:
   - every month during treatment
   - at the end of treatment
   - and 1 month after stopping treatment

   I must not start taking isotretinoin until I am sure that I am not pregnant, have negative results from 2 pregnancy tests, and the second test has been done in a lab.
   Initial: _____
10. I have read and understand the materials my doctor has given to me, including *The iPLEDGE Program Guide for Isotretinoin for Female Patients Who Can Get Pregnant, The iPLEDGE Birth Control Workbook* and *The iPLEDGE Program Patient Introductory Brochure.*

    My doctor gave me and asked me to watch the DVD containing a video about birth control and a video about birth defects and isotretinoin.

    I was told about a private counseling line that I may call for more information about birth control. I have received information on emergency birth control.
    Initial: _____
11. I must stop taking isotretinoin right away and call my doctor if I get pregnant, miss my expected menstrual period, stop using birth control, or have sexual intercourse without using my 2 birth control methods at any time.
    Initial: _____
12. My doctor gave me information about the purpose and importance of providing information to the iPLEDGE program should I become pregnant while taking isotretinoin or within 1 month of the last dose. I understand that if I become pregnant, information about my pregnancy, my health, and my baby's health may be shared with the makers of isotretinoin, authorized parties who maintain the iPLEDGE program for the makers of isotretinoin, and government health regulatory authorities.
    Initial: _____
13. I understand that being qualified to receive isotretinoin in the iPLEDGE program means that I:
    - have had 2 negative urine or blood pregnancy tests before receiving the first isotretinoin prescription. The second test must be done in a lab. I must have a negative result from a urine or blood pregnancy test done in a lab repeated each month before I receive another isotretinoin prescription.
    - have chosen and agreed to use 2 forms of effective birth control at the same time. At least 1 method must be a primary form of birth control, **unless I have chosen never to have sexual contact with a male (abstinence)**, or I have undergone a hysterectomy. I must use 2 forms of birth control for at least 1 month before I start isotretinoin therapy, during therapy, and for 1 month after stopping therapy. I must receive counseling, repeated on a monthly basis, about birth control and behaviors associated with an increased risk of pregnancy.
    - have signed a Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) that contains warnings about the chance of possible birth defects if I am pregnant or become pregnant and my unborn baby is exposed to isotretinoin.
    - have interacted with the iPLEDGE program before starting isotretinoin and on a monthly basis to answer questions on the program requirements and to enter my two chosen forms of birth control.

    Initial: _____

My doctor has answered all my questions about isotretinoin and I understand that it is my responsibility not to get pregnant 1 month before, during isotretinoin treatment, or for 1 month after I stop taking isotretinoin.

Initial: _____

I now authorize my doctor _____ to begin my treatment with isotretinoin.

Patient Signature: _____ Date: _____

Parent/Guardian Signature (if under age 18): _____ Date: _____

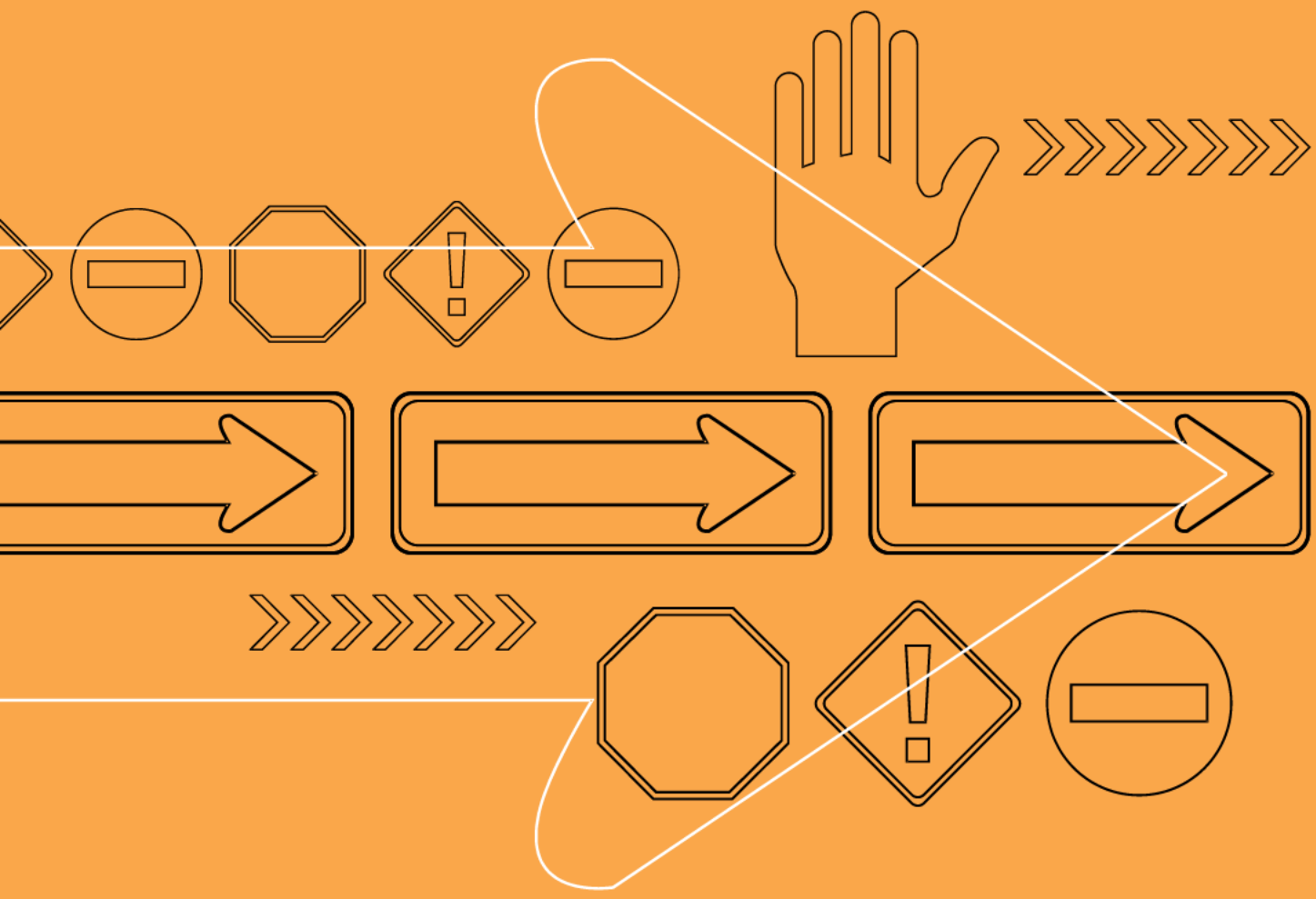
Please print: Patient Name and Address _____ Telephone _____

I have fully explained to the patient, _____, the nature and purpose of the treatment described above and the risks to female patients of childbearing potential. I have asked the patient if she has any questions regarding her treatment with isotretinoin and have answered those questions to the best of my ability.

Doctor Signature: _____ Date: _____

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT'S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

Patient Flowchart



A flowchart to assist you with the iPLEDGE program requirements

REGISTERED PATIENTS

iPLEDGE™ Committed to Pregnancy Prevention

Female patients of childbearing potential (FCBP)

BEFORE TREATMENT

- **Sign** a Patient Information/Informed Consent (for all patients) form for treatment
- **Sign** a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form
- **Get** a screening urine/blood pregnancy test
- **Receive** patient ID card
- **Choose** 2 effective forms of birth control
- **Start** using the 2 forms of birth control simultaneously for at least 1 month
- **Get** a second pregnancy test within the first 5 days of your menstrual period (patient with irregular cycle please check with your prescriber) in an approved lab
- **Access*** the iPLEDGE system to answer questions and to enter the 2 chosen forms of birth control. You can only answer your questions after your doctor has entered your test results into the iPLEDGE System
- **Get** a prescription for a maximum 30-day supply

EACH MONTH DURING THERAPY

- **Use** the 2 forms of birth control simultaneously
- **See** your doctor for a monthly pregnancy test in an approved lab
- **Access*** the iPLEDGE system to answer questions and confirm the 2 forms of birth control
- **Get** a prescription for a maximum 30-day supply
- **Do not** donate blood

AFTER TREATMENT

- **Get** a pregnancy test in an approved lab after the last dose
- **Continue** to use the 2 forms of birth control simultaneously for 1 month after the last dose
- **Do not** donate blood for 1 month after the last dose
- **Get** a final pregnancy test 1 month after the last dose

Male patients/Female patients not of childbearing potential (FNCBP)

BEFORE TREATMENT

- **Sign** a Patient Information/Informed Consent (for all patients) form for treatment
- **Receive** patient ID card
- **Get** a prescription for a maximum 30-day supply

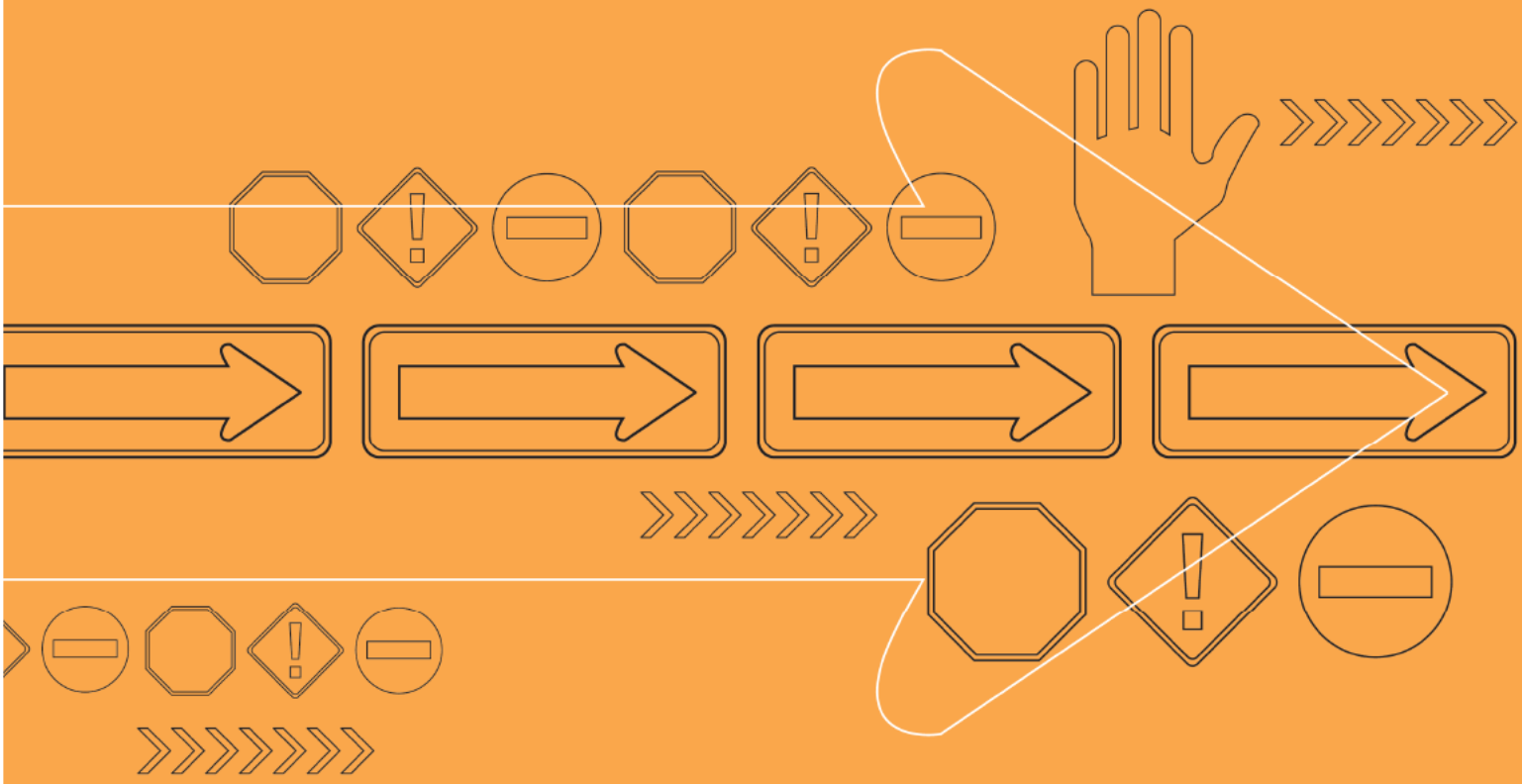
EACH MONTH DURING THERAPY

- **See** your doctor to get a prescription
- **Get** a prescription for a maximum 30-day supply
- **Do not** donate blood

AFTER TREATMENT

- **Do not** donate blood for 1 month after your last dose

*You can access the system via the web site, **www ipledgeprogram.com**, or the telephone, **1-866-495-0654**.



www.ipledgeprogram.com 1-866-495-0654

WARNING

For your health and safety, please read this booklet carefully. Also, be sure you understand what your doctor has told you about isotretinoin before starting treatment.

Do not take isotretinoin if you are pregnant, plan to become pregnant, or become pregnant during isotretinoin treatment. Isotretinoin causes severe birth defects (deformed babies), loss of a baby before birth (miscarriage), death of a baby and early (premature) births. There is no accurate means of determining whether an exposed fetus has been affected.

IMPORTANT NOTICE

Use only isotretinoin products approved by the US Food and Drug Administration.

Fill and pick up your isotretinoin prescriptions *only* at pharmacies that are licensed in the United States and are registered with and activated in the iPLEDGE program.

iPLEDGE™

Committed to Pregnancy Prevention

Reference ID: 3122588

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Patient Information/Informed Consent (for all patients):

To be completed by patient (and parent or guardian if patient is under age 18) and signed by the doctor.

Read each item below and initial in the space provided if you understand each item and agree to follow your doctor's instructions. A parent or guardian of a patient under age 18 must also read and understand each item before signing the agreement.

Do not sign this agreement and do not take isotretinoin if there is anything that you do not understand about all the information you have received about using isotretinoin.

1. I, _____
(Patient's Name)
understand that isotretinoin is a medicine used to treat severe nodular acne that cannot be cleared up by any other acne treatments, including antibiotics. In severe nodular acne, many red, swollen, tender lumps form in the skin. If untreated, severe nodular acne can lead to permanent scars.
Initials: _____
2. My doctor has told me about my choices for treating my acne.
Initials: _____
3. I understand that there are serious side effects that may happen while I am taking isotretinoin. These have been explained to me. These side effects include serious birth defects in babies of pregnant patients. [Note: There is a second Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)].
Initials: _____
4. I understand that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, "anxious" or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts). Some people tried to end their own lives. And some people have ended their own lives. There were reports that some of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. No one knows if isotretinoin caused these behaviors or if they would have happened even if the person did not take isotretinoin. Some people have had other signs of depression while taking isotretinoin (see #7).
Initials: _____
5. Before I start taking isotretinoin, I agree to tell my doctor if I have **ever** had symptoms of depression (see #7), been psychotic, attempted suicide, had any other mental problems, or take medicine for any of these problems. Being psychotic means having a loss of contact with reality, such as hearing voices or seeing things that are not there.
Initials: _____
6. Before I start taking isotretinoin, I agree to tell my doctor if, to the best of my knowledge, anyone in my family has ever had symptoms of depression, been psychotic, attempted suicide, or had any other serious mental problems.
Initials: _____
7. Once I start taking isotretinoin, I agree to stop using isotretinoin and tell my doctor right away if any of the following signs and symptoms of depression or psychosis happen. I:
   - Start to feel sad or have crying spells
   - Lose interest in activities I once enjoyed
   - Sleep too much or have trouble sleeping
   - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
   - Have a change in my appetite or body weight
   - Have trouble concentrating
   - Withdraw from my friends or family
   - Feel like I have no energy
   - Have feelings of worthlessness or guilt
   - Start having thoughts about hurting myself or taking my own life (suicidal thoughts)
   - Start acting on dangerous impulses
   - Start seeing or hearing things that are not real

   Initials: _____
8. **I agree to return to see my doctor every month I take isotretinoin to get a new prescription for isotretinoin, to check my progress, and to check for signs of side effects.**
Initials: _____
9. Isotretinoin will be prescribed just for me — I will not share isotretinoin with other people because it may cause serious side effects, including birth defects.
Initials: _____
10. I will not give blood while taking isotretinoin or for 1 month after I stop taking isotretinoin. I understand that if someone who is pregnant gets my donated blood, her baby may be exposed to isotretinoin and may be born with serious birth defects.
Initials: _____
11. I have read *The iPLEDGE Program Patient Introductory Brochure* and other materials my provider gave me containing important safety information about isotretinoin. I understand all the information I received.
Initials: _____
12. My doctor and I have decided I should take isotretinoin. I understand that I must be qualified in the iPLEDGE program to have my prescription filled each month. I understand that I can stop taking isotretinoin at any time. I agree to tell my doctor if I stop taking isotretinoin.
Initials: _____

I now allow my doctor _____ to begin my treatment with isotretinoin.

Patient Signature: _____ Date: _____

Parent/Guardian Signature (if under age 18): _____ Date: _____

Patient Name (print) _____

Patient Address _____ Telephone_____–_____–_____

I have:

- fully explained to the patient, _____, the nature and purpose of isotretinoin treatment, including its benefits and risks
- given the patient the appropriate educational materials, *The iPLEDGE Program Patient Introductory Brochure* and asked the patient if he/she has any questions regarding his/her treatment with isotretinoin
- answered those questions to the best of my ability

Doctor Signature: _____ Date: _____

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT'S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE–Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant)

To be completed by the patient (and her parent or guardian* if patient is under age 18) and signed by her doctor.

Read each item below and initial in the space provided to show that you understand each item and agree to follow your doctor's instructions. **Do not sign this consent and do not take isotretinoin if there is anything that you do not understand.**

*A parent or guardian of a minor patient (under age 18) must also read and initial each item before signing the consent.

_____
(Patient's Name)

1. I understand that there is a very high chance that my unborn baby could have severe birth defects if I am pregnant or become pregnant while taking isotretinoin. This can happen with any amount and even if taken for short periods of time. This is why I must not be pregnant while taking isotretinoin.
   Initial: _____
2. I understand that I must not get pregnant 1 month before, during the entire time of my treatment, and for 1 month after the end of my treatment with isotretinoin.
   Initial: _____
3. I understand that I must avoid sexual intercourse completely, or I must use 2 separate, effective forms of birth control (contraception) **at the same time**. The only exceptions are if I have had surgery to remove the uterus (a hysterectomy) or both of my ovaries (bilateral oophorectomy), or my doctor has medically confirmed that I am post-menopausal.
   Initial: _____
4. I understand that hormonal birth control products are among the most effective forms of birth control. Combination birth control pills and other hormonal products include skin patches, shots, under-the-skin implants, vaginal rings, and intrauterine devices (IUDs). Any form of birth control can fail. That is why I must use 2 different birth control methods at the same time, starting 1 month before, during, and for 1 month after stopping therapy every time I have sexual intercourse, even if 1 of the methods I choose is hormonal birth control.
   Initial: _____
5. I understand that the following are effective forms of birth control:

Primary forms	Secondary forms
• tubal sterilization (tying your tubes) • partner's vasectomy • intrauterine device • hormonal (combination birth control pills, skin patches, shots, under-the-skin implants, or vaginal ring)	*Barrier forms* • male latex condom with or without spermicide • diaphragm with spermicide • cervical cap with spermicide *Others:* • vaginal sponge (contains spermicide)

   A diaphragm and cervical cap must each be used with spermicide, a special cream that kills sperm

   I understand that at least 1 of my 2 forms of birth control must be a primary method.
   Initial: _____
6. I will talk with my doctor about any medicines including herbal products I plan to take during my isotretinoin treatment because hormonal birth control methods may not work if I am taking certain medicines or herbal products.
   Initial: _____
7. I may receive a free birth control counseling session from a doctor or other family planning expert. My isotretinoin doctor can give me an isotretinoin Patient Referral Form for this free consultation.
   Initial: _____
8. I must begin using the birth control methods I have chosen as described above at least 1 month before I start taking isotretinoin.
   Initial: _____
9. I cannot get my first prescription for isotretinoin unless my doctor has told me that I have 2 negative pregnancy test results. The first pregnancy test should be done when my doctor decides to prescribe isotretinoin. The second pregnancy test must be done in a lab during the first 5 days of my menstrual period right before starting isotretinoin therapy treatment, or as instructed by my doctor. I will then have 1 pregnancy test; in a lab:
   - every month during treatment
   - at the end of treatment
   - and 1 month after stopping treatment

   I must not start taking isotretinoin until I am sure that I am not pregnant, have negative results from 2 pregnancy tests, and the second test has been done in a lab.
   Initial: _____
10. I have read and understand the materials my doctor has given to me, including *The iPLEDGE Program Guide for Isotretinoin for Female Patients Who Can Get Pregnant, The iPLEDGE Birth Control Workbook* and *The iPLEDGE Program Patient Introductory Brochure.*

    My doctor gave me and asked me to watch the DVD containing a video about birth control and a video about birth defects and isotretinoin.

    I was told about a private counseling line that I may call for more information about birth control. I have received information on emergency birth control.
    Initial: _____
11. I must stop taking isotretinoin right away and call my doctor if I get pregnant, miss my expected menstrual period, stop using birth control, or have sexual intercourse without using my 2 birth control methods at any time.
    Initial: _____
12. My doctor gave me information about the purpose and importance of providing information to the iPLEDGE program should I become pregnant while taking isotretinoin or within 1 month of the last dose. I understand that if I become pregnant, information about my pregnancy, my health, and my baby's health may be shared with the makers of isotretinoin, authorized parties who maintain the iPLEDGE program for the makers of isotretinoin, and government health regulatory authorities.
    Initial: _____
13. I understand that being qualified to receive isotretinoin in the iPLEDGE program means that I:
    - have had 2 negative urine or blood pregnancy tests before receiving the first isotretinoin prescription. The second test must be done in a lab. I must have a negative result from a urine or blood pregnancy test done in a lab repeated each month before I receive another isotretinoin prescription.
    - have chosen and agreed to use 2 forms of effective birth control at the same time. At least 1 method must be a primary form of birth control, **unless I have chosen never to have sexual contact with a male (abstinence)**, or I have undergone a hysterectomy. I must use 2 forms of birth control for at least 1 month before I start isotretinoin therapy, during therapy, and for 1 month after stopping therapy. I must receive counseling, repeated on a monthly basis, about birth control and behaviors associated with an increased risk of pregnancy.
    - have signed a Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) that contains warnings about the chance of possible birth defects if I am pregnant or become pregnant and my unborn baby is exposed to isotretinoin.
    - have interacted with the iPLEDGE program before starting isotretinoin and on a monthly basis to answer questions on the program requirements and to enter my two chosen forms of birth control.

    Initial: _____

My doctor has answered all my questions about isotretinoin and I understand that it is my responsibility not to get pregnant 1 month before, during isotretinoin treatment, or for 1 month after I stop taking isotretinoin.

Initial: _____

I now authorize my doctor _____ to begin my treatment with isotretinoin.

Patient Signature: _____ Date: _____

Parent/Guardian Signature (if under age 18): _____ Date: _____

Please print: Patient Name and Address_____ Telephone_____

I have fully explained to the patient, _____, the nature and purpose of the treatment described above and the risks to female patients of childbearing potential. I have asked the patient if she has any questions regarding her treatment with isotretinoin and have answered those questions to the best of my ability.

Doctor Signature: _____ Date: _____

PLACE THE ORIGINAL SIGNED DOCUMENTS IN THE PATIENT'S MEDICAL RECORD.
PLEASE PROVIDE A COPY TO THE PATIENT.

II.D.2 Patient Understanding

Patient Comprehension Questions

Program Steps	
One goal of iPLEDGE is making sure pregnant women do not take isotretinoin	1. True
	2. False
You are in your third month of treatment, in order to get your isotretinoin prescription, you must	1. Have a urine test for infection.
	2. Have a negative pregnancy test done in a laboratory, discuss birth control with your doctor and answer questions in the iPLEDGE system.
The confidential iPLEDGE Program Pregnancy Registry collects information on pregnancies that happen during isotretinoin treatment or within 1 month after the last dose	1. True
	2. False
Each month you need to answer questions and:	1. Enter 2 forms of birth control you are using.
	2. Do a home pregnancy test to show the pharmacist.
For 1 month after your last dose, you must use 2 effective forms of birth control together all the time	1. True
	2. False
Your doctor tells you that you to come back 1 month after your final dose. You return to the office to:	1. Get a prescription for 30 days.
	2. Talk with your doctor about birth control.
	3. Get the last pregnancy test.
Your doctor tells you that you need to have a pregnancy test each month. You would:	1. Refuse the test because you know you are not pregnant.
	2. Agree to have the pregnancy test because it is important to know if you are pregnant before taking isotretinoin.
	3. Wait a week before getting the test done.
You must keep your appointment every month because:	1. It is important for you and your doctor to interact before you get a maximum 30 day supply of isotretinoin each month.
	2. You need to sign a consent form each month.
	You need to tell your doctor where to call in your prescription.

General Contraception Requirements	
Many women who became pregnant while taking isotretinoin were using only 1 form of birth control.	1. True 2. False
Using alcohol and drugs can make it more difficult to use your birth control properly when having sex.	1. True 2. False
You can change one primary form of birth control for another without talking with the doctor first.	1. True 2. False
You can use any forms of birth control for iPLEDGE	1. True 2. False
You are using 2 effective forms of birth control in the month after your last dose. Your partner's condom breaks. You would:	1. Forget about it since you have finished isotretinoin 2. Call your doctor to see if you might need emergency birth control. 3. Get a home pregnancy test kit to see if you are pregnant.
While you are taking isotretinoin, you must use 2 effective forms of birth control together all the time	1. True 2. False
You should talk to your doctor about birth control:	1. Each month during your office visit. 2. Only when you have a problem. 3. Only when you sign the second consent form.
You have finished your last dose of isotretinoin. Your doctor has ordered a pregnancy test. For the next month, you:	1. Continue to use 2 effective forms of birth control together all the time. 2. Stop using your secondary form because you are not taking isotretinoin. 3. Go for the pregnancy test at any time during the month.

Birth Defects and Pregnancy	
Which of the following are signs you might be pregnant?	1. You miss your menstrual period
	2. You have nausea, sometimes referred to as morning sickness.
	3. Your breasts feel tender, like at the beginning of a menstrual period.
	4. Any of the above is a sign you might be pregnancy.
The risk for birth defects for a baby whose mother took isotretinoin is	1. So low that you do not have to worry.
	2. Low enough so you do not need birth control.
	3. Very high even if a woman takes a small amount of isotretinoin.
You cannot get pregnant if you have sex under water	1. True
	2. False
You can get pregnant any time and anywhere you have sex, particularly unprotected sex.	1. True
	2. False
You can get pregnant if you have not started having menstrual periods.	1. True
	2. False
Which of the following birth defects may be caused by isotretinoin?	1. No ears
	2. Heart problems
	3. Small jaw and misshaped head
	4. A child could have any or all of these birth defects.
You think you may be pregnant and you have taken isotretinoin. You would:	1. Not worry because it was only a few doses.
	2. Stop isotretinoin and call your doctor. Even the smallest amount of isotretinoin may cause birth defects.
It's okay to take isotretinoin when	1. You are using one effective form of birth control.
	2. You are using 2 effective forms of birth control all the time.
	3. You may be pregnant.
You cannot get pregnant if:	1. You never have sex with a man.
	2. You miss your hormone shots.
	3. You use only a condom with spermicide.

Safety Information	
I must not give blood while taking isotretinoin and 1 month after stopping isotretinoin.	1. True
	2. False
I will not share my isotretinoin with anyone.	1. Agree
	2. Disagree
Your neighbor wants to try your isotretinoin. You tell her or him:	1. I must not share isotretinoin.
	2. It might be harmful to her or him.
	3. You tell her or him both of these reasons.
The Red Cross calls you to give blood right after your last dose. You tell them:	1. I can never give blood again.
	2. I cannot give blood until 1 month after my last dose of isotretinoin.
The Red Cross calls you to give blood during your first month after your last dose. You tell them:	1. Giving blood is not safe for me.
	2. I cannot give blood until 1 month after my last dose of isotretinoin.
	I can never give blood again.

Filling a prescription	
Your pharmacist can fill and dispense your prescription only after:	1. You phone it in. 2. Checking with the iPLEDGE system to see if you can get isotretinoin. 3. You email it in.
You can get a prescription for isotretinoin only if:	1. You pregnancy test is negative. 2. You answered the questions correctly. 3. You entered your 2 forms of birth control. 4. Your doctor entered your 2 forms of birth control. 5. All of these.
You had a pregnancy test on Tuesday for your next prescription. What is the last day you can fill and pick up your prescription?	1. Later that same day (7 hours later) 2. By Friday before the pharmacy closes 3. On Monday of the next week
You can fill and pick up your prescription any time you want	1. True 2. False
Your doctor has entered your negative pregnancy test results and your two forms of birth control into the iPLEDGE system and gives you a prescription. Before you can fill and pick up the prescription you must:	1. Answer your comprehension questions in the iPLEDGE system. 2. Schedule your next appointment with your doctor 3. Sign your informed consent each month.

Contraception Choices	
You missed 2 birth control pills earlier this week. You would:	1. Not have sex for the rest of the cycle, but keep taking the birth control pills as prescribed
	2. Have sex whenever you want.
I have been using birth control pills for 5 years and have not gotten pregnant. Why do I need another form of birth control now?	1. Any form of birth control can fail
	2. The birth defects are too severe to risk getting pregnant
	3. Isotretinoin may change how well some forms of birth control work
	4. All of these
Birth control pills work best when you take them every day as prescribed.	1. True
	2. False
You can switch to the progesterone-only mini-pill for your primary form of birth control while you are taking isotretinoin.	1. True
	2. False
Birth control pills may not work as well when you are taking isotretinoin. It is important to:	1. Take two birth control pills every day.
	2. Remember to take your birth control pill every day and always use a second effective method to help prevent pregnancy.
	3. Take your birth control pill only before having sex
I use my primary form of birth control exactly as prescribed and my partner uses condoms as the second form. My partner does not have any condoms with him tonight. We would:	1. Have sex anyway.
	2. Wait until he can buy a condom.
	3. Have sex but use withdrawal.
I use my primary form of birth control exactly as prescribed and my partner uses condoms with spermicide as the second form. My partner's condom breaks. I would:	1. Not worry about getting pregnant.
	2. Worry that I may become pregnant but not do anything.
	3. Call my doctor to talk about emergency birth control.
My partner has only one condom with him. We would:	1. Have sex more than once and reuse the condom.
	2. Have sex once and wait until he can buy more condoms.
	3. Have sex but use withdrawal.

For the iPLEDGE program, condoms can be used with or without spermicide.	1. True
	2. False
If you use lubricant with a latex condom, it should be a water-based lubricant.	1. True
	2. False
Your partner should put his condom on:	1. Any time during sex.
	2. As soon as he gets an erection, because waiting too long lets sperm leak out.
	3. Only when he remembers.
You find a hole in your diaphragm after you had sex. You should:	1. Forget about it since you were near your period.
	2. Call your doctor to see if you might need emergency birth control.
For the iPLEDGE program, diaphragms can be used with or without spermicide.	1. True
	2. False
After sex, your diaphragm should stay in place for:	1. 24 hours or more.
	2. 2 to 4 hours
	3. At least 6 hours and up to 24 hours.
You and your partner want to have sex a second time after you put in your diaphragm. You must:	1. Put spermicide in your vagina again before you have sex.
	2. Have sex again without using more spermicide for up to 24 hours at a time.
	3. Take out your diaphragm and clean it before having sex again.
Your gynecologist or family doctor needs to check how your diaphragm fits:	1. Every time you have sex.
	2. Every 2 years or if you gain or lose 10 pounds.
	3. Every 2 months.
The diaphragm with spermicide can help prevent:	1. Pregnancy
	2. The spread of HIV (AIDS)
	3. The spread of other sexually transmitted diseases (STD's)
I use my primary form of birth control exactly as prescribed and a cervical cap with spermicide as my second form. I forgot my cap at home. I would:	1. Have sex anyway.
	2. Wait until I can use the cervical cap with spermicide.
	3. Have sex but use withdrawal.
For the iPledge program cervical caps can be used with or without spermicide.	1. True
	2. False
If you use a lubricant with your cervical Cap, it should be a water-based lubricant.	1. True
	2. False

You find a hole in your cervical cap after you had sex. You should:	1. Forget about it since you were near your period.
	2. Call your doctor to see if you might need emergency birth control.
You and your partner want to have sex a second time after you put in your cervical cap. You do not need to put in more spermicide.	1. True
	2. False
After sex, your cervical cap should stay in place for:	1. 24 hours.
	2. 4 to 8 hours.
	3. At least 6 hours and up to 48 hours.
The cervical cap with spermicide can help prevent:	1. Pregnancy.
	2. The spread of HIV (AIDS)
	3. The spread of other sexually transmitted diseases (STD's)
I use my primary form of birth control exactly as prescribed and use a vaginal sponge as my second form. I ran out of sponges tonight. My partner and I would:	1. Wait until I can buy more sponges or some other secondary form of birth control.
	2. Have sex anyway.
	3. Have sex but use withdrawal.
I use my primary form of birth control exactly as prescribed, but I forgot to put in my vaginal sponge this one time. I would:	1. Not worry that I could have gotten pregnant.
	2. Worry that I may become pregnant, but do nothing.
	3. Call my doctor to talk about emergency birth control.
The vaginal sponge can help prevent:	1. The spread of HIV (AIDS)
	2. The spread of other sexually transmitted diseases (STD's)
	3. Pregnancy
You should insert your sponge:	1. Any time during sex.
	2. Any time up to 30 hours before you have sex.
	3. Only when you remember.
After sex, your sponge should stay in place for:	1. 24 hours or more.
	2. 2 to 4 hours.
	3. At least 6 hours.
If you and your partner want to have sex a second time after you put in your sponge:	1. You must put spermicide in your vagina again before you have sex.
	2. You can have sex again without using a new sponge for up to 30 hours at a time.
	3. You must take out your sponge and out in a new one before having sex.
I have been using the hormonal skin patch perfectly for over a year and have not gotten pregnant. Why do I need another form of birth control now?	1. Any form of birth control can fail.
	2. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.

	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.
I have been using the hormonal skin patch, but I was 2 days late changing it. I would:	1. Not have sex for the rest of my cycle, but keep using the hormonal patch as prescribed.
	2. Have sex when I want to, my partner's condom is enough.
I am using the hormonal skin patch exactly as my doctor tells me. I should not put it on:	1. My upper outer arm.
	2. My stomach or upper body.
	3. My breasts.
The hormonal skin patch works best when you change it every week as prescribed.	1. True
	2. False
You can get pregnant using the hormonal patch if:	1. It becomes loose or falls off for more than 24 hours.
	2. You leave the same hormonal patch on more than one week.
	3. Both 1 and 2.
My hormonal vaginal ring slipped out and I did not replace it within 3 hours, I would:	1. Not have sex for the rest of my cycle, but keep using the hormonal vaginal ring as prescribed.
	2. Have sex when I want to, my partner's condom with spermicide is enough.
I have been using a hormonal vaginal ring for 1 year and have not gotten pregnant. Why do I need another form of birth control now?	1. Any form of birth control can fail.
	2. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.
	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.
I am using the hormonal vaginal ring as my primary form. I can use it with which of the following barrier methods?	1. Cervical cap with spermicide.
	2. Condom with or without spermicide.
	3. Diaphragm with spermicide.
The hormonal ring works best when you change it on time every month, as prescribed.	1. True
	2. False
Pregnancy can happen when you are using a hormonal vaginal ring if:	1. The unopened package containing the hormonal vaginal ring is put into direct sunlight or gets hot.
	2. It slips out of your vagina and you do not replace it within 3 hours.
	3. It does not stay in your vagina for 3 weeks.

	4. You leave it in your vagina for more than 3 weeks.
	5. All of these reasons.
I have been getting hormone shots for 1 year and have not gotten pregnant. Why do I need another form of birth control now?	1. Any form of birth control can fail.
	2. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.
	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.
You get hormone shots:	1. Every 4 or 12 weeks, depending on the brand of the product.
	2. In your arm, belly, or buttocks.
	3. Both are true.
You are using hormonal shots as your primary form of birth control, you should remember:	1. You are not protected against HIV (AIDS)
	2. You need to see your doctor to get the hormonal shot
	3. They might delay your ability to get pregnant after you stop using hormonal shots.
	4. All of the above.
One advantage of Hormone shots is that they also protect against sexually transmitted diseases.	1. True
	2. False
You have chosen hormone shots as your primary method of birth control. Another acceptable form for you to use would be:	1. Female condoms
	2. IUD Progesterone T
	3. Withdrawal
	4. None of the above
You have received a prescription for isotretinoin from your doctor but have not had the prescription filled. It is OK to have unprotected sex since you have had a negative pregnancy test.	1. True
	2. False
You check for the strings on your IUD, but cannot feel them. You would:	1. Not worry because you are also using a diaphragm with spermicide.
	2. Call your gynecologist.
I have been using an IUD for 3 years and have not gotten pregnant. Why do I need another form of birth control now?	1. Any form of birth control can fail.
	2. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.
	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.

Your IUD needs to be checked by your doctor:	1. Within 3 months after you had it inserted.
	2. If you can feel the strings.
	3. If your weight stays the same.
You have chosen an IUD as your primary method of birth control. Another acceptable form for you to use would be:	1. Female condoms
	2. IUD Progesterone T
	3. Withdrawal
	4. None of the above
I had tubal sterilization (my tubes tied) 5 years ago and have not gotten pregnant. Why do I need another form of birth control now?	1. Any form of birth control can fail, including tubal sterilization (having my tubes tied).
	2. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.
	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.
My primary form of birth control is tubal sterilization (having my tubes tied). I also need to use a secondary form or another primary form of birth control while I am taking isotretinoin:	1. True
	2. False
Important information to know about tubal sterilization (tying your tubes) is:	1. Tubal sterilization (Tying your tubes) does not protect against sexually transmitted diseases.
	2. Tubal sterilization (Tying your tubes) does not require surgery.
	3. It is easy to re-open the tubes.
Tubal sterilization (Tying your tubes) is a highly effective form of birth control and does not require use of another effective form of birth control while taking isotretinoin:	1. True
	2. False
You have chosen tubal sterilization (tying your tubes) as your primary method of birth control. Another acceptable form for you to use would be:	1. Female condoms
	2. IUD Progesterone T
	3. Withdrawal
	4. None of the above
My only partner had a vasectomy 5 years ago and I have not gotten pregnant. Why do I need another form of birth control now?	1. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.
	2. Any form of birth control can fail.
	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.

My primary form of birth control is my only partner's vasectomy. I also need to use a secondary form or another primary form of birth control while I am taking Isotretinoin.	1. True
	2. False
Important information to know about your partner's vasectomy is:	1. Your partner's vasectomy does not protect against sexually transmitted diseases.
	2. Your partner's vasectomy does not require surgery.
	3. It is easy to open the tubes again if your partner wants a child later.
Your partner's vasectomy is a highly effective form of birth control and does not require use of another effective form of birth control while taking isotretinoin:	1. True
	2. False
You have chosen your partner's vasectomy as your primary method of birth control. Another acceptable form for you to use would be:	1. Female condoms
	2. IUD Progesterone T
	3. Withdrawal
	4. None of the above
I have had implanted hormones for 2 years and have not gotten pregnant. Why do I need another form of birth control now?	1. Using two forms of birth control all the time drastically reduces the chance that you will get pregnant.
	2. Any form of birth control can fail.
	3. Most female patients who got pregnant during isotretinoin treatment were using only 1 form of birth control.
	4. All of these.
My primary form of birth control is implanted hormones. I also need to use a secondary form or another primary form of birth control while I am taking isotretinoin.	1. True
	2. False
My implantable hormone will only be effective through the first month while I am taking isotretinoin, after that I only need to use one effective form of birth control for the rest of my treatment.	1. True
	2. False
You have chosen implantable hormones as your primary method of birth control. Another acceptable form for you to use would be:	1. Female condoms
	2. IUD Progesterone T
	3. Withdrawal
	4. None of the above
Abstinence means no sex at all, 24 hours a day, 7 days a week.	1. True
	2. False
One of the most common causes of unplanned pregnancy is not being able to avoid sex.	1. True
	2. False

You planned not to have sex while taking isotretinoin, so you do not use any birth control. If you decide to have sex, you need to:	1. Work with your doctor to develop a plan to go on birth control before having sex.
	2. Stop having sex until you use your new birth control form for at least 1 month and have a negative pregnancy test.
	3. Start using three forms of effective birth control, just to be sure.
	4. 1 and 2 are correct.
Isotretinoin is not recommended if you do not follow the birth control requirements of the iPledge.	1. True
	2. False
Important information to know about birth control pills is:	1. You cannot get pregnant while using birth control pills even if you skip pills.
	2. Birth control pills do not protect against STDs 9sexually transmitted diseases) or HIV (AIDS)
	3. There are no side effects from using birth control pills.
The male condom can help prevent:	1. Pregnancy.
	2. The spread of HIV (AIDS)
	3. The spread of other sexually transmitted diseases (STD's)
	4. All of the above.
For 1 month after your last dose, you must use 2 effective forms of birth control together all the time.	1. True
	2. False

iPLEDGE™
Committed to Pregnancy Prevention

iPLEDGE – Committed to Pregnancy Prevention
P.O. Box 29094
Phoenix, AZ 85038

On Behalf of the Wholesaler Listed Below, I Acknowledge That:

For the purpose of the iPLEDGE program, the term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its individual distribution centers, and/or each warehousing chain pharmacy distribution center. To distribute isotretinoin, wholesalers must be registered with iPLEDGE and agree to meet all iPLEDGE requirements for wholesale distribution of isotretinoin products. Wholesalers must register with iPLEDGE by signing and returning this agreement that affirms they will comply with all iPLEDGE requirements for distribution of isotretinoin. The registration of wholesalers that do not abide by the terms of the agreement will be revoked after an investigation process and manufacturers of FDA-approved isotretinoin products will not continue to provide them with isotretinoin for distribution. Each distribution center operated by a wholesaler must register if they are to distribute isotretinoin. These requirements include:

- Registering prior to distributing isotretinoin and reregistering annually thereafter
- Distributing only FDA-approved isotretinoin product obtained directly from the isotretinoin manufacturers (or delegate) or another registered wholesaler
- Beginning November 1, 2005 only ship isotretinoin to
  - wholesalers registered in the iPLEDGE program with prior written consent from the manufacturer, or
  - pharmacies licensed in the US and registered and activated in the iPLEDGE program
- Notifying immediately the isotretinoin manufacturer (or delegate) of any non-registered and/or non-activated pharmacy or unregistered wholesaler that attempts to order isotretinoin
- Complying with inspection of wholesaler records by the isotretinoin manufacturer (or delegate) for verification of compliance with the iPLEDGE program
- Returning to the manufacturer (or delegate) any undistributed product if registration is revoked by the iPLEDGE program or if the wholesaler chooses to not reregister annually

An agreement must be completed for each distribution center.

I am authorized to execute this agreement on behalf of the Wholesaler (and its distribution centers, if applicable).

Wholesaler's Name _____
(Type or Print)

Distribution Center's DEA# _____

Distribution Center's Address _____

Distribution Center's City _____

Distribution Center's State _____ Distribution Center's ZIP _____

Distribution Center's Phone Number _____

Distribution Center's Fax Number _____

Authorized Representative _____
(print-first, MI, last)

Title _____

E-mail Address for Key Contact _____

E-mail Address for Pharmacy Eligibility File Delivery* _____

Authorized Representative's Signature _____

Date ____/____/____
M D Y

This agreement expires 12 months from agreement date. Annual registration is required.

* The list of registered and activated pharmacies will be e-mailed to this address daily

[Name of Manufacturer]

{Product Name and Generic Designation} Wholesaler to Wholesaler Shipment Request

REQUESTING PARTY INFORMATION: (Please print or type)

Requester Name: _____Telephone: _____

E-Mail Address: _____ Date of Request: _____

Wholesaler Name: _____ DEA: _____

Address: _____City:_____State:_____Zip:_____

Requesting Party represents and warrants that the Receiving Party listed below is registered with the iPLEDGE program.

Requester Signature: _____ Date: _____

RECEIVING PARTY INFORMATION

Wholesaler Name: _____ DEA: _____

Address: _____City:_____State:_____Zip:_____

Ship to Address: _____City: _____State: _____Zip: _____

MANUFACTURER'S CONSENT

Shipments of [Product Name and Generic Designation] between wholesalers* must be in compliance with the iPLEDGE program. Labeling for [Product Name] states that wholesalers registered in iPLEDGE may only ship to other registered wholesalers with prior written consent from the manufacturer. Pursuant to the labeling for [Product Name], the authorized signature below shall serve as written consent from the manufacturer provided that the requesting and receiving party's registration is verified prior to each shipment. Registration will be verified by [Maunfacturer Name] upon receipt of shipment request.

**The term wholesaler refers to a wholesaler and each of its individual distribution centers, a distributor and each of its individual distribution centers, and/or each warehousing chain pharmacy distribution center.*

[Name of Manufacturer]

By: _____Title: _____

Print Name: _____Date: _____

Please return completed forms to [Insert Appropriate Information Including Fax Number, Email URL, Telephone Number, etc.]

Please note that this approval is for a one time shipment. Further shipments require consent from [Manufacturer].

ATTACHMENT

Annual iPLEDGE Report Contents

a. Background
   i. Program Overview
   ii. Stakeholder Process and Requirements
   iii. Non-Compliance Process
   iv. Post-Isotretinoin Therapy Follow-up
   v. Isotretinoin Pregnancy Registry with Root Cause Analysis
   vi. Exemption for Patients with Serious Medical Reasons
b. Methodology
   i. Pregnancy Categorization
      1. (iPLEDGE pregnancy: an isotretinoin-exposed or indeterminate-exposure pregnancy whether medically confirmed or unconfirmed in a patient who was registered in iPLEDGE; Non-iPLEDGE pregnancy: an isotretinoin-exposed or indeterminate-exposure pregnancy whether medically confirmed or unconfirmed in a patient who was not registered in iPLEDGE and who became pregnant after iPLEDGE was fully implemented; Pre-iPLEDGE pregnancy).
   ii. Date of Conception
   iii. Timing of Isotretinoin Exposure Relative to Date of Conception
   iv. Pregnancy Status
   v. Study Period
c. Patient Information
   i. Patient Statistics
   ii. Compliance with End of Treatment Pregnancy Testing
   iii. Lost to Follow-up
d. Pregnancies
   i. iPLEDGE Pregnancies
      1. Timing of Isotretinoin Exposure Relative to Pregnancy Conception
      2. Deviations from the iPLEDGE Process and Requirements
      3. Number of Risk Management Authorizations
      4. Patient Age
      5. Contraceptive Choices
      6. Reasons for Pregnancy as Reported by the Prescriber and Patient
      7. Patient Understanding of the iPLEDGE Program
      8. Contraceptive Counseling
      9. Root Cause Analysis
      10. Pregnancy Outcome
      11. Number of deviations per pregnant patient vs. number of deviations per non-pregnant female of childbearing potential
   ii. Non-iPLEDGE Pregnancies
      1. Isotretinoin Source
      2. Reasons for Pregnancy as Reported by the Prescriber and Patient

3. Root Cause Analysis
4. Pregnancy Outcome

iii. Pre-iPLEDGE Pregnancies

e. Exemption for Patients with Serious Medical Reasons
   i. Number of prescribers who requested an exemption
   ii. Number of patients per prescriber
   iii. Age and risk category of each patient

f. Operations Assessment
   i. Wholesalers - to include wholesaler to wholesaler shipment compliance
   ii. Prescribers
   iii. Pharmacies
   iv. Prescriptions
   v. Summary of iPLEDGE Deviations
   vi. Call Center

g. Overall Assessment

h. Tables
   i. Table 1 Key iPLEDGE Requirements by Stakeholder
   ii. Table 2 Stakeholder Deviation Categories
   iii. Table 3 Violations that Have Resulted in iPLEDGE Deactivation
   iv. Table 4 Number of Patients Registered in iPLEDGE by Patient Risk Category (Male, Female Not of Childbearing Potential, Female of Childbearing Potential)
   v. Table 5 Patients with at least One Isotretinoin Prescription Authorized through iPLEDGE by Risk Category and Age
   vi. Table 6 Number of Females of Childbearing Potential who Completed Isotretinoin Treatment and Completed Post-Treatment Pregnancy Tests
   vii. Table 7 Females of Childbearing Potential who were Exposed to Isotretinoin and Lost to Follow-up
   viii. Table 8 Total Number of Pregnancies Reported to the Pregnancy Registry by iPLEDGE Status
   ix. Table 9 Total Pregnancies by iPLEDGE Year
   x. Table 10 iPLEDGE Pregnancies by Isotretinoin Exposure Category
   xi. Table 11 Number of iPLEDGE Pregnancies by Month
   xii. Table 12 Pregnancies Detected by iPLEDGE Before Initiation of Isotretinoin Treatment
   xiii. Table 13 Timing of Isotretinoin Exposure Relative to Pregnancy Conception
   xiv. Table 14 Information other than Last Menstrual Period that was Used to Estimate the Date of Conception for Women who Initiated Isotretinoin Treatment While Pregnant
   xv. Table 15 Number of Risk Management Authorizations During the Course of Therapy that the Patient Became Pregnant
   xvi. Table 16 Number of Pregnancies by Total Number of Risk Management Authorizations from iPLEDGE Run-In Period through Year of report
   xvii. Table 17 Age of Pregnant and Non-Pregnant Females of Childbearing Potential
   xviii. Table 18 Most Common Contraceptive Choices for Pregnant and Non-Pregnant Females of Childbearing Potential

xix. Table 19 Reasons Reported by Prescriber and Patient for iPLEDGE Pregnancies
xx. Table 20 First Month Questions about Avoiding Pregnancy and the Educational Components of iPLEDGE
xxi. Table 21 Monthly Comprehension Testing for Females of Childbearing Potential about the Use of Contraception and the Risk of Birth Defects
xxii. Table 22 Number of Patients Who Passed/Failed Their Monthly Comprehension Test on the First Try of the Month
xxiii. Table 23 First Month Questions about Contraceptive Counseling
xxiv. Table 24 Pregnancy Outcomes for iPLEDGE Pregnancies
xxv. Table 25 Non-iPLEDGE Pregnancies by Isotretinoin Exposure
xxvi. Table 26 Number of Non-iPLEDGE Pregnancies by Month
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xxx. Table 30 Number of Registered Wholesalers by iPLEDGE Year
xxxi. Table 31 Number of Registered and Activated Prescribers Who Prescribed at Least One Isotretinoin Prescription
xxxii. Table 32 Number of Registered and Activated Pharmacies
xxxiii. Table 33 Number of Pharmacies Registered and Activated in iPLEDGE by Pharmacy Type
xxxiv. Table 34 Reasons for Pharmacy Deactivations
xxxv. Table 35 Number of Prescriptions Authorized
xxxvi. Table 36 Number of Prescription Authorization Attempts Denied by Risk Category
xxxvii. Table 37 Reasons for Prescription Denial

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST

04/30/2012

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 076485Orig1s003

LABELING REVIEW

Labeling Review Branch
Division of Labeling and Program Support
Office of Generic Drugs

Labeling Supplement Review

Application Number: 76-485/S-003 (10 mg, 20 mg, and 40 mg)

Name of Drug: Myorisan™ (Isotretinoin Capsules USP), 10 mg, 20 mg and 40 mg.

Applicant: Douglas Pharmaceuticals America LTD

Material Reviewed:

Submission Dates: March 22, 2012 (REMS modification) and amendment dated **April 12, 2012** (Revised REMS attachments to reflect the address change from Pennsylvania to Arizona, and revised REMS document per agency's recommendations).

Background and Summary - (REMS: Single Shared System for Isotretinoin)

As required under section 505-1(i) of the FDCA, this REMS will use a single shared system for the elements to assure safe use and implementation system in the approved REMS. This single shared system, iPLEDGE, includes the following products:

ANDA 075945 Amnesteem® (isotretinoin) Capsules, 10, 20, and 40 mg
ANDA 076135 Clavaris™ (isotretinoin) Capsules, 20, 30, and 40 mg
ANDA 076356 Claravis™ (isotretinoin) Capsules, 10 mg
ANDA 076041 Sotret® (isotretinoin) Capsules, 10, 20 and 40 mg
ANDA 076503 Sotret® (isotretinoin) Capsules, 30 mg
ANDA 076485 Myorisan™ (isotretinoin) Capsules, 10, 20, and 40 mg

The REMS for Myorisan™ (isotretinoin) was originally approved on January 19, 2012. The REMS consists of a Medication Guide, elements to assure safe use, and an implementation system.

Review

The proposed modification to the REMS consists of the following:

1. removal of (b) (4) and (b) (4) from the iPLEDGE materials,

In addition, the following agreed-upon modifications are also included:

2. Relocating the Non-Compliance Action Policy from the REMS document into the REMS supporting documents
3. Relocating the following iPLEDGE website screen shots from the REMS document into the REMS supporting documents:
    a. iPLEDGE website Prescriber web pages
    b. iPLEDGE website Pharmacy web pages
    c. iPLEDGEprogram.com home page
4. Relocating the "What's New" document from the REMS document to the REMS supporting document
5. Removal of references to specific brand names, and respective sponsor names, for isotretinoin from the REMS educational materials
6. Revised "Effective Date" on the REMS educational materials to reflect the approved REMS modification approval date.
7. Section 2.2.3 bii – added the word "as"

8. Section 2.3. d – added the following text '…(patients, pharmacies, prescribers/delegates, designees and wholesalers). The Non-Compliance Action Policy shall describe the types of non-compliance, and corresponding corrective or remedial actions (notice of non- compliance, warning, suspension, temporary or permanent deactivation) that will be taken by the iPLEDGE sponsors for each category of non-compliant stakeholder.'
9. Revised to consistently reflect the Arizona address in all instances where it appears.

Medication Guide: Editorial changes have been made to the Medication Guide as follows:

1. Deletion of "USP" from established name in product title line
2. Deletion of established name from first bullet under "What is the most important information I should know about Myorisan?"
3. Replacing the word "one" with the number "1" in first and third bullets under the "Birth defects (deformed babies), loss of a baby before birth (miscarriage), death of the baby and early (premature) births."
4. Switching the order of the temperatures and parenthesis as they appear in the first bullet under "How should I store Myorisan?"
5. Deleting the statement in brackets "[See USP Controlled Room Temperature.]" in the first bullet under "How should I store Myorisan?"
6. Adding a hard return to create a new paragraph for the last sentence under "General Information about is"

Recommendation

Your proposed modified REMS, submitted on March 22, 2012 and April 12, 2012 are satisfactory.

Approve the Labeling Supplement.

{see appended electronic signature}

_____
Beverly Weitzman
Labeling Reviewer

Supervisory Comment/Concurrence:

{see appended electronic signature}

_____
John Grace
Team Leader

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BEVERLY WEITZMAN
04/24/2012

JOHN F GRACE
04/30/2012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 076485Orig1s003

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

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March 21, 2012

ANDA 076485
REMS ASSESSMENT

NEW SUPPLEMENT FOR ANDA 076485
PROPOSED REMS MODIFICATION

Office of Generic Drugs, CDER, FDA
Keith Webber, Ph.D., Acting Director
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, MD 20855-2810

Re: MYORISAN™ (ISOTRETINOIN CAPSULES USP), 10 MG, 20 MG, AND 40 MG
ANDA 076485
NEW SUPPLEMENT - PROPOSED REMS MODIFICATION

Dear Dr. Webber:

Reference is made to Douglas Pharmaceuticals America LTD approved ANDA 076485 for Myorisan™ (Isotretinoin Capsules USP), 10 mg, 20 mg and 40 mg. Reference is also made to the replacement approval letter dated January 19, 2012 with instructions for submitting proposed modifications to the approved REMS.

Reference is made to the iPLEDGE REMS modification supplement submitted by the other isotretinoin sponsors, Mylan, Teva and Ranbaxy (collectively the Isotretinoin Product Manufacturer Group (IPMG)) dated September 7, 2011, and their subsequent REMS modification supplement dated February 14, 2012. Reference is also made to the email correspondence received by IPMG dated March 2, 2012 from J. Paul Phillips, of the Division of Dermatology and Dental Drug Products, which provided recommended changes to the proposed iPLEDGE Risk Evaluation and Mitigation Strategy Proposal.

At this time, VersaPharm Incorporated, U.S. Agent for Douglas Pharmaceuticals and labeled distributor of Myorisan™, is submitting a supplement to modify the approved REMS and to incorporate all comments and revisions requested by the Agency referenced above to the IPMG. Please note that no additional changes have been made to the REMS proposal, supporting documentation, or any of the iPLEDGE materials except for those that are indicated in the tracked changes document provided herein. Please note that the REMS and SUPPORTING REMS materials submitted herein, are an exact duplication of the REMS /SUPPORTING REMS materials submitted by the other members of IPMG on March 13, 2012.

Specifically, the Agency recommended the following:

FDA Comment 1
The "Effective" date should be updated on all of the REMS educational materials to reflect the date of the REMS modification approval as: "Most Recent Modification: March xx, 2012".

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Sponsor Response 1
As requested by the Agency, the sponsors have updated the "Effective" date on all of the REMS educational materials to reflect the date of the REMS modification approval as "Most Recent Modification: March xx, 2012". We have included Word versions of these documents to facilitate entry of the Agency's regulatory action date.

FDA Comment 2
All references to the sponsors names and product names should be removed from the REMS & REMS attachment. The following are examples of such references and all instances where such references appear should be modified as follow:

Current	Revised
(b) (4)	"A complete list of FDA-approved isotretinoin products that may be prescribed, dispensed may be found by calling 1-866-495-0654 or via www.ipledgeprogram.com."
	"For More Information About Isotretinoin To get information about specific brands of isotretinoin the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com."
	"Isotretinoin Products To get information about specific brands of isotretinoin the contact information for individual makers can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com."

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Current	Revised
(b) (4)	"Reporting adverse events Specific information about adverse events that may occur during isotretinoin therapy may be reported to the individual makers of isotretinoin and/or to the Food and Drug Administration MedWatch Program at 1-800-FDA-1088 or via www.fda.gov/medwatch/report.htm. The contact information for specific brands of isotretinoin can be obtained by calling 1-866-495-0654 or via www.ipledgeprogram.com."

Sponsor Response 2
As requested by the Agency, the sponsors have removed all references to the sponsor names and product names from the REMS and REMS attachments where appropriate. Please note that the sponsors used the revised language proposed in the above table with a few minor grammatical edits. Specifically, we deleted a comma after prescribed from the first part of the table and changed it to read "A complete list of FDA-approved isotretinoin products that may be prescribed and dispensed may be…" We also added a comma after isotretinoin in the second and third part of the table. The fourth part remains unchanged.

FDA Comment 3
The website and automated phone system should be updated to include a list of the FDA-approved isotretinoin products that are included in the iPLEDGE program and their respective contact information.

Sponsor Response 3
The sponsors commit to updating both the website and automated phone system to include the list of the FDA approved isotretinoin products and their respective contact information that are included in the iPLEDGE program.

Please note that VersaPharm's product name, NDC#s, and contact information will be included in the website and automated phone system upon completion of VersaPharm's integration into iPLEDGE and prior to marketing of the product.

Please refer to the Table of Contents for the REMS document and the Supporting Document. Each Table of Contents links to the individual files that make up the REMS document and Supporting Document. These also include those documents that were red-lined.

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In addition, the sponsors acknowledge the FDA's request to submit our proposed REMS and other materials in MS Word documents as it makes the review of these materials more efficient and it is easier for the web posting staff to make the document 508 compliant. The sponsors complied with this request whenever it was possible.

Please note that it will take approximately 90 days from FDA approval for the sponsors to implement and launch the iPLEDGE REMS as described herein.

Please direct all written or telephone communications to the undersigned.

Sincerely,

John D. Franolic, Ph.D.
Vice President of Regulatory Affairs
VersaPharm Incorporated
Phone: (770) 373-5635
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April 12, 2012

ANDA 076485
REMS MODIFICATION

AMENDMENT TO S-003

Office of Generic Drugs, CDER, FDA
Keith Webber, Ph.D., Acting Director
Document Control Room, Metro Park North VII
7620 Standish Place
Rockville, MD 20855-2810

Re: MYORISAN™ (ISOTRETINOIN CAPSULES USP), 10 MG, 20 MG, AND 40 MG
ANDA 076485 (SEQUENCE 0005)
AMENDMENT TO S-003 - REMS MODIFICATION

Dear Dr. Webber:

Reference is made to Douglas Pharmaceuticals America LTD ("Douglas") ANDA 076485 for Myorisan™ (Isotretinoin Capsules USP), 10 mg, 20 mg and 40 mg approved on January 19, 2012. Reference is also made to the REMS Modification Supplement (S-003) submitted on March 21, 2012.

Reference is also made to the iPLEDGE REMS modification supplement amendments submitted by the other isotretinoin sponsors, Mylan, Teva and Ranbaxy (collectively the Isotretinoin Product Manufacturer Group (IPMG)) on March 26, 2012 and April 2, 2012, respectively. These amendments consisted of the following: (1) update of the address on some REMS documents and supporting REMS documents to reflect transition of the iPLEDGE program operations from (b) (4) to (b) (4) (Arizona), and (2) update of the proposed REMS document as per email recommendations made by J. Paul Phillips, of the Division of Dermatology and Dental Drug Products on March 30, 2012.

At this time, VersaPharm Incorporated, U.S. Agent for Douglas and labeled distributor of Myorisan™, is submitting an amendment to S-003 to include the changes submitted by the IPMG in the above amendments. Please note that the REMS and SUPPORTING REMS materials submitted herein, are an exact duplication of the REMS /SUPPORTING REMS materials submitted by the other members of IPMG in the above amendments.

Specifically, the following changes are included in this amendment:

(1) Update of all REMS and Supporting REMS documents to consistently reflect the Arizona address in all instances where it appears. This change is instituted as a result of the transition of the iPLEDGE program operations from (b) (4) who is currently located in (b) (4) to (b) (4) who is currently located in Arizona. The affected REMS documents and Supporting REMS documents are provided in the Table 1 and Table 2, respectively. Each table has links to the individual files which were revised with the address change.

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Table 1- Revised REMS Documents with Address Change from (b) (4) to (b) (4) Arizona

Document Name	Page Number Impacted	Location of Address Block
Educational Kit for Females of Childbearing Potential	72	Top of page
Exemption for Patients with Serious Medical Conditions	1	Bottom of page
Instructions and Managing Office Staff Designees	1	Top of page
Office Staff Designee Registration Form	1	Top and bottom of the page
Patient Informed Consent Form (All Patients)	1	Top of the page
Patient Informed Consent Form (for females of childbearing potential)	1	Top of the page
Pharmacy Enrollment Form	1	Top and bottom of the page
Prescriber Enrollment Form	1	Top and bottom of the page
Wholesaler Agreement	1	Top of the page

Table 2- Revised Supporting REMS Documents with Address Change from (b) (4) (b) (4) to (b) (4) Arizona

Document Name	Page Number Impacted	Location of Address Block
Dear Doctor Letter	1 and 2	Top of both pages, and below heading on page 2
Dear Healthcare Provider Letter for Oncology Patients	1 and 2	Heading
Dear Pharmacist Letter	1 and 2	Top and middle of page 1 and top of page 2
iPLEDGE Program Frequently Asked Questions	26	Bottom of the page
Pharmacy Activation Instructions	1	Top of the page
Pharmacy Letter of Non-Compliance	32, 44 and 47	Top of page 32, top of page 44 and the top of page 47
Pharmacy Successful Registration Letter	1 and 2	Top of both pages
Prescriber Activation Instructions	1	Top of the page
Prescriber Designee Registration Letter	1 and 2	Top of both pages
Prescriber Successful Activation Letter	1 and 2	Top of both pages
Prescriber Successful Registration Letter	1 and 2	Top of both pages
Steps to Request and Exception for Patients with Serious Medical Conditions	1	Bottom on the page
Wholesaler's Letter of Non-Compliance	2, 5, 8, 26 and 29	Top of all pages

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(2) In accordance with the Agency's recommendations received by IPMG on March 30, 2012 from J. Paul Phillips, of the Division of Dermatology and Dental Drug Products, the pending REMS document is to incorporate all comments and revisions requested by the Agency.

Specifically, the Agency requested the following changes:

a. Section 2.2.3.b.ii – add the word 'as'

b. Section 2.3.d – add the following text '…(patients, pharmacies, prescribers/delegates, designees and wholesalers). The Non-Compliance Action Policy shall describe the types of non-compliance, and corresponding corrective or remedial actions (notice of non-compliance, warning, suspension, temporary or permanent deactivation) that will be taken by the iPLEDGE sponsors for each category of non-compliant stakeholder.'

Please refer to Table 3 which contains the revisions and page numbers of the proposed REMS Document requested by the Agency.

Table 3- Revisions to the Proposed REMS Document

Document Name	Page Number / Section impacted	Location of Address Block
Risk Evaluation and Mitigation Strategy (REMS); The iPLEDGE Program- Single Shared System for Isotretinoin	Page 5- Section 2.2.3.b.ii	Added the word 'as'.
	Page 8 Section 2.3.d	Added the following text '…(patients, pharmacies, prescribers/delegates, designees and wholesalers). The Non-Compliance Action Policy shall describe the types of non-compliance, and corresponding corrective or remedial actions (notice of non-compliance, warning, suspension, temporary or permanent deactivation) that will be taken by the iPLEDGE sponsors for each category of non-compliant stakeholder'

In addition to the above changes, we are including a clean version of the "What's New" supporting REMS document. This document was inadvertently left out of our original REMS modification supplement dated March 21, 2012.

With respect to the appropriate location of the Prescriber Flow Chart, the sponsors would like to clarify that it is included as part of the REMS supporting documents.

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Please note that no additional changes have been made to the REMS proposal, supporting documentation, or any of the iPLEDGE materials except for those indicated above.

Please note that it will take approximately 90 days from FDA approval for the sponsors to implement and launch the iPLEDGE REMS as described herein.

Please direct all written or telephone communications to the undersigned.

Sincerely,

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