

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Plan B safely and effectively. See full prescribing information for Plan B.

Plan B (levonorgestrel) tablets, 0.75 mg, for oral use

Initial U.S. Approval: 1982

INDICATIONS AND USAGE

Plan B is a progestin-only emergency contraceptive, indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. Plan B is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older. Plan B is not intended for routine use as a contraceptive. (1)

DOSAGE AND ADMINISTRATION

The first tablet is taken orally as soon as possible within 72 hours after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Efficacy is better if Plan B is taken as soon as possible after unprotected intercourse. (2)

DOSAGE FORMS AND STRENGTHS

A total of two 0.75 mg tablets taken 12 hours apart as a single course of treatment. (3)

CONTRAINDICATIONS

Known or suspected pregnancy. (4)

WARNINGS AND PRECAUTIONS

- Ectopic Pregnancy: Women who become pregnant or complain of lower abdominal pain after taking Plan B should be evaluated for ectopic pregnancy. (5.1)
- Plan B is not effective in terminating an existing pregnancy. (5.2)

- Effect on menses: Plan B may alter the next expected menses. If menses is delayed beyond 1 week, pregnancy should be considered. (5.3)
- STI/HIV: Plan B does not protect against STI/HIV. (5.4)

ADVERSE REACTIONS

The most common adverse reactions ($\geq 10\%$) in the clinical trial included menstrual changes (26%), nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), dizziness (11%) and breast tenderness (11%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals at 1-888-483-8279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Drugs or herbal products that induce certain enzymes, such as CYP3A4, may decrease the effectiveness of progestin-only pills. (7)

USE IN SPECIFIC POPULATIONS

- Nursing Mothers: Small amounts of progestin pass into the breast milk of nursing women taking progestin-only pills for long-term contraception, resulting in detectable steroid levels in infant plasma. (8.3)
- Plan B is not intended for use in pediatric (premenarcheal) (8.4) or postmenopausal women (8.5).
- Clinical trials demonstrated a higher pregnancy rate in the Chinese population. (8.6)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 9/2017

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Plan B[®] is a progestin-only emergency contraceptive indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet should be taken 12 hours later.

Plan B is available only by prescription for women younger than age 17 years, and available over the counter for women 17 years and older.

Plan B is not indicated for routine use as a contraceptive.

2 DOSAGE AND ADMINISTRATION

Take one tablet of Plan B orally as soon as possible within 72 hours after unprotected intercourse or a known or suspected contraceptive failure. Efficacy is better if the tablet is taken as soon as possible after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Plan B can be used at any time during the menstrual cycle.

If vomiting occurs within two hours of taking either dose of medication, consideration should be given to repeating the dose.

3 DOSAGE FORMS AND STRENGTHS

Each Plan B tablet is supplied as a white, round tablet containing 0.75 mg of levonorgestrel and is marked with INOR on one side.

4 CONTRAINDICATIONS

Plan B is contraindicated for use in the case of known or suspected pregnancy.

5 WARNINGS AND PRECAUTIONS

5.1 Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of all reported pregnancies. Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic.

A history of ectopic pregnancy is not a contraindication to use of this emergency contraceptive method. Healthcare providers, however, should consider the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Plan B. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Plan B.

5.2 Existing Pregnancy

Plan B is not effective in terminating an existing pregnancy.

5.3 Effects on Menses

Some women may experience spotting a few days after taking Plan B. Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and women using levonorgestrel for postcoital and emergency contraception.

If there is a delay in the onset of expected menses beyond 1 week, consider the possibility of pregnancy.

5.4 STI/HIV

Plan B does not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

5.5 Physical Examination and Follow-up

A physical examination is not required prior to prescribing Plan B. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Plan B.

5.6 Fertility Following Discontinuation

A rapid return of fertility is likely following treatment with Plan B for emergency contraception; therefore, routine contraception should be continued or initiated as soon as possible following use of Plan B to ensure ongoing prevention of pregnancy.

6 ADVERSE REACTIONS

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

A double-blind, controlled clinical trial in 1,955 evaluable women compared the efficacy and safety of Plan B (one 0.75 mg tablet of levonorgestrel taken within 72 hours of unprotected intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets each containing 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol, taken within 72 hours of intercourse, and two tablets taken 12 hours later).

The most common adverse events (>10%) in the clinical trial for women receiving Plan B included menstrual changes (26%), nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), dizziness (11%), and breast tenderness (11%). Table 1 lists those adverse events that were reported in $\geq 5\%$ of Plan B users.

Table 1: Adverse Events in $\geq 5\%$ of Women, by % Frequency

	Plan B Levonorgestrel N=977 (%)
Nausea	23.1
Abdominal Pain	17.6
Fatigue	16.9
Headache	16.8
Heavier Menstrual Bleeding	13.8
Lighter Menstrual Bleeding	12.5
Dizziness	11.2
Breast Tenderness	10.7
Vomiting	5.6
Diarrhea	5.0

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Plan B. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal Disorders

Abdominal Pain, Nausea, Vomiting

General Disorders and Administration Site Conditions

Fatigue

Nervous System Disorders

Dizziness, Headache

Reproductive System and Breast Disorders

Dysmenorrhea, Irregular Menstruation, Oligomenorrhea, Pelvic Pain

7 DRUG INTERACTIONS

Drugs or herbal products that induce enzymes, including CYP3A4, that metabolize progestins may decrease the plasma concentrations of progestins, and may decrease the effectiveness of progestin-only pills. Some drugs or herbal products that may decrease the effectiveness of progestin-only pills include:

- barbiturates (including primidone)
- bosentan

- carbamazepine
- felbamate
- griseofulvin
- oxcarbazepine
- phenytoin
- rifampin
- St. John's wort
- topiramate

Significant changes (increase or decrease) in the plasma levels of the progestin have been noted in some cases of co-administration with HIV protease inhibitors or with non-nucleoside reverse transcriptase inhibitors. Concomitant administration of efavirenz has been found to reduce plasma levels of levonorgestrel (AUC) by around 50%, which may reduce the effectiveness of Plan B.

Consult the labeling of all concurrently used drugs to obtain further information about interactions with progestin-only pills or the potential for enzyme alterations.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Many studies have found no harmful effects on fetal development associated with long-term use of contraceptive doses of oral progestins. The few studies of infant growth and development that have been conducted with progestin-only pills have not demonstrated significant adverse effects.

8.3 Nursing Mothers

In general, no adverse effects of progestin-only pills have been found on breastfeeding performance or on the health, growth or development of the infant. However, isolated post-marketing cases of decreased milk production have been reported. Small amounts of progestins pass into the breast milk of nursing mothers taking progestin-only pills for long-term contraception, resulting in detectable steroid levels in infant plasma.

8.4 Pediatric Use

Safety and efficacy of progestin-only pills for long-term contraception have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of Plan B emergency contraception before menarche is not indicated.

8.5 Geriatric Use

This product is not intended for use in postmenopausal women.

8.6 Race

No formal studies have evaluated the effect of race. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both Plan B and the Yuzpe regimen (another form of emergency contraception). The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown.

8.7 Hepatic Impairment

No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Plan B.

8.8 Renal Impairment

No formal studies were conducted to evaluate the effect of renal disease on the disposition of Plan B.

9 DRUG ABUSE AND DEPENDENCE

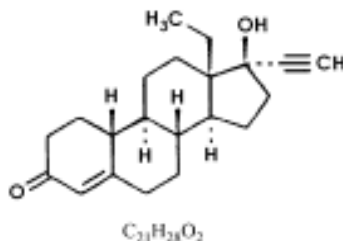
Levonorgestrel is not a controlled substance. There is no information about dependence associated with the use of Plan B.

10 OVERDOSAGE

There are no data on overdosage of Plan B, although the common adverse event of nausea and associated vomiting may be anticipated.

11 DESCRIPTION

Each Plan B tablet contains 0.75 mg of a single active steroid ingredient, levonorgestrel [18,19-Dinorepregn-4-en-20-yn-3-one-13-ethyl-17-hydroxy-, (17 α)-(-)-], a totally synthetic progestogen. The inactive ingredients present are colloidal silicon dioxide, potato starch, gelatin, magnesium stearate, talc, corn starch, and lactose monohydrate. Levonorgestrel has a molecular weight of 312.45, and the following structural and molecular formulas:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Emergency contraceptive pills are not effective if a woman is already pregnant. Plan B is believed to act as an emergency contraceptive principally by preventing ovulation or fertilization (by altering tubal transport of sperm and/or ova). In addition, it may inhibit implantation (by altering the endometrium). It is not effective once the process of implantation has begun.

12.3 Pharmacokinetics

Absorption

No specific investigation of the absolute bioavailability of Plan B in humans has been conducted. However, literature indicates that levonorgestrel is rapidly and completely absorbed after oral administration (bioavailability about 100%) and is not subject to first pass metabolism.

After a single dose of Plan B (0.75 mg) administered to 16 women under fasting conditions, maximum serum concentrations of levonorgestrel were 14.1 + 7.7 ng/mL (mean + SD) at an average of 1.6 + 0.7 hours.

Table 2: Pharmacokinetic Parameter Values Following Single Dose Administration of Plan B (Levonorgestrel) Tablets 0.75 mg to Healthy Female Volunteers under Fasting Conditions

	Mean (\pm SD)					
	C _{max} (ng/mL)	T _{max} (h)	CL (L/h)	V _d (L)	t _{1/2} (h)	AUC _{inf} (ng/mL.h)
Levonorgestrel	14.1 (7.7)	1.6 (0.7)	7.7 (2.7)	260.0	24.4 (5.3)	123.1 (50.1)

C_{max} = maximum concentration

T_{max} = time to maximum concentration

CL = clearance

V_d = volume of distribution

t_{1/2} = elimination half life

AUC_{inf} = area under the drug concentration curve from time 0 to infinity

Effect of Food: The effect of food on the rate and the extent of levonorgestrel absorption following single oral administration of Plan B has not been evaluated.

Distribution

The apparent volume of distribution of levonorgestrel is reported to be approximately 1.8 L/kg. It is about 97.5 to 99% protein-bound, principally to sex hormone binding globulin (SHBG) and, to a lesser extent, serum albumin.

Metabolism

Following absorption, levonorgestrel is conjugated at the 17 β -OH position to form sulfate conjugates and, to a lesser extent, glucuronide conjugates in plasma. Significant amounts of

conjugated and unconjugated 3 α , 5 β -tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3 α , 5 α -tetrahydrolevonorgestrel and 16 β hydroxylevonorgestrel. Levonorgestrel and its phase I metabolites are excreted primarily as glucuronide conjugates. Metabolic clearance rates may differ among individuals by several-fold, and this may account in part for the wide variation observed in levonorgestrel concentrations among users.

Excretion

About 45% of levonorgestrel and its metabolites are excreted in the urine and about 32% are excreted in feces, mostly as glucuronide conjugates.

Specific Populations

Pediatric: This product is not intended for use in the pediatric (pre-menarcheal) population, and pharmacokinetic data are not available for this population.

Geriatric: This product is not intended for use in postmenopausal women and pharmacokinetic data are not available for this population.

Race: No formal studies have evaluated the effect of race on pharmacokinetics of Plan B. However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both Plan B and the Yuzpe regimen (another form of emergency contraception). The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown [*see USE IN SPECIFIC POPULATIONS (8.6)*].

Hepatic Impairment: No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Plan B.

Renal Impairment: No formal studies were conducted to evaluate the effect of renal disease on the disposition of Plan B.

Drug-Drug Interactions

No formal drug-drug interaction studies were conducted with Plan B [*see DRUG INTERACTIONS (7)*].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity: There is no evidence of increased risk of cancer with short-term use of progestins. There was no increase in tumorigenicity following administration of levonorgestrel to rats for 2 years at approximately 5 μ g/day, to dogs for 7 years at up to 0.125 mg/kg/day, or to rhesus monkeys for 10 years at up to 250 μ g/kg/day. In another 7 year dog study, administration of levonorgestrel at 0.5 mg/kg/day did increase the number of mammary adenomas in treated dogs compared to controls. There were no malignancies.

Genotoxicity: Levonorgestrel was not found to be mutagenic or genotoxic in the Ames Assay, in vitro mammalian culture assays utilizing mouse lymphoma cells and Chinese hamster ovary cells, and in an in vivo micronucleus assay in mice.

Fertility: There are no irreversible effects on fertility following cessation of exposures to levonorgestrel or progestins in general.

14 CLINICAL STUDIES

A double-blind, randomized, multinational controlled clinical trial in 1,955 evaluable women (mean age 27) compared the efficacy and safety of Plan B (one 0.75 mg tablet of levonorgestrel taken within 72 hours of unprotected intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets each containing 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol, taken within 72 hours of intercourse, and two additional tablets taken 12 hours later). After a single act of intercourse occurring anytime during the menstrual cycle, the expected pregnancy rate of 8% (with no contraceptive use) was reduced to approximately 1% with Plan B.

Emergency contraceptives are not as effective as routine hormonal contraception since their failure rate, while low based on a single use, would accumulate over time with repeated use [*see INDICATIONS AND USAGE (1)*].

At the time of expected menses, approximately 74% of women using Plan B had vaginal bleeding similar to their normal menses, 14% bled more than usual, and 12% bled less than usual. The majority of women (87%) had their next menstrual period at the expected time or within + 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses.

16 HOW SUPPLIED/STORAGE AND HANDLING

Plan B (levonorgestrel) tablets, 0.75 mg, are available for a single course of treatment in PVC/aluminum foil blister packages of two tablets each. The tablet is white, round and marked INOR on one side.

Available as: Unit-of-use NDC 51285-769-93

Store Plan B tablets at controlled room temperature, 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP].

17 PATIENT COUNSELING INFORMATION

17.1 Information for Patients

- Take Plan B as soon as possible and not more than 72 hours after unprotected intercourse or a known or suspected contraceptive failure.
- If you vomit within two hours of taking either tablet, immediately contact your healthcare provider to discuss whether to take another tablet.
- Seek medical attention if you experience severe lower abdominal pain 3 to 5 weeks after taking Plan B, in order to be evaluated for an ectopic pregnancy.
- After taking Plan B, consider the possibility of pregnancy if your period is delayed more than one week beyond the date you expected your period.

- Do not use Plan B as routine contraception.
- Plan B is not effective in terminating an existing pregnancy.
- Plan B does not protect against HIV-infection (AIDS) and other sexually transmitted diseases/infections.
- For women younger than age 17 years, Plan B is available only by prescription.

Mfg. by Gedeon Richter, Ltd., Budapest, Hungary
for Teva Women's Health, Inc.
Subsidiary of Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454

PLA-001
Rev. 9/2017

Plan B[®]

Emergency Contraceptive.

Because the unexpected happens.

Important Information About Plan B[®], Birth Control & Sexually Transmitted Diseases

For additional information intended for healthcare professionals, please see enclosed Product Information for Plan B[®].

Plan B[®] logo

Emergency Contraceptive

From the makers of Plan B[®], Teva Women's Health, Inc., a subsidiary of Teva Pharmaceuticals USA, Inc.

What is Plan B[®]?

Plan B[®] is emergency contraception that helps prevent pregnancy after birth control failure or unprotected sex. It is a **backup** method of preventing pregnancy and should not be used as regular birth control.

What Plan B[®] is not.

Plan B[®] will not work if you are already pregnant and will not affect an existing pregnancy. Plan B[®] will not protect you from HIV infection (the virus that causes AIDS) and other sexually transmitted diseases (STDs).

When should I use Plan B[®]?

The sooner you take emergency contraception, the better it works. You should use Plan B[®] within 72 hours (3 days) **after you have had unprotected sex.**

Plan B[®] is a backup or emergency method of birth control you can use when:

- your regular birth control was used incorrectly or failed
- You did not use any birth control method

When not to use Plan B[®]?

Plan B[®] should not be used:

- as a regular birth control method, because it's not as effective as regular birth control.
- if you are already pregnant, because it will not work.

- if you are allergic to levonorgestrel or any other ingredients in Plan B[®].

When should I talk to a doctor or pharmacist?

Ask a doctor or pharmacist before use if you are taking efavirenz (HIV medication) or rifampin (tuberculosis treatment) or medication for seizures (epilepsy). These medications may reduce the effectiveness of Plan B[®] and increase your chance of becoming pregnant. Your doctor may prescribe another form of emergency contraception that may not be affected by these medications.

How does Plan B[®] work?

Plan B[®] is two tablets with levonorgestrel, a hormone that has been used in many birth control pills for several decades. Plan B[®] contains a higher dose of levonorgestrel than birth control pills, but works in a similar way to prevent pregnancy. It works mainly by stopping the release of an egg from the ovary. It is possible that Plan B[®] may also work by preventing fertilization of an egg (the uniting of sperm with the egg) or by preventing attachment (implantation) to the uterus (womb).

How can I get the best results from Plan B[®]?

You have 72 hours (3 days) to try to prevent pregnancy after birth control failure or unprotected sex. **The sooner you take Plan B[®], the better it works.** Take the first Plan B[®] tablet **as soon as possible within 72 hours (3 days)** after unprotected sex. Take the second tablet **12 hours** later.

How effective is Plan B[®]?

If Plan B[®] is taken as directed, it can significantly decrease the chance that you will get pregnant. About 7 out of every 8 women who would have gotten pregnant will not become pregnant.

How will I know Plan B[®] worked?

You will know Plan B[®] has been effective when you get your next period, which should come at the expected time, or within a week of the expected time. If your period is delayed beyond 1 week, it is possible you may be pregnant. You should get a pregnancy test and follow up with your healthcare professional.

Will I experience any side effects?

- some women may have changes in their period, such as a period that is heavier or lighter or a period that is early or late. **If your period is more than a week late, you may be pregnant.**
- if you have severe abdominal pain, you may have an ectopic pregnancy, and should get immediate medical attention.
- when used as directed, Plan B[®] is safe and effective. Side effects may include changes in your period, nausea, lower stomach (abdominal) pain, tiredness,

headache, dizziness, and breast tenderness.

- if you vomit within 2 hours of taking the medication, call a healthcare professional to find out if you should repeat the dose.

What are the directions for using Plan B®?

Women 17 years of age and older:

- Take the first Plan B® tablet as soon as possible within 72 hours (3 days) after unprotected sex.
- Take the second tablet 12 hours after you take the first tablet.
- If you vomit within 2 hours of taking either dose of medication, call a healthcare professional to find out if you should repeat that dose.

Prescription only for women younger than age 17. If you are younger than 17, see a healthcare professional.

What if I still have questions about Plan B®?

If you have questions or need more information, call our toll-free number, 1-800-330-1271 or ask a healthcare professional.

Other information

Keep out of reach of children:

In case of overdose, get medical help or contact a Poison Control Center right away at 1-800-222-1222.

Do not use if the blister seal is open.

Store at room temperature 20–25°C (68–77°F).

You may report side effects to FDA at 1-800-FDA-1088.

Active ingredient: levonorgestrel 0.75 mg in each tablet

Inactive ingredients: colloidal silicon dioxide, potato starch, gelatin, magnesium stearate, talc, corn starch, lactose monohydrate

1-800-330-1271

If you are sexually active, you should see a healthcare provider for routine checkups. Your healthcare provider will talk to you about and, if necessary, test you for sexually transmitted diseases, teach you about effective methods of routine birth control, and answer any other questions you may have.

This label may not be the latest approved by FDA.
For current labeling information, please visit <https://www.fda.gov/drugsatfda>

Manufacturer logo lock up

Plan B logo lock up

Mfg. by Gedeon Richter, Ltd., Budapest, Hungary
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