CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

020747Orig1s050

Trade Name:	**ACTIQ**
Generic or Proper Name:	fentanyl citrate
Sponsor:	CEPHALON LLC
Approval Date:	December 23, 2020
Indication:	**ACTIQ** is an opioid agonist indicated for the management of breakthrough pain in cancer patients 16 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

CENTER FOR DRUG EVALUATION AND RESEARCH

020747Orig1s050

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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APPROVAL LETTER

NDA 020747/S-050

SUPPLEMENT APPROVAL

Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380

Attention: Angela Randall
Director, Regulatory Affairs Labeling

Dear Ms. Randall:

Please refer to your supplemental new drug application (sNDA) dated and received July 30, 2019, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Actiq (fentanyl citrate) oral transmucosal lozenge.

We also refer to our REMS MODIFICATION NOTIFICATION letter, dated March 27, 2019, informing you that the Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) must be modified to ensure that the benefits of the drug outweigh its risks. This determination was based on information contained in the REMS assessment reports suggesting many patients prescribed a TIRF medicine may not have been opioid-tolerant when they received a new prescription for a TIRF medicine, as well as recommendations from the August 3, 2018, joint meeting of the Drug Safety and Risk Management, and the Anesthetic and Analgesic Drug Products advisory committees.

This supplemental new drug application proposes REMS modifications required under section 505-1 of the FDCA, consistent with those outlined in the March 27, 2019, letter.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for TIRF products, of which Actiq is a member, was originally approved on December 28, 2011, and the most recent REMS modification was approved on September 7, 2017. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

In order to ensure the benefits of Actiq outweigh its risks, we determined that you were required to make the REMS modifications outlined in our REMS Modification letter dated March 27, 2019.

Your proposed modified REMS, submitted to Drug Master File (DMF) (b) (4) on December 7, 2020, and appended to this letter, is approved.

The modifications to the approved REMS must be fully implemented within 120 calendar days of the date of this letter.

The REMS uses a shared system for the elements to assure safe use, an implementation system, and a timeable for assessments of the REMS. This shared system, known as the TIRF REMS program, currently includes products listed on the FDA REMS, website, available at: https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=60

Other products may be added in the future if additional NDAs or ANDAs are approved.

The timetable for submission of assessments of the REMS must be revised to 12 months from the date of the approval of this REMS modification (December 23, 2020) and annually thereafter.

The revised REMS assessment plan must include, but is not limited to, the following:

Program Outreach and Communication

1. **Communication (1-year assessment post-modification approval only)**
    a. Sources of the distribution list(s) for the Dear Healthcare Provider Letter to healthcare providers likely to prescribe TIRF medicines
    b. Number of targeted healthcare providers who can prescribe
    c. The number of Dear Healthcare Provider letters sent by date(s), medical specialty, and method of distribution.
        i. The number and percentage of emailed letters successfully delivered, opened, and unopened.
        ii. The number and percentage of mailed letters successfully delivered or returned as undeliverable.
        iii. The number and percentage of faxed letters successfully delivered or returned as undeliverable.
    d. The number of professional societies sent the Dear Healthcare Provider Letter by date(s) and method of distribution. In addition, include which professional societies distributed the Dear Healthcare Provider Letter or the content of the letter to their respective members.

e. Sources of the distribution list(s) for the Dear Pharmacy Letter to inpatient and outpatient pharmacies that dispense Schedule II drugs and may be involved in dispensing TIRF medicines

f. The number of pharmacies sent the Dear Pharmacy Letter date(s), type of pharmacy, and by method of distribution

   i. The number and percentage of emailed letters successfully delivered, opened, and unopened.

   ii. The number and percentage of mailed letters successfully delivered or returned as undeliverable.

   iii. The number and percentage of faxed letters successfully delivered or returned as undeliverable.

g. The number of professional societies sent the Dear Pharmacy by dates(s) and by method of distribution. In addition, include which professional societies distributed the Dear Pharmacy Letter or the content of the letter to their respective members.

h. Date(s) and name(s) of Professional meetings where TIRF REMS materials were disseminated or displayed.

Program Implementation and Operations

2. REMS Program Implementation (1-year assessment post-modification approval only)

a. Date when the modified TIRF REMS website went live and was fully operational

b. Date when healthcare providers who can prescribe could become certified in the modified REMS

c. Date when pharmacies could become certified in the modified REMS

d. Date when patients could be enrolled in the modified REMS

e. Date when distributors/wholesalers could be registered in the modified REMS

f. Date when the REMS Call Center for the modified TIRF REMS program went live and was fully operational

3. REMS Certification and Enrollment Statistics (provide previous, current, and cumulative reporting periods)

a. Patients (number and percent)

   i. For the one-year assessment report only:

1) Patients previously enrolled in the TIRF REMS Access program (i.e. enrolled prior to implementation of the modified REMS)
2) Patients re-enrolled (i.e., previously enrolled in the TIRF REMS Access program and transitioned to new program)

ii. Newly enrolled into the new program

iii. Active patients (i.e., received at least one dispensation of a TIRF product during the reporting period)

iv. For metrics 3.a.i. through iii, stratify by demographics (age, gender, ethnicity, race, and geographic region [as defined by US Census]), around-the-clock opioid(s) (moiety, daily dose, and duration of greater than seven days), medical reasons related to pain (cancer or non-cancer pain), TIRF medicine use in the prior six months, and concomitant benzodiazepines and other central nervous system (CNS) depressants

v. A summary of the methods of patient enrollment (e.g., online, fax)

vi. Number of patients who were unable to become enrolled, accompanied by a summary of the reasons they were unable to be enrolled

b. Healthcare Providers who can Prescribe (number and percent)

i. For the one-year assessment report only:

1) Healthcare providers who can prescribe who previously certified in the TIRF REMS Access program (i.e. enrolled prior to implementation of the modified REMS)
2) Healthcare providers who can prescribe who re-certified (i.e., previously certified in the TIRF REMS Access program and transitioned to new program)

ii. Healthcare providers who can prescribe who are newly certified

iii. Active prescribers (i.e. who have prescribed a TIRF at least once during the reporting period)

iv. For metrics 3.a.i. through iii, stratify by credentials, (e.g., Doctor of Medicine, Doctor of Osteopathic Medicine, Nurse Practitioner, Physician Assistant, Other), medical specialty (e.g., Pain Medicine, Oncology, Internal Medicine, Other, etc.) and geographic region [as defined by US Census])

v. A summary of the methods of healthcare provider certification (e.g., online, fax)

vi. Number of healthcare providers who can prescribe who were unable to become certified, accompanied by a summary of the reasons they were unable to be certified

vii. For the 2-year assessment report, conduct an outreach to healthcare providers that did not re-certify in the REMS to ascertain the reasons why they did not re-certify. Submit the methodology protocol 120 days prior to initiating the outreach.

c. Pharmacies (number and percent)

i. For the one-year assessment report only:

1) Pharmacies previously certified in the TIRF REMS Access program (i.e. enrolled prior to implementation of the modified REMS)

2) Pharmacies re-certified (i.e., previously certified in the TIRF REMS Access program and transitioned to new program)

ii. Pharmacies newly certified into the new program

iii. Active pharmacies (i.e., have dispensed a TIRF at least once during the reporting period)

iv. For metrics 3.a.i. through iii, stratify by pharmacy type (inpatient, chain, independent [retail, mail, institutional], or closed system [provide identity of closed system entities]) and by geographic region [as defined by US Census])

v. A summary of the methods of pharmacy certification (e.g., online, fax)

vi. Number of pharmacies that were unable to become certified, accompanied by a summary of the reasons they were unable to be certified

vii. For the 2-year REMS assessment report, conduct an outreach to pharmacies that did not re-certify in the REMS to ascertain the reasons why they did not re-certify. Submit the methodology protocol 120 days prior to initiating the outreach.

d. Wholesalers-Distributors (number)

i. Previously enrolled (i.e. enrolled prior to implementation of the modified REMS)

ii. Re-enrolled (i.e., enrolled prior to implementation of the modified REMS and transitioned to new program)

iii. Newly enrolled into the new program

iv. Active (i.e., distributed a TIRF product during the reporting period)

4. **TIRF Utilization Data (provide previous, current, and cumulative reporting periods)**
    a. Number of prescriptions/transactions authorized for dispensing and those dispensed stratified by:
        i. Prescriber specialty, degree/credentials, and geographic region.
        ii. Pharmacy type (specialty, central fill, inpatient, chain, independent [retail, mail, institutional], or closed system [provide identity of closed system entities])
        iii. Patient demographics (age, gender, ethnicity, race, and geographic region [as defined by US Census])
        iv. Identify the source of this information

5. **REMS Infrastructure and Performance (provide previous, current, and cumulative reporting periods)**
    a. REMS Website
        i. Number of visits and unique visits to the REMS website
        ii. Number of REMS materials downloaded or printed for each material
    b. REMS program Call Center Report
        i. Number of contacts by stakeholder type (patient/caregiver, healthcare provider, pharmacy, wholesalers/distributors, other)
        ii. A table summarizing the most frequently asked questions (e.g., enrollment question) and by stakeholder type (e.g., patient/caregiver, healthcare provider, pharmacy, wholesalers/ distributors, etc.).
        iii. Summary of reasons for calls (e.g., enrollment question) and by reporter (authorized representative, patient/caregiver, healthcare provider, other)
        iv. If the summary reason for the call(s) indicates a complaint, provide details on the nature of the complaint(s) and whether they indicate potential REMS burden or patient access issues
        v. Summary of frequently asked questions (FAQ) by stakeholder type
        vi. A summary report of corrective actions resulting from issues identified

c. Infrastructure Performance

i. Number of times a backup system was used with reason(s) for each instance (for example, pharmacy level problem, or REMS database problem) clearly defined and described with description of corrective actions taken

ii. Number of times unintended system interruptions occurred for each reporting period. Describe the number of stakeholders affected, how the issue was resolved, and steps put into place to minimize the impact of future interruptions

6. REMS Compliance (current reporting period)

a. Audits of pharmacies, wholesalers/distributors, and the REMS program Call Center) will be conducted to ensure that all REMS processes and procedures are in place, functioning, and support the REMS program, and will be submitted with each assessment report. The audit reports are to include:

i. A copy of the audit plan used for the reporting period

ii. A detailed description of audit findings including the number with no findings, minor, moderate, or serious findings; include information about the root cause of the noncompliance

iii. Number of audited sites in each stakeholder category listed directly above.

iv. Number of audits expected, and the number of audits performed

v. Number and types of deficiencies noted for each group of audited stakeholders

vi. Include a unique ID for each stakeholder that had deviations to track deviations by stakeholder over time.

vii. Documentation of completion of training for relevant staff

viii. The existence of documented processes and procedures for complying with the REMS

ix. Verification that at each audited stakeholder's site, the designated authorized representative remains the same. If different, include the number of new authorized representatives and verification of the site's recertification.

x. For inpatient hospital pharmacies, also report:

1) The number of units of use of TIRFs ordered per inpatient hospital pharmacy audited per 12-month period

2) Verification that processes such as order sets/protocols are in place to assure compliance with the REMS

xi. For closed systems, also report:

1) Numbers of prescription authorizations per closed system;

2) Numbers of prescriptions dispensed that did not receive REMS authorization

xii. Describe any corrective actions taken for any non-compliance as identified above during the audits as well as preventative measures that were developed because of uncovering these non-compliance events

1) For those with deficiencies noted, report the number that successfully completed a corrective and preventive action (CAPA) plan within one month of the audit.

2) For any that did not complete the CAPA within one month of the audit, describe additional actions taken.

b. Description of number, specialties, and affiliations of the personnel that constitute the Non-Compliance Review Team (NCRT) as well as the Non-Compliance Working Group

c. For each non-compliance event, provide the source of the report, a description of the event, the cause of the event, if any patient harm resulted, and any corrective actions taken. Also provide a summary of non-compliance identified by stakeholder, including but not limited to:

i. For Prescribers, provide:

1) Number of prescribing healthcare providers who were non-compliant with TIRF REMS requirements

2) Number of prescriptions written by non-certified healthcare providers

3) Number of healthcare providers that were suspended or de-certified and reasons for decertification. Include if any healthcare providers were re-certified.

ii. For Pharmacies provide:

1) Number and types of pharmacies for which non-compliance with the REMS is detected

2) Number and type of non-certified pharmacies that dispensed TIRFs and the number of incidents for each

3) Number of TIRF prescriptions dispensed that were written by non-certified prescribers and include steps taken to prevent future occurrences

4) Number of prescriptions dispensed by non-certified pharmacies and include steps taken to prevent future occurrences

5) Number of times certified pharmacies dispensed TIRFs to unenrolled patients

6) Number of times a TIRF prescription was dispensed because a pharmacy (closed or open system) was able to bypass REMS edits and if any such events occurred, describe how these events occurred and were identified

7) Number of TIRF prescriptions dispensed to non-enrolled patients and the actions taken to prevent future occurrences

8) Number of pharmacies suspended or decertified by pharmacy type, the reasons for such actions, and actions to address non-compliance

iii. For Wholesalers/distributors provide:

1) The number of enrolled wholesalers/distributors for which non-compliance with the REMS is detected

2) Number of times TIRF products were distributed to a non-certified pharmacy or directly to patients, and actions taken to recover the TIRF product

3) Number of wholesalers suspended or de-enrolled, reasons for such action, and actions to address non-compliance

iv. For patients provide:

1) Number of patients unenrolled, and reasons for such

2) Number of patients not enrolled in the REMS who were dispensed TIRFs

d. For each non-patient stakeholder referred to in section 6.c. above:

i. Describe any moderate or serious non-compliance with the REMS that occurred during the first year of transitioning to the modified REMS

ii. Provide an assessment of stakeholder compliance in following the proposed transition plan in transitioning to the modified REMS

e. For each reporting period, include a copy of the non-compliance plan used during that reporting period

f. Number of times a TIRF was prescribed to an opioid non-tolerant individual by falsifying information. Include what was done to minimize such instances; if any such events occurred, describe how these events were identified

Safe Use Behaviors

7. **Patient Enrollment and Patient Status and Opioid Tolerance Forms**

   a. Report on the Patient Enrollment Form and Patient Status and Opioid Tolerance Form (the "Forms") (data presented for each individual form as well as combined):

      i. (For the 1-, 2-, and 3-year assessment reports only) The most common modes of submission of Forms to the REMS (e.g., Fax, online)

      ii. Number of Forms received compared to the number of TIRF prescriptions authorized for dispensing

         1) Explain any discrepancies between these two metrics

         2) Provide a description of the outcome/resolution of such event

      iii. Provide an analysis of cases where multiple submissions of a Form for the same patient were required prior to the pharmacy dispensing a prescription:

         1) Provide the mean, median, and range of the number of re-submissions

         2) Provide the reason(s) for the re-submissions grouped by commonly encountered situations

         3) Include an analysis of the number of Forms that were submitted that indicated that the patient was not opioid tolerant

      iv. Number of Forms submitted to the REMS with incomplete, erroneous, or altered fields; provide:

         1) An accounting of the sections of the Forms affected

         2) A description of the outcome/resolution of any incomplete, erroneous, or altered Forms

      v. For each TIRF dispense authorization (i.e., the prescriber provided documentation of opioid tolerance), provide the following:

         1) The number of these prescriptions that were dispensed by the pharmacy.

         2) For those prescriptions that were not dispensed, provide the reasons (e.g., patient not opioid tolerant as per the pharmacist, insurance/financial, etc.)

vi. For all dispensed TIRF prescriptions, provide an evaluation to confirm opioid tolerance based on the specific product, strength, frequency and duration provided on the Forms.

1) Conduct a quarterly analysis of patients prescribed TIRFs to assess whether they met the threshold for opioid tolerance. Provide the results of these analyses in the annual assessment reports. The performance thresholds for this analysis have been set as follows:

a) By the Year One assessment report, at least 80% of prescriptions written for TIRFs will be for opioid tolerant patients, as defined in labeling

b) By the Year Two assessment report, at least 90% of prescriptions written for TIRFs will be for opioid tolerant patients, as defined in labeling

c) By the Year Three assessment report, as well as for all subsequent assessment reports, at least 95% of prescriptions written for TIRFs will be for opioid tolerant patients, as defined in labeling

2) Provide the number of prescriptions dispensed as well as the number determined to have been dispensed to opioid non-tolerant patients.

a) Describe if any such events recurred in the same patients.

b) Conduct a follow-up in these patients for any adverse events of special interest.

Health Outcomes and/or Surrogates of Health Outcomes (data collected per reporting period)

8. Surveillance Data

a. Data from the REMS Patient Registry (REMS Data, Postmarketing Adverse Event Data): Surveillance data focused on Adverse Events of Special Interest (AESI) such as Accidental Exposure, Misuse, Abuse, Addiction, Overdose, Death, Serious Adverse Event.

i. Average number of patients for each enrolled prescriber

ii. Reports of inappropriate interchanges between TIRF products (a switch from a TIRF product to second TIRF product that is not initiated at the lowest dose when beginning the second TIRF)

iii. Number and percentage of patients experiencing an Adverse Event of Special Interest AESI

iv. The total number of AESIs reported and total number of each AESI (includes cases reported to the TIRF REMS by all sources including phone, REMS Forms, and spontaneous reports received directly by the application holders) per report source

v. Risk of each AESI, as a cumulative estimate from all patients enrolled in the new program, and stratified by:

1) REMS Assessment Period

2) Patients with and without any concomitant CNS depressant medication at enrollment, as documented on the Patient Enrollment Form

3) Patients with each specific category of concomitant CNS depressant medication at enrollment

4) Type of pain noted at enrollment: cancer pain, non-cancer pain

5) Child in the home/caregiver for small children, yes or no

vi. Summary of details of AESIs reported, and outcomes of AESIs (if known)

vii. Specifically, regarding the Patient Discontinuation Form:

1) The number of such forms submitted

2) The number reporting AESI or death

3) The reasons for discontinuation indicated

viii. The number of Targeted AESI Forms expected, the number completed, and the reasons for this discrepancy

ix. Monitor whether the percentage of patients who experience AESIs is increasing or decreasing over time

b. Surveillance data to monitor events of accidental exposure, misuse, abuse, addiction, overdose, death, and pediatric cases should also be drawn from poison control center data, including case narratives.

i. Depending on results of REMS assessment reports, additional surveillance data sources may be required

c. Healthcare data to monitor events of pediatric accidental exposure requiring medical evaluation. FDA determined that the REMS assessment must include a medical record review of drug-related hospitalizations and hospital emergency department visits. Depending on the study results, administrative claims data may be required in addition to or instead of medical records data.

d. Death certificate data to monitor drug-related deaths, especially involving pediatric subjects

e. Regarding spontaneous adverse event reports:

   i. AESI reports related to specific TIRF products will be reported to the FDA in accordance with 21 CFR 314.80.

   ii. AESI reports are to be linked to the registry and de-duplicated as is possible.

   iii. AESI reports from an inpatient setting, or outpatient reports that cannot be linked to enrolled patient data will be summarized separately.

   iv. The FAERS public dashboard is to be utilized.

   v. TIRF product application holders will retrieve AESI reports from their respective safety databases and calculate reporting rates.

   vi. Each TIRF product application holder is to submit MedWatch reports in conjunction with un-blinded line listings directly to the FDA.

Knowledge

9. Periodic Surveys of Prescribers, Pharmacists, and Patients (due with the 2-Year REMS Assessment Report and annually thereafter with each assessment report)

A Knowledge, Attitude and Behavior (KAB) Survey will be conducted with random samples of prescribers, pharmacists, and patients who have prescribed, dispensed, or received a TIRF medicine.

a. Certified Prescriber KAB surveys will assess if prescribers are educated on the following:

   i. TIRF medicines contain fentanyl. Serious, life-threatening, and/or fatal respiratory depression has occurred.

   ii. Patients must be opioid tolerant to be prescribed a TIRF Medicine.

   iii. Accidental exposure to children and others and may cause severe or fatal respiratory depression.

   iv. Prescribers must counsel their patients on the risk of misuse, abuse, addiction, and overdose.

b. Certified Outpatient Pharmacist KAB surveys will assess understanding of the following key risk messages:

i. TIRF medicines contain fentanyl. Serious life-threatening, and/or fatal respiratory depression has occurred.

ii. Patients must be opioid tolerant to be prescribed a TIRF Medicine.

iii. For each outpatient prescription, the pharmacist must obtain a prescription authorization number from the TIRF REMS Access program prior to dispensing each TIRF medicine.

iv. Accidental exposure to children and others and may cause severe or fatal respiratory depression.

c. Certified Inpatient Pharmacist KAB surveys will assess understanding of the following key risk messages:

i. TIRF medicines contain fentanyl. Serious, life-threatening, and/or fatal respiratory depression has occurred.

ii. Develop internal policies and procedures to verify opioid tolerant inpatients who require TIRF medicine while hospitalized.

d. Patient KAB surveys will assess patient understanding of the following key risk messages:

i. TIRF medicines can cause you to stop breathing which can lead to death.

ii. Accidental poisoning by a child or others could cause harm or even death.

10. Knowledge Assessments (provide for each reporting period and cumulatively)

a. The number of completed post-training knowledge assessments for healthcare providers who can prescribe and pharmacy authorized representatives including the method of completion and the number of attempts to complete.

b. A summary of the most frequently missed knowledge assessment questions.

c. A summary of potential comprehension or perception issues identified with the knowledge assessment.

11. The requirement for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of the last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing

the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 020747 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g., UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

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

NDA 020747 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 020747/S-000/
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 020747/S-000/
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 020747/S-000/
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES
SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 020747/S-000/

REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA 020747

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the prescribing information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must submit final promotional materials and prescribing information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call LCDR Jessica Voqui, PharmD, MS; Safety Regulatory Project Manager, at 301-796-2915.

Sincerely,

{See appended electronic signature page}

LCDR Mark A. Liberatore, PharmD, RAC
Deputy Director for Safety
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE:
- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARK A LIBERATORE
12/23/2020 04:05:28 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

020747Orig1s050

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ACTIQ safely and effectively. See full prescribing information for ACTIQ.

ACTIQ® (fentanyl citrate) oral transmucosal lozenge, CII
Initial U.S. Approval: 1968

WARNING: SERIOUS AND LIFE-THREATENING RISKS FROM USE OF ACTIQ

See full prescribing information for complete boxed warning.

- **ACTIQ exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and reassess regularly for these behaviors and conditions. (5.1)**
- **Serious, life-threatening, or fatal respiratory depression has occurred in patients treated with ACTIQ, including following use in opioid non-tolerant patients and improper dosing. Regularly evaluate patients, especially upon initiation or following a dosage increase. To reduce the risk of respiratory depression, proper dosing and titration of ACTIQ are essential. The substitution of ACTIQ for any other fentanyl product may result in fatal overdose. Due to the risk of fatal respiratory depression, ACTIQ is contraindicated in opioid non-tolerant patients and in management of acute or postoperative pain, including headache/migraines. (1, 4, 5.2)**
- **Accidental ingestion of ACTIQ, especially by children, can result in a fatal overdose of fentanyl. Keep out of reach of children. Ensure proper storage and disposal. (2.8, 5.3)**
- **Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate. (5.4, 7)**
- **If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of Neonatal Opioid Withdrawal Syndrome, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery. (5.8)**
- **ACTIQ is available only through a restricted program called the TIRF REMS. Pharmacies, outpatients, and healthcare professionals who prescribe to outpatients are required to enroll in the program. Patients must be opioid tolerant to receive a TIRF medicine (5.7)**
- **When prescribing, do not convert patients on a mcg per mcg basis from any other fentanyl product to ACTIQ. (5.5)**
- **When dispensing, do not substitute with any other fentanyl products. (5.5)**
- **Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of fentanyl. (5.6, 7, 12.3)**

RECENT MAJOR CHANGES

Boxed Warning	12/2023
Dosage and Administration (2.1, 2.5)	12/2023
Warnings and Precautions (5.9)	12/2023

INDICATIONS AND USAGE

ACTIQ is an opioid agonist indicated for the management of breakthrough pain in cancer patients 16 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain. (1)

Patients considered opioid tolerant are those who are taking, for one week or longer, around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg of transdermal fentanyl per hour, at least 30 mg of oral oxycodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg oral oxymorphone per day, at least 60 mg of oral hydrocodone per day, or an equianalgesic dose of another opioid. Patients must remain on around-the-clock opioids while taking ACTIQ.

Limitations of Use:

- Not for use in opioid non-tolerant patients.
- Not for use in the management of acute or postoperative pain, including headache/migraine or dental pain. (4)
- As a part of the TIRF REMS, ACTIQ may be dispensed by outpatient pharmacies only to outpatients enrolled in the program. (5.7) For inpatient administration of ACTIQ, patient and prescriber enrollment are not required.

DOSAGE AND ADMINISTRATION

- Patients must require and use around-the-clock opioids when taking ACTIQ. (1)
- ACTIQ should be prescribed only by healthcare professionals who are knowledgeable about the use of opioids and how to mitigate the associated risks. (2.1)
- Use the lowest effective dosage for the shortest duration of time consistent with individual patient treatment goals. Reserve titration to higher doses of ACTIQ for patients in whom lower doses are insufficiently effective and in whom the expected benefits of using a higher dose opioid clearly outweigh the substantial risks. (2.1, 5)
- Initiate the dosing regimen for each patient individually, taking into account the patient's underlying cause and severity of pain, patient response, prior analgesic experience, and risk factors for addiction, abuse, and misuse. (2.1, 5.1)
- Respiratory depression can occur at any time during opioid therapy, especially when initiating and following dosage increases with ACTIQ. Consider this risk when selecting an initial dose and when making dose adjustments. (2.1, 5.2)
- Discuss availability of naloxone with the patient and caregiver and assess each patient's need for access to naloxone, both when initiating and renewing treatment with ACTIQ. Consider prescribing naloxone based on the patient's risk factors for overdose. (2.2, 5.1, 5.2, 5.4)
- Initial dose of ACTIQ: 200 mcg. Prescribe an initial supply of six 200 mcg ACTIQ units. (2.3)
- Individually titrate to a tolerable dose that provides adequate analgesia using single ACTIQ dosage unit per breakthrough cancer pain episode. (2.4)
- No more than two doses can be taken per breakthrough pain episode. (2.4, 2.5)
- Wait at least 4 hours before treating another episode of breakthrough pain with ACTIQ. (2.4, 2.5)
- Limit consumption to four or fewer units per day once successful dose is found. (2.5)
- When opioid therapy is no longer required, consider discontinuing ACTIQ along with a gradual downward of other opioids to minimize possible withdrawal effects. (2.7)

DOSAGE FORMS AND STRENGTHS

- Solid oral transmucosal lozenge: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, and 1600 mcg. (3)

CONTRAINDICATIONS

- Opioid non-tolerant patients. (4)
- Significant respiratory depression. (4)
- Management of acute or postoperative pain, including headache/migraine and dental pain. (4)
- Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment. (4)
- Known or suspected gastrointestinal obstruction, including paralytic ileus. (4)
- Known hypersensitivity to fentanyl or components of ACTIQ. (4)

WARNINGS AND PRECAUTIONS

- Opioid-Induced Hyperalgesia and Allodynia: Opioid-Induced Hyperalgesia (OIH) occurs when an opioid analgesic paradoxically causes an increase in pain, or an increase in sensitivity to pain. If OIH is suspected, carefully consider appropriately decreasing the dose of the current opioid analgesic or opioid rotation. (5.9)
- Serotonin Syndrome: Potentially life-threatening condition could result from concomitant serotonergic drug administration. Discontinue ACTIQ if serotonin syndrome is suspected. (5.10)
- Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients: Regularly evaluate patients, particularly during initiation and titration. (5.11)
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid. (5.12)
- Severe Hypotension: Regularly evaluate patients during dosage initiation and titration. Avoid use of ACTIQ in patients with circulatory shock. (5.13)
- Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of ACTIQ in patients with impaired consciousness or coma. (5.14)

ADVERSE REACTIONS

Most common (frequency ≥5%): nausea, dizziness, somnolence, vomiting, asthenia, and headache, dyspnea, constipation, anxiety, confusion, depression, rash, and insomnia. (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

- Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics: Avoid the use of mixed agonist/antagonist or partial agonist analgesics in patients who are already receiving a full opioid agonist analgesic (including ACTIQ) because they may reduce analgesic effect of ACTIQ or precipitate withdrawal symptoms. (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Not recommended. (8.2)
- Renal and Hepatic Impairment: Administer ACTIQ with caution. (8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 12/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

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* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: SERIOUS AND LIFE-THREATENING RISKS FROM USE OF ACTIQ

Addiction, Abuse, and Misuse

Because the use of ACTIQ exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death, assess each patient's risk prior to prescribing and reassess all patients regularly for the development of these behaviors and conditions *[see Warnings and Precautions (5.1)]*.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has occurred in patients treated with ACTIQ, including following use in opioid non-tolerant patients and improper dosing. Evaluate patients for respiratory depression, especially during initiation of ACTIQ or following a dosage increase. To reduce the risk of respiratory depression, proper dosing and titration of ACTIQ are essential. The substitution of ACTIQ for any other fentanyl product may result in fatal overdose *[see Warnings and Precautions (5.2)]*.

Due to the risk of respiratory depression, ACTIQ is contraindicated in the management of acute or postoperative pain including headache/migraine and in opioid non-tolerant patients *[see Contraindications (4)]*.

Accidental Ingestion

Accidental ingestion of even one dose of ACTIQ, especially by children, can result in a fatal overdose of fentanyl. Death has been reported in children who have accidentally ingested ACTIQ. ACTIQ must be kept out of reach of children *[see Warnings and Precautions (5.3)]*.

Risks From Concomitant Use with Benzodiazepines or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of ACTIQ and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate *[see Warnings and Precautions (5.4), Drug Interactions (7)]*.

Risk of Medication Errors

Substantial differences exist in the pharmacokinetic profile of ACTIQ compared to other fentanyl products that result in clinically important differences in the extent of absorption of fentanyl and that could result in fatal overdose *[see Dosage and Administration (2.1), Warnings and Precautions (5.5)]*.

- **When prescribing, do not convert patients on a mcg per mcg basis from any other fentanyl products to ACTIQ *[see Dosage and Administration (2.1)]*.**
- **When dispensing, do not substitute an ACTIQ prescription for other fentanyl products.**

Cytochrome P450 3A4 Interaction

The concomitant use of ACTIQ with all cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse reactions and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in fentanyl plasma concentration. Evaluate patients at frequent intervals receiving ACTIQ and any CYP3A4 inhibitor or inducer *[see Warnings and Precautions (5.6), Drug Interactions (7), Clinical Pharmacology (12.3)].*

Risk Evaluation and Mitigation Strategy (REMS)

Because of the risk for accidental exposure, misuse, abuse, addiction, and overdose, ACTIQ is available only through a restricted program required by the Food and Drug Administration, called a Risk Evaluation and Mitigation Strategy (REMS). Under the Transmucosal Immediate Release Fentanyl (TIRF) REMS, pharmacies, outpatients, and healthcare professionals who prescribe to outpatients must enroll in the program. Inpatient pharmacies must develop policies and procedures to verify opioid tolerance in inpatients who require ACTIQ while hospitalized. Further information is available at www.TIRFREMSAccess.com or by calling 1-866-822-1483 *[see Warnings and Precautions (5.7)].*

Neonatal Opioid Withdrawal Syndrome (NOWS)

If opioid use is required for an extended period of time in a pregnant woman, advise the patient of the risk of NOWS, which may be life-threatening if not recognized and treated. Ensure that management by neonatology experts will be available at delivery *[see Warnings and Precautions (5.8)].*

1 INDICATIONS AND USAGE

ACTIQ is indicated for the management of breakthrough pain in cancer patients 16 years of age and older who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Patients considered opioid tolerant are those who are taking, for one week or longer, around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg of transdermal fentanyl per hour, at least 30 mg of oral oxycodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg oral oxymorphone per day, at least 60 mg of oral hydrocodone per day, or an equianalgesic dose of another opioid. Patients must remain on around-the-clock opioids when taking ACTIQ.

Limitations of Use:

- Not for use in opioid non-tolerant patients.
- Not for use in the management of acute or postoperative pain, including headache/migraine and dental pain *[see Contraindications (4)]*.
- As a part of the TIRF REMS, ACTIQ may be dispensed by outpatient pharmacies only to outpatients enrolled in the program *[see Warnings and Precautions (5.7)]*. For inpatient administration of ACTIQ, patient and prescriber enrollment are not required.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

- Healthcare professionals who prescribe ACTIQ for outpatients must enroll in the TIRF REMS and comply with the requirements of the REMS to ensure safe use of ACTIQ *[see Warnings and Precautions (5.7)]*.
- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals *[see Warnings and Precautions (5)]*. Because the risk of overdose increases as opioid doses increase, reserve titration to higher doses of ACTIQ for patients in whom lower doses are insufficiently effective and in whom the expected benefits of using a higher dose opioid clearly outweigh the substantial risks.
- It is important to minimize the number of strengths available to patients at any time to prevent confusion and possible overdose.
- There is variability in the opioid analgesic dose and duration needed to adequately manage pain due both to the cause of pain and to individual patient factors. Initiate the dosing regimen for each patient individually, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse *[see Warnings and Precautions (5.1)]*.
- Respiratory depression can occur at any time during opioid therapy, especially when initiating and following dosage increases with ACTIQ. Consider this risk when selecting an initial dose and when making dose adjustments *[see Warnings and Precautions (5)]*.
- Instruct patients and caregivers to take steps to store ACTIQ securely and to properly dispose of unused ACTIQ as soon as no longer needed *[see Warnings and Precautions (5.1, 5.3)]*.
- Other TIRF formulations and ACTIQ are not equivalent. DO NOT substitute an ACTIQ prescription for any other TIRF formulation under any circumstances. Do not convert patients on a mcg per mcg basis from any other fentanyl product to ACTIQ *[see Warnings and Precautions (5.5)]*.

2.2 Patient Access to Naloxone for the Emergency Treatment of Opioid Overdose

Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver and assess the potential need for access to naloxone, both when initiating and renewing treatment with ACTIQ *[see Warnings and Precautions (5.2)]*.

Inform patients and caregivers about the various ways to obtain naloxone as permitted by individual state naloxone dispensing and prescribing requirements or guidelines (e.g., by prescription, directly from a pharmacist, or as part of a community-based program).

Consider prescribing naloxone, based on the patient’s risk factors for overdose, such as concomitant use of CNS depressants, a history of opioid use disorder, or prior opioid overdose.

The presence of risk factors for overdose should not prevent the proper management of pain in any given patient *[see Warnings and Precautions (5.1, 5.2, 5.4)]*.

Consider prescribing naloxone if the patient has household members (including children) or other close contacts at risk for accidental ingestion or overdose.

2.3 Initial Dosage

Individually titrate ACTIQ to a dose that provides adequate analgesia and minimizes side effects. The initial dose of ACTIQ to treat episodes of breakthrough cancer pain is always 200 mcg. The ACTIQ unit should be consumed over 15 minutes. Patients should be prescribed an initial titration supply of six 200 mcg ACTIQ units, thus limiting the number of units in the home during titration. Patients should use up all units before increasing to a higher dose to prevent confusion and possible overdose.

Repeat Dosing

a. In cases where the breakthrough pain episode is not relieved after 15 minutes after completion of the ACTIQ unit (30 minutes after the start of the unit), patients may take ONLY ONE additional dose using the same strength for that episode. Thus patients should take a maximum of two doses of ACTIQ for any episode of breakthrough pain.

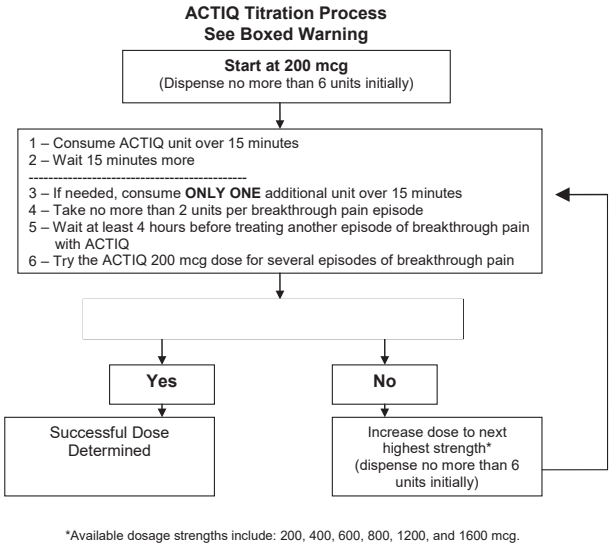
b. Patients MUST wait at least 4 hours before treating another episode of breakthrough pain with ACTIQ.

2.4 Dose Titration

From an initial dose, closely follow patients and change the dosage strength until the patient reaches a dose that provides adequate analgesia using a single ACTIQ dosage unit per breakthrough cancer pain episode. If signs of excessive opioid effects appear before the unit is consumed, the dosage unit should be removed from the patient's mouth immediately, disposed of properly, and subsequent doses should be decreased. Patients should record their use of ACTIQ over several episodes of breakthrough cancer pain and review their experience with their healthcare providers to determine if a dosage adjustment is warranted.

In cases where the breakthrough pain episode is not relieved 15 minutes after completion of the ACTIQ unit (30 minutes after the start of the unit), patients may take ONLY ONE additional dose of the same strength for that episode. Thus, patients should take a maximum of two doses of ACTIQ for any breakthrough pain episode.

Patients must wait at least 4 hours before treating another episode of breakthrough pain with ACTIQ. To reduce the risk of overdosing during titration, patients should have only one strength of ACTIQ available at any one time.



*Available dosage strengths include: 200, 400, 600, 800, 1200, and 1600 mcg.

2.5 Maintenance Dosing

a. Once titrated to an effective dose, patients should generally use ONLY ONE ACTIQ unit of the appropriate strength per breakthrough pain episode.

b. On those occasions when the breakthrough pain episode is not relieved 15 minutes after completion of the ACTIQ unit, patient may take ONLY ONE additional dose using the same strength for that episode.

c. Patients MUST wait at least 4 hours before treating another episode of breakthrough pain with ACTIQ. Once a successful dose has been found (i.e., an average episode is treated with a single unit), patients should limit consumption to four or fewer units per day.

d. Dosage adjustment of ACTIQ may be required in some patients in order to continue to provide adequate relief of breakthrough pain. If after increasing the dosage, unacceptable opioid-related adverse reactions are observed (including an increase in pain after dosage increase), consider reducing the dosage *[see Warnings and Precautions (5)]*. Adjust the dosage to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

e. Generally, the ACTIQ dose should be increased only when a single administration of the current dose fails to adequately treat the breakthrough pain episode for several consecutive episodes.

f. If the patient experiences greater than four breakthrough pain episodes per day, the dose of the maintenance (around-the-clock) opioid used for persistent pain should be re-evaluated.

2.6 Administration of ACTIQ

Open the blister package with scissors immediately prior to product use. The patient should place the ACTIQ unit in his or her mouth between the cheek and lower gum, occasionally moving the drug matrix from one side to the other using the handle. The ACTIQ unit should be sucked, not chewed. A unit dose of ACTIQ, if chewed and swallowed, might result in lower peak

concentrations and lower bioavailability than when consumed as directed *[see Clinical Pharmacology (12.3)]*.

The ACTIQ unit should be consumed over a 15-minute period. Longer or shorter consumption times may produce less efficacy than reported in ACTIQ clinical trials. If signs of excessive opioid effects appear before the unit is consumed, remove the drug matrix from the patient's mouth immediately and decrease future doses.

2.7 Discontinuation of ACTIQ

When opioid therapy is no longer required, consider discontinuing ACTIQ along with a gradual downward tapering (titration) of other opioids to minimize possible withdrawal effects. In patients who continue to take their chronic opioid therapy for persistent pain but no longer require treatment for breakthrough pain, ACTIQ therapy can usually be discontinued immediately *[see Drug Abuse and Dependence (9.3)]*.

2.8 Disposal of ACTIQ

After consumption of the unit is complete and the matrix is totally dissolved, throw away the handle in a trash container that is out of the reach of children.

- If any of the drug matrix remains on the handle, place the handle under hot running tap water until all of the drug matrix is dissolved, and then dispose of the handle in a place that is out of the reach of children.
- Dispose of handles in the child-resistant container (as described in steps 1 and 2) at least once a day.

If the temporary storage bottle provided as part of the ACTIQ Child Safety Kit is available, partially consumed units may be stored in the specially provided child-resistant container out of the reach of children until proper disposal is possible.

Unopened units remaining from a prescription must be properly disposed as soon as they are no longer needed.

To dispose of the unused ACTIQ units:

- Remove the ACTIQ unit from its blister package using scissors, and hold ACTIQ by its handle over the toilet bowl.
- Using wire-cutting pliers cut off the drug matrix end so that it falls into the toilet.
- Dispose of the handle in a place that is out of the reach of children.
- Repeat steps 1, 2, and 3 for each ACTIQ unit. Flush the toilet twice after 5 units have been cut and deposited into the toilet.

Do not flush the entire ACTIQ units, ACTIQ handles, blister packages, or cartons down the toilet. Dispose of the handle where children cannot reach it.

In the event that a caregiver requires additional assistance in disposing of excess unusable units that remain in the home after a patient has expired, instruct them to call the toll-free number for Teva Pharmaceuticals (1-888-483-8279) or seek assistance from their local DEA office.

3 DOSAGE FORMS AND STRENGTHS

Solid oral transmucosal lozenge: Each dosage unit has white to off-white color and is a solid drug matrix on a handle. Each strength is marked on the individual solid drug matrix and the handle tag. ACTIQ is available in 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg and 1600 mcg strengths *[see How Supplied/Storage and Handling (16)]*.

4 CONTRAINDICATIONS

ACTIQ is contraindicated in:

- Opioid non-tolerant patients: Life-threatening respiratory depression and death could occur at any dose in opioid non-tolerant patients *[see Indications and Usage (1), Warnings and Precautions (5.2)]*.
- Significant respiratory depression *[see Warnings and Precautions (5.2)]*.
- Acute or postoperative pain including headache/migraine and dental pain, or acute pain in the emergency department *[see Indications and Usage (1)]*.
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment *[see Warnings and Precautions (5.11)]*.
- Known or suspected gastrointestinal obstruction, including paralytic ileus *[see Warnings and Precautions (5.15)]*.
- Known hypersensitivity to fentanyl or components of ACTIQ (e.g., anaphylaxis, hypersensitivity) *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Addiction, Abuse, and Misuse

ACTIQ contains fentanyl, a Schedule II controlled substance. As an opioid, ACTIQ exposes users to the risks of addiction, abuse, and misuse *[see Drug Abuse and Dependence (9)]*.

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed ACTIQ. Addiction can occur at recommended dosages and if the drug is misused or abused.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing ACTIQ, and reassess all patients receiving ACTIQ for the development of these behaviors and conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as ACTIQ, but use in such patients necessitates intensive counseling about the risks and proper use of ACTIQ along with frequent reevaluation for signs of addiction, abuse, and misuse. Consider prescribing naloxone for the emergency treatment of opioid overdose *[see Dosage and Administration (2.2), Warnings and Precautions (5.2)]*.

Opioids are sought for nonmedical use and are subject to diversion from legitimate prescribed use. Consider these risks when prescribing or dispensing ACTIQ. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on careful storage of the drug during the course of treatment and proper disposal of unused drug. Contact local state professional licensing board or state-controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

5.2 Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status *[see Overdosage (10)]*. Carbon dioxide (CO_2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of ACTIQ, the risk is greatest during the initiation of therapy or following a dosage increase.

To reduce the risk of respiratory depression, proper dosing and titration of ACTIQ are essential *[see Dosage and Administration (2)]*. Overestimating the ACTIQ dosage can result in a fatal overdose with the first dose. The substitution of ACTIQ for any other fentanyl product may result in fatal overdose *[see Warnings and Precautions (5.5)]*.

ACTIQ could be fatal to individuals for whom it is not prescribed and for those who are not opioid-tolerant.

Accidental ingestion of even one dose of ACTIQ, especially by children, can result in respiratory depression and death due to an overdose of fentanyl *[see Warnings and Precautions (5.3)]*.

Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help right away in the event of a known or suspected overdose.

Opioids can cause sleep-related breathing disorders including central sleep apnea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper *[see Dosage and Administration (2.7)]*.

Patient Access to Naloxone for the Emergency Treatment of Opioid Overdose

Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver and assess the potential need for access to naloxone, both when initiating and renewing treatment with ACTIQ. Inform patients and caregivers about the various ways to obtain naloxone as permitted by individual state naloxone dispensing and prescribing requirements or guidelines (e.g., by prescription, directly from a pharmacist, or as part of a community-based program). Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help, even if naloxone is administered.

Consider prescribing naloxone, based on the patient's risk factors for overdose, such as concomitant use of CNS depressants, a history of opioid use disorder, or prior opioid overdose. The presence of risk factors for overdose should not prevent the proper management of pain in any given patient. Also consider prescribing naloxone if the patient has household members (including children) or other close contacts at risk for accidental ingestion or overdose. If naloxone is prescribed, educate patients and caregivers on how to treat with naloxone *[see Dosage and Administration (2.2), Warnings and Precautions (5.1, 5.4), Overdosage (10)]*.

5.3 Increased Risk of Overdose in Children Due to Accidental Ingestion or Exposure

Death has been reported in children who have accidentally ingested ACTIQ.

Patients and their caregivers must be informed that ACTIQ contains a medicine in an amount which can be fatal to a child. Healthcare providers and dispensing pharmacists must specifically question patients or caregivers about the presence of children in the home (on a full time or visiting basis) and counsel them regarding the dangers to children from inadvertent exposure.

Patients and their caregivers must be instructed to keep both used and unused dosage units out of the reach of children. While all units should be disposed of immediately after use, partially consumed units represent a special risk to children. In the event that a unit is not completely consumed it must be properly disposed as soon as possible.

Detailed instructions for the proper storage, administration, disposal, and important instructions for managing an overdose of ACTIQ are provided in the ACTIQ *Medication Guide*. Encourage patients to read this information in its entirety and give them an opportunity to have their questions answered.

5.4 Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants (including Alcohol)

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of ACTIQ with benzodiazepines and/or other CNS depressants, including alcohol (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics *[see Drug Interactions (7)]*.

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a

benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Inform patients and caregivers of this potential interaction and educate them on the signs and symptoms of respiratory depression (including sedation).

If concomitant use is warranted, consider prescribing naloxone for the emergency treatment of opioid overdose *[see Dosage and Administration (2.2), Warnings and Precautions (5.2)]*.

Advise both patients and caregivers about the risks of respiratory depression and sedation when ACTIQ is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs *[see Drug Interactions (7)]*.

5.5 Risk of Medication Errors

When prescribing, do not convert a patient to ACTIQ from any other fentanyl product on a mcg per mcg basis as ACTIQ and other fentanyl products are not equivalent on a microgram per microgram basis.

ACTIQ is not a generic version of other transmucosal immediate release fentanyl (TIRF) formulations. When dispensing, do not substitute an ACTIQ prescription for any other TIRF formulation under any circumstances. Other TIRF formulations and ACTIQ are not equivalent. Substantial differences exist in the pharmacokinetic profile of ACTIQ compared to other fentanyl products including other TIRF formulations that result in clinically important differences in the rate and extent of absorption of fentanyl. As a result of these differences, the substitution of ACTIQ for any other fentanyl product may result in a fatal overdose.

There are no safe conversion directions available for patients on any other fentanyl products. (Note: This includes oral, transdermal, or parenteral formulations of fentanyl.) Therefore, for opioid tolerant patients, the initial dose of ACTIQ should always be 200 mcg. Each patient should be individually titrated to provide adequate analgesia while minimizing side effects *[see Dosage and Administration (2.4)]*.

5.6 Risks of Concomitant Use or Discontinuation of Cytochrome P450 3A4 Inhibitors and Inducers

Concomitant use of ACTIQ with a CYP3A4 inhibitor, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir), may increase plasma concentrations of fentanyl and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression *[see Warnings and Precautions (5.2)]*, particularly when an inhibitor is added after a stable dose of ACTIQ is achieved. Similarly, discontinuation of a CYP3A4 inducer, such as rifampin, carbamazepine, and phenytoin, in ACTIQ-treated patients may increase fentanyl plasma concentrations and prolong opioid adverse reactions. When using ACTIQ with CYP3A4 inhibitors or discontinuing CYP3A4 inducers in ACTIQ-treated patients, evaluate patients at frequent intervals and consider dosage reduction of ACTIQ until stable drug effects are achieved *[see Drug Interactions (7)]*.

Concomitant use of ACTIQ with CYP3A4 inducers or discontinuation of a CYP3A4 inhibitor could decrease fentanyl plasma concentrations, decrease opioid efficacy or, possibly, lead to a withdrawal syndrome in a patient who had developed physical dependence to fentanyl. When using ACTIQ with CYP3A4 inducers or discontinuing CYP3A4 inhibitors, evaluate patients at frequent intervals and consider increasing the opioid dosage if needed to maintain adequate analgesia or if symptoms of opioid withdrawal occur *[see Drug Interactions (7)].*

5.7 Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS)

Because of the risk for accidental exposure, misuse, abuse, addiction, and overdose *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9)],* ACTIQ is available only through a restricted program called the TIRF REMS. Under the TIRF REMS, healthcare professionals who prescribe to outpatients, the outpatients themselves, and pharmacies are required to enroll in the program.

Notable requirements of the TIRF REMS are:

- Prescribers for outpatient use must be certified with the REMS program by enrolling and completing training. Prescribers must document opioid tolerance with every ACTIQ prescription.
- Outpatients must be enrolled in the REMS program and must be opioid-tolerant to receive ACTIQ *[see Dosage and Administration (2.1)]*.
- Outpatient pharmacies must be certified with the REMS program and verify documentation of opioid tolerance with every ACTIQ prescription.
- Inpatient pharmacies must be certified with the REMS program and develop policies and procedures to verify opioid tolerance in inpatients who require ACTIQ while hospitalized.
- Wholesalers and distributors must enroll in the REMS program and distribute only to certified pharmacies.

Further information, including a list of certified pharmacies and enrolled distributors, is available at www.TIRFREMSAccess.com or by calling 1-866-822-1483.

5.8 Neonatal Opioid Withdrawal Syndrome

Use of ACTIQ for an extended period of time during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for an extended period of time of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available *[see Use in Specific Populations (8.1)]*.

5.9 Opioid-Induced Hyperalgesia and Allodynia

Opioid-Induced Hyperalgesia (OIH) occurs when an opioid analgesic paradoxically causes an increase in pain, or an increase in sensitivity to pain. This condition differs from tolerance, which is the need for increasing doses of opioids to maintain a defined effect *[see Dependence (9.3)]*. Symptoms of OIH include (but may not be limited to) increased levels of pain upon opioid dosage increase, decreased levels of pain upon opioid dosage decrease, or pain from ordinarily non-painful stimuli (allodynia). These symptoms may suggest OIH only if there is no evidence of underlying disease progression, opioid tolerance, opioid withdrawal, or addictive behavior.

Cases of OIH have been reported, both with short-term and longer-term use of opioid analgesics. Though the mechanism of OIH is not fully understood, multiple biochemical pathways have been implicated. Medical literature suggests a strong biologic plausibility between opioid analgesics and OIH and allodynia. If a patient is suspected to be experiencing OIH, carefully consider appropriately decreasing the dose of the current opioid analgesic or opioid rotation (safely switching the patient to a different opioid moiety) *[see Dosage and Administration (2.7)]*.

5.10 Serotonin Syndrome with Concomitant Use of Serotonergic Drugs

Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of ACTIQ with serotonergic drugs. Serotonergic drugs include selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonergic neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), certain muscle relaxants (i.e., cyclobenzaprine, metaxalone), and drugs that impair metabolism of serotonin (including MAO inhibitors, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue) *[see Drug Interactions (7)]*. This may occur within the recommended dosage range.

Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea) and can be fatal. The onset of symptoms generally occurs within several hours to a few days of concomitant use, but may occur later than that. Discontinue ACTIQ if serotonin syndrome is suspected.

5.11 Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of ACTIQ in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: ACTIQ-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of ACTIQ *[see Warnings and Precautions (5.2)]*.

Elderly, Cachectic, or Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients *[see Warnings and Precautions (5.2)]*.

Regularly evaluate patients, particularly when initiating and titrating ACTIQ and when ACTIQ is given concomitantly with other drugs that depress respiration *[see Warnings and Precautions (5.2), Drug Interactions (7)]*. Alternatively, consider the use of non-opioid analgesics in these patients.

5.12 Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

5.13 Severe Hypotension

ACTIQ may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g. phenothiazines or general anesthetics) *[see Drug Interactions (7)]*. Regularly evaluate these patients for signs of hypotension after initiating or titrating the dosage of ACTIQ. In patients with circulatory shock, ACTIQ may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of ACTIQ in patients with circulatory shock.

5.14 Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

In patients who may be susceptible to the intracranial effects of CO_2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), ACTIQ may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with ACTIQ.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of ACTIQ in patients with impaired consciousness or coma.

5.15 Risks of Use in Patients with Gastrointestinal Conditions

ACTIQ is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

The fentanyl in ACTIQ may cause spasm of the sphincter of Oddi. Opioids may cause increases in serum amylase. Regularly evaluate patients with biliary tract disease, including acute pancreatitis for worsening symptoms.

5.16 Increased Risk of Seizures in Patients with Seizure Disorders

The fentanyl in ACTIQ may increase the frequency of seizures in patients with seizure disorders, and may increase the risk of seizures occurring in other clinical settings associated with seizures. Regularly evaluate patients with a history of seizure disorders for worsened seizure control during ACTIQ therapy.

5.17 Risks of Driving and Operating Machinery

ACTIQ may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of ACTIQ and know how they will react to the medication.

5.18 Cardiac Disease

Intravenous fentanyl may produce bradycardia. Therefore, use ACTIQ with caution in patients with bradyarrhythmias.

6 ADVERSE REACTIONS

The following serious adverse reactions are described, or described in greater detail, in other sections:

- Addiction, Abuse, and Misuse *[see Warnings and Precautions (5.1)]*
- Life-Threatening Respiratory Depression *[see Warnings and Precautions (5.2)]*
- Interactions with Benzodiazepines and Other CNS Depressants *[see Warnings and Precautions (5.4)]*
- Neonatal Opioid Withdrawal Syndrome *[see Warnings and Precautions (5.8)]*
- Opioid-Induced Hyperalgesia and Allodynia *[see Warnings and Precautions (5.9)]*
- Serotonin Syndrome *[see Warnings and Precautions (5.10)]*
- Adrenal Insufficiency *[see Warnings and Precautions (5.12)]*
- Severe Hypotension *[see Warnings and Precautions (5.13)]*
- Gastrointestinal Adverse Reactions *[see Warnings and Precautions (5.15)]*
- Seizures *[see Warnings and Precautions (5.16)]*

6.1 Clinical Studies 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 practice.

The safety of ACTIQ has been evaluated in 257 opioid-tolerant chronic cancer pain patients. The duration of ACTIQ use varied during the open-label study. Some patients were followed for over 21 months. The average duration of therapy in the open-label study was 129 days.

The most serious adverse reactions associated with ACTIQ are respiratory depression (potentially leading to apnea or respiratory arrest), circulatory depression, hypotension, and shock.

Because the clinical trials of ACTIQ were designed to evaluate safety and efficacy in treating breakthrough cancer pain, all patients were also taking concomitant opioids, such as sustained-release morphine or transdermal fentanyl, for their persistent cancer pain. The adverse event data presented here reflect the actual percentage of patients experiencing each adverse effect among patients who received ACTIQ for breakthrough cancer pain along with a concomitant opioid for persistent cancer pain. There has been no attempt to correct for concomitant use of other opioids, duration of ACTIQ therapy, or cancer-related symptoms.

Three short-term clinical trials with similar titration schemes were conducted in 257 patients with malignancy and breakthrough cancer pain. Data are available for 254 of these patients. Table 1 lists, by dose groups, adverse reactions with an overall frequency of 1% or greater that occurred during titration. The ability to assign a dose-response relationship to these adverse reactions is limited by the titration schemes used in these studies. Adverse reactions are listed in descending order of frequency within each body system.

Table 1. Percent of Patients with Specific Adverse Events Commonly Associated with Opioid Administration or of Particular Clinical Interest Which Occurred During Titration (Events in 1% or More of Patients)

Dose Group	Percentage of Patients Reporting Event				
	200-600 mcg (n=230)	800-1400 mcg (n=138)	1600 mcg (n=54)	>1600 mcg (n=41)	Any Dose* (n=254)
Body As A Whole					
Asthenia	6	4	0	7	9
Headache	3	4	6	5	6
Accidental Injury	1	1	4	0	2
Digestive					
Nausea	14	15	11	22	23
Vomiting	7	6	6	15	12
Constipation	1	4	2	0	4
Nervous					
Dizziness	10	16	6	15	17

Somnolence	9	9	11	20	17
Confusion	1	6	2	0	4
Anxiety	3	0	2	0	3
Abnormal Gait	0	1	4	0	2
Dry Mouth	1	1	2	0	2
Nervousness	1	1	0	0	2
Vasodilatation	2	0	2	0	2
Hallucinations	0	1	2	2	1
Insomnia	0	1	2	0	1
Thinking Abnormal	0	1	2	0	1
Vertigo	1	0	0	0	1
Respiratory					
Dyspnea	2	3	6	5	4
Skin					
Pruritus	1	0	0	5	2
Rash	1	1	0	2	2
Sweating	1	1	2	2	2
Special Senses					
Abnormal Vision	1	0	2	0	2

* Any Dose = A patient who experienced the same adverse event at multiple doses was only counted once.

The following adverse reactions not reflected in Table 1 occurred during titration with an overall frequency of 1% or greater and are listed in descending order of frequency within each body system.

Body as a Whole: Pain, fever, abdominal pain, chills, back pain, chest pain, infection

Digestive: Diarrhea, dyspepsia, flatulence

Metabolic and Nutritional: Peripheral edema, dehydration

Nervous: Hypesthesia, migraine

Respiratory: Pharyngitis, cough increased

The following reactions occurred during titration with an overall frequency of less than 1% and are listed in descending order of frequency within each body system.

Body as a Whole: Bone pain

Cardiovascular: Deep thrombophlebitis, hypertension, hypotension

Digestive: Anorexia, eructation, fecal impaction, gum hemorrhage, mouth ulceration, oral moniliasis

Hemic and Lymphatic: Anemia, leukopenia

Metabolic and Nutritional: Edema, hypercalcemia, weight loss

Musculoskeletal: Myalgia, pathological fracture, myasthenia

Nervous: Abnormal dreams, urinary retention, agitation, amnesia, emotional lability, euphoria, incoordination, libido decreased, neuropathy, paresthesia, speech disorder

Respiratory: Hemoptysis, pleural effusion, rhinitis, asthma, hiccup, pneumonia, respiratory insufficiency, sputum increased

Skin and Appendages: Alopecia, exfoliative dermatitis

Special Senses: Taste perversion

Urogenital: Vaginal hemorrhage, dysuria, hematuria, urinary incontinence, urinary tract infection

A long-term extension study was conducted in 156 patients with malignancy and breakthrough cancer pain who were treated for an average of 129 days. Data are available for 152 of these patients. Table 2 lists by dose groups, adverse reactions with an overall frequency of 1% or greater that occurred during the long-term extension study. Adverse reactions are listed in descending order of frequency within each body system.

Table 2. Percent of Patients with Adverse Events Commonly Associated with Opioid Administration or of Particular Clinical Interest Which Occurred During Long Term Treatment (Events in 1% or More of Patients)

Dose Group	Percentage of Patients Reporting Event				
	200-600 mcg (n=98)	800-1400 mcg (n=83)	1600 mcg (n=53)	>1600 mcg (n=27)	Any Dose* (n=152)
Body As A Whole					
Asthenia	25	30	17	15	38
Headache	12	17	13	4	20
Accidental Injury	4	6	4	7	9
Hypertonia	2	2	2	0	3
Digestive					
Nausea	31	36	25	26	45
Vomiting	21	28	15	7	31
Constipation	14	11	13	4	20
Intestinal Obstruction	0	2	4	0	3
Cardiovascular					
Hypertension	1	1	0	0	1
Nervous					
Dizziness	12	10	9	0	16
Anxiety	9	8	8	7	15
Somnolence	8	13	8	7	15

Confusion	2	5	13	7	10
Depression	9	4	2	7	9
Insomnia	5	1	8	4	7
Abnormal Gait	5	1	0	0	4
Dry Mouth	3	1	2	4	4
Nervousness	2	2	0	4	3
Stupor	4	1	0	0	3
Vasodilatation	1	1	4	0	3
Thinking Abnormal	2	1	0	0	2
Abnormal Dreams	1	1	0	0	1
Convulsion	0	1	2	0	1
Myoclonus	0	0	4	0	1
Tremor	0	1	2	0	1
Vertigo	0	0	4	0	1
Respiratory					
Dyspnea	15	16	8	7	22
Skin					
Rash	3	5	8	4	8
Sweating	3	2	2	0	4
Pruritus	2	0	2	0	2
Special Senses					
Abnormal Vision	2	2	0	0	3
Urogenital					
Urinary Retention	1	2	0	0	2

* Any Dose = A patient who experienced the same adverse event at multiple doses was only counted once.

The following reactions not reflected in Table 2 occurred with an overall frequency of 1% or greater in the long-term extension study and are listed in descending order of frequency within each body system.

Body as a Whole: Pain, fever, back pain, abdominal pain, chest pain, flu syndrome, chills, infection, abdomen enlarged, bone pain, ascites, sepsis, neck pain, viral infection, fungal infection, cachexia, cellulitis, malaise, pelvic pain

Cardiovascular: Deep thrombophlebitis, palpitation, vascular disorder

Digestive: Diarrhea, anorexia, dyspepsia, dysphagia, oral moniliasis, mouth ulceration, rectal disorder, stomatitis, flatulence, gastrointestinal hemorrhage, gingivitis, jaundice, periodontal abscess, eructation, glossitis, rectal hemorrhage

Hemic and Lymphatic: Anemia, leukopenia, thrombocytopenia, ecchymosis, lymphadenopathy, lymphedema, pancytopenia

Metabolic and Nutritional: Peripheral edema, edema, dehydration, weight loss, hyperglycemia, hypokalemia, hypercalcemia, hypomagnesemia

Musculoskeletal: Myalgia, pathological fracture, joint disorder, leg cramps, arthralgia, bone disorder

Nervous: Hypesthesia, paresthesia, hypokinesia, neuropathy, speech disorder, migraine

Respiratory: Cough increased, pharyngitis, pneumonia, rhinitis, sinusitis, bronchitis, epistaxis, asthma, hemoptysis, sputum increased

Skin and Appendages: Skin ulcer, alopecia

Special Senses: Tinnitus, conjunctivitis, ear disorder, taste perversion

Urogenital: Urinary tract infection, urinary incontinence, breast pain, dysuria, hematuria, scrotal edema, hydronephrosis, kidney failure, urinary urgency, urination impaired, breast neoplasm, vaginal hemorrhage, vaginitis

The following reactions occurred with a frequency of less than 1% in the long-term extension study and are listed in descending order of frequency within each body system.

Body as a Whole: Allergic reaction, cyst, face edema, flank pain, granuloma, bacterial infection, mucous membrane disorder, neck rigidity

Cardiovascular: Angina pectoris, hemorrhage, hypotension, peripheral vascular disorder, postural hypotension, tachycardia

Digestive: Cheilitis, esophagitis, fecal incontinence, gastroenteritis, gastrointestinal disorder, gum hemorrhage, hemorrhage of colon, hepatorenal syndrome, liver tenderness, tooth caries, tooth disorder

Hemic and Lymphatic: Bleeding time increased

Metabolic and Nutritional: Acidosis, generalized edema, hypocalcemia, hypoglycemia, hyponatremia, hypoproteinemia, thirst

Musculoskeletal: Arthritis, muscle atrophy, myopathy, synovitis, tendon disorder

Nervous: Acute brain syndrome, agitation, cerebral ischemia, facial paralysis, foot drop, hallucinations, hemiplegia, miosis, subdural hematoma

Respiratory: Hiccup, hyperventilation, lung disorder, pneumothorax, respiratory failure, voice alteration

Skin and Appendages: Herpes zoster, maculopapular rash, skin discoloration, urticaria, vesiculobullous rash

Special Senses: Ear pain, eye hemorrhage, lacrimation disorder, partial permanent deafness, partial transitory deafness

Urogenital: Kidney pain, nocturia, oliguria, polyuria, pyelonephritis

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of ACTIQ. 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.

Digestive:

- *Dental decay*: Dental decay, including dental caries, tooth loss, and gum line erosion.

Nervous System Disorders:

- *Serotonin syndrome*: Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of opioids with serotonergic drugs.

- *Hyperalgesia and Allodynia*: Cases of hyperalgesia and allodynia have been reported with opioid therapy of any duration *[see Warnings and Precautions (5.9)]*.

Endocrine Disorders:

- *Adrenal insufficiency*: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.

- *Androgen deficiency*: Cases of androgen deficiency have occurred with use of opioids for an extended period of time *[see Clinical Pharmacology (12.2)]*.

Immune System Disorders:

- *Anaphylaxis*: Anaphylaxis has been reported with ingredients contained in ACTIQ.

General Disorders and Administration Site Conditions:

- *Application site reactions* including irritation, pain, ulcer, and drug withdrawal syndrome.

Metabolic and Nutritional Disorders:

- *Hypoglycemia*: Cases of hypoglycemia have been reported in patients taking opioids. Most reports were in patients with at least one predisposing risk factor (e.g., diabetes).

7 DRUG INTERACTIONS

Table 3 includes clinically significant drug interactions with ACTIQ.

Table 3: Clinically Significant Drug Interactions with ACTIQ

Inhibitors of CYP3A4	
Clinical Impact:	The concomitant use of ACTIQ and CYP3A4 inhibitors can increase the plasma concentration of fentanyl, resulting in increased or prolonged opioid effects, particularly when an inhibitor is added after a stable dose of ACTIQ is achieved *[see Warnings and Precautions (5.6)]*. After stopping a CYP3A4 inhibitor, as the effects of the inhibitor decline, the fentanyl plasma concentration will decrease *[see Clinical Pharmacology (12.3)]*, resulting in decreased opioid efficacy or a withdrawal syndrome in patients who had developed physical dependence to fentanyl.

Intervention:	If concomitant use is necessary, consider dosage reduction of ACTIQ until stable drug effects are achieved. Evaluate patients at frequent intervals for respiratory depression and sedation. If a CYP3A4 inhibitor is discontinued, consider increasing the ACTIQ dosage until stable drug effects are achieved. Evaluate for signs of opioid withdrawal.
Examples:	Macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), protease inhibitors (e.g., ritonavir), grapefruit juice
CYP3A4 Inducers	
Clinical Impact:	The concomitant use of ACTIQ and CYP3A4 inducers can decrease the plasma concentration of fentanyl *[see Clinical Pharmacology (12.3)]*, resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to fentanyl *[see Warnings and Precautions (5.6)]*. After stopping a CYP3A4 inducer, as the effects of the inducer decline, the fentanyl plasma concentration will increase *[see Clinical Pharmacology (12.3)]*, which could increase or prolong both the therapeutic effects and adverse reactions, and may cause serious respiratory depression.
Intervention:	If concomitant use is necessary, consider increasing the ACTIQ dosage until stable drug effects are achieved. Evaluate for signs of opioid withdrawal. If a CYP3A4 inducer is discontinued, consider ACTIQ dosage reduction and evaluate patients at frequent intervals for signs of respiratory depression and sedation.
Examples:	Rifampin, carbamazepine, phenytoin
Benzodiazepines and Other Central Nervous System (CNS) Depressants	
Clinical Impact:	Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants including alcohol, increases the risk of respiratory depression, profound sedation, coma, and death.
Intervention:	Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Inform patients and caregivers of this potential interaction and educate them on the signs and symptoms of respiratory depression (including sedation). If concomitant use is warranted, consider prescribing naloxone for the emergency treatment of opioid overdose *[see Dosage and Administration (2.2), Warnings and Precautions (5.1, 5.2, 5.4)]*.
Examples:	Benzodiazepines and other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol.
Serotonergic Drugs	
Clinical Impact:	The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome *[see Warnings and Precautions (5.10)]*.
Intervention:	If concomitant use is warranted, frequently evaluate the patient, particularly during treatment initiation and dose adjustment. Discontinue ACTIQ if serotonin syndrome is suspected.
Examples:	Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), certain muscle relaxants (i.e., cyclobenzaprine, metaxalone), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).
Monoamine Oxidase Inhibitors (MAOIs)	

Clinical Impact:	MAOI interactions with opioids may manifest as serotonin syndrome *[see Warnings and Precautions (5.10)]* or opioid toxicity (e.g., respiratory depression, coma) *[see Warnings and Precautions (5.2)]*.
Intervention:	The use of ACTIQ is not recommended for patients taking MAOIs or within 14 days of stopping such treatment.
Examples:	Phenelzine, tranylcypromine, linezolid
Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics	
Clinical Impact:	May reduce the analgesic effect of ACTIQ and/or precipitate withdrawal symptoms.
Intervention:	Avoid concomitant use.
Examples:	Butorphanol, nalbuphine, pentazocine, buprenorphine
Muscle Relaxants	
Clinical Impact:	Fentanyl may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
Intervention:	Because respiratory depression may be greater than otherwise expected, decrease the dosage of ACTIQ and/or the muscle relaxant as necessary. Due to the risk of respiratory depression with concomitant use of skeletal muscle relaxants and opioids, consider prescribing naloxone for the emergency treatment of opioid overdose *[see Dosage and Administration (2.2), Warnings and Precautions (5.2, 5.4)]*.
Examples:	Cyclobenzaprine, metaxalone
Diuretics	
Clinical Impact:	Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.
Intervention:	Evaluate patients for signs of diminished diuresis and/or effects on blood pressure and increase the dosage of the diuretic as needed.
Anticholinergic Drugs	
Clinical Impact:	The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Intervention:	Evaluate patients for signs of urinary retention or reduced gastric motility when ACTIQ is used concomitantly with anticholinergic drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Use of opioid analgesics for an extended period of time during pregnancy may cause neonatal opioid withdrawal syndrome *[see Warnings and Precautions (5.8)]*. Available data with ACTIQ in pregnant women are insufficient to inform a drug-associated risk for major birth defects and miscarriage. There are risks to the mother and infant associated with use of ACTIQ for an extended period of time during pregnancy *(see Clinical Considerations)*.

In animal reproduction studies, fentanyl administration to pregnant rats during organogenesis was embryocidal at doses within the range of the human recommended dosing. When

administered during gestation through lactation fentanyl administration to pregnant rats resulted in reduced pup survival at doses within the range of the human recommended dosing. No evidence of malformations were noted in animal studies completed to date *[see Data]*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Use of opioid analgesics for an extended period of time during pregnancy for medical or nonmedical purposes can result in physical dependence in the neonate and neonatal opioid withdrawal syndrome shortly after birth.

Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea, and failure to gain weight. The onset of neonatal withdrawal symptoms usually occurs in the first days after birth. The duration and severity of neonatal opioid withdrawal syndrome may vary. Observe newborns for symptoms of neonatal opioid withdrawal syndrome and manage accordingly *[see Warnings and Precautions (5.8)]*.

Labor or Delivery

Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist, such as naloxone, must be available for reversal of opioid-induced respiratory depression in the neonate. ACTIQ is not recommended for use in pregnant women during or immediately prior to labor, when other analgesic techniques are more appropriate. Opioid analgesics, including ACTIQ, can prolong labor through actions which temporarily reduce the strength, duration, and frequency of uterine contractions. However, this effect is not consistent and may be offset by an increased rate of cervical dilation, which tends to shorten labor. Monitor neonates exposed to opioid analgesics during labor for signs of excess sedation and respiratory depression.

Data

Human Data

In women treated acutely with intravenous or epidural fentanyl during labor, symptoms of neonatal respiratory or neurological depression were no more frequent than would be expected in infants of untreated mothers.

Transient neonatal muscular rigidity has been observed in infants whose mothers were treated with intravenous fentanyl.

Animal Data

Fentanyl (25, 50, or 100 mcg/kg) citrate was administered subcutaneously to pregnant rats during the period of organogenesis (Gestation Day, GD 6 to 17). Maternal toxicity and a decrease in fetal weights were observed at 100 mcg/kg but no teratogenicity was seen in the study (the no observed effect level of 50 mcg/kg is equivalent to 0.7 times the exposure of a single human dose

of 1600 mcg per pain episode, based on an AUC comparison). Fentanyl (50, 100, or 250 mcg/kg) was also administered subcutaneously to pregnant rabbits during the period of organogenesis (GD 6-18). Maternal toxicity was noted at doses >100 mcg/kg. No teratogenicity was seen in the study (250 mcg/kg dose is equivalent to 3.5 times the exposure of a single human dose of 1600 mcg per pain episode, based on an AUC comparison).

Fentanyl has been shown to be embryocidal in pregnant rats at doses of 30 mcg/kg intravenously (0.2 times the 1600 mcg dose of ACTIQ on a mg/m^2 basis) from GD 6 to 18 and 160 mcg/kg subcutaneously (1 times the 1600 mcg dose of ACTIQ based on a mg/m^2 basis). No evidence of teratogenicity was reported.

No evidence of malformations or adverse effects on the fetus was reported in a published study in which pregnant rats were administered fentanyl continuously via subcutaneously implanted osmotic minipumps at doses of 10, 100, or 500 mcg/kg/day starting 2-weeks prior to breeding and throughout pregnancy. The high dose was approximately 3 times the human dose of 1600 mcg ACTIQ per pain episode on a mg/m^2 basis and produced mean steady-state plasma levels that are 3.4 times higher than the mean C_{max} observed following administration of 1600 mcg dose of ACTIQ in humans.

In a postnatal development study, pregnant rats were treated from GD 6 through Lactation Day (LD) 20 with subcutaneous doses of fentanyl (25, 50, 100, and 400 mcg/kg). Maternal toxicity was noted at doses >100 mcg/kg. A reduction in pup growth and delayed attainment of developmental indices were observed at >100 mcg/kg. No difference in the number of live pups/litter was seen at birth, however, pup survival at LD 4 was reduced to 48% at 400 mcg/kg and by LD 21 pup survival was reduced to 30% and 26% at 100 and 400 mcg/kg, respectively. During lactation, fentanyl-related clinical signs (decreased activity, skin cold to touch, and moribund appearance) were noted in the F1 pups, most prominently in the 400 mcg/kg group. Pups from this group also had significantly reduced body weights throughout the lactation period. The dose of fentanyl administered to rats at which no developmental toxicity in the F1 generation was seen was 50 mcg/kg which is 0.6 times the exposure of a single human dose of 1600 mcg per pain episode, based on an AUC comparison.

8.2 Lactation

Risk Summary

Fentanyl is present in breast milk. One published lactation study reports a relative infant dose of fentanyl of 0.024%. However, there is insufficient information to determine the effects of fentanyl on the breastfed infant and the effects of fentanyl on milk production. Because of the potential for serious adverse reactions, including excess sedation and respiratory depression in a breastfed infant, advise patients that breastfeeding is not recommended during treatment with ACTIQ.

Clinical Considerations

Monitor infants exposed to ACTIQ through breast milk for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breastfeeding is stopped.

8.3 Females and Males of Reproductive Potential

Infertility

Use of opioids for an extended period of time may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible *[see Adverse Reactions (6.2), Clinical Pharmacology (12.2), Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients below 16 years of age have not been established.

In a clinical study, 15 opioid-tolerant pediatric patients with breakthrough pain, ranging in age from 5 to 15 years, were treated with ACTIQ. The study was too small to allow conclusions on safety and efficacy in this patient population. Twelve of the fifteen opioid-tolerant children and adolescents aged 5 to 15 years in this study received ACTIQ at doses ranging from 200 mcg to 600 mcg. The mean (CV%; range) dose-normalized (to 200 mcg) C_{max} and AUC_{0-8} values were 0.87 ng/mL (51%; 0.42-1.30) and 4.54 ng·h/mL (42%; 2.37-6.0), respectively, for children ages 5 to <11 years old (N = 3) and 0.68 ng/mL (72%; 0.15-1.44) and 8.38 (192%; 0.84-50.78), respectively, for children ages ≥11 to <16 y (N = 9).

8.5 Geriatric Use

Of the 257 patients in clinical studies of ACTIQ in breakthrough cancer pain, 61 (24%) were 65 years of age and older, while 15 (6%) were 75 years of age and older. Those patients over the age of 65 years were titrated to a mean dose that was about 200 mcg less than the mean dose titrated to by younger patients. No difference was noted in the safety profile of the group over 65 years of age as compared to younger patients in ACTIQ clinical trials.

Elderly patients have been shown to be more sensitive to the effects of fentanyl when administered intravenously, compared with the younger population. Therefore, exercise caution when individually titrating ACTIQ in elderly patients to provide adequate efficacy while minimizing risk.

Respiratory depression is the chief risk for elderly patients treated with opioids, and has occurred after large initial doses were administered to patients who were not opioid-tolerant or when opioids were co-administered with other agents that depress respiration. Titrate the dosage of ACTIQ slowly in geriatric patients and frequently reevaluate the patient for signs of central nervous system and respiratory depression *[see Warnings and Precautions (5.11)]*.

Fentanyl is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to regularly evaluate renal function.

8.6 Patients with Renal or Hepatic Impairment

Insufficient information exists to make recommendations regarding the use of ACTIQ in patients with impaired renal or hepatic function. Fentanyl is metabolized primarily via human cytochrome P450 3A4 isoenzyme system and mostly eliminated in urine. If the drug is used in

these patients, it should be used with caution because of the hepatic metabolism and renal excretion of fentanyl.

8.7 Sex

Both male and female opioid-tolerant patients with cancer were studied for the treatment of breakthrough cancer pain. No clinically relevant sex differences were noted either in dosage requirement or in observed adverse reactions.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

ACTIQ contains fentanyl, a Schedule II controlled substance.

9.2 Abuse

ACTIQ contains fentanyl, a substance with high potential for misuse and abuse, which can lead to the development of substance use disorder, including addiction *[see Warnings and Precautions (5.1)]*.

Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a healthcare provider or for whom it was not prescribed.

Abuse is the intentional, non-therapeutic use of a drug, even once, for its desirable psychological or physiological effects.

Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

Misuse and abuse of ACTIQ increases risk of overdose, which may lead to central nervous system and respiratory depression, hypotension, seizures, and death. The risk is increased with concurrent abuse of ACTIQ with alcohol and/or other CNS depressants. Abuse of and addiction to opioids in some individuals may not be accompanied by concurrent tolerance and symptoms of physical dependence. In addition, abuse of opioids can occur in the absence of addiction.

All patients treated with opioids require careful and frequent reevaluation for signs of misuse, abuse, and addiction, because use of opioid analgesic products carries the risk of addiction even under appropriate medical use. Patients at high risk of ACTIQ abuse include those with a history of prolonged use of any opioid, including products containing fentanyl, those with a history of drug or alcohol abuse, or those who use ACTIQ in combination with other abused drugs.

“Drug-seeking” behavior is very common in persons with substance use disorders. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing, or referral, repeated “loss” of prescriptions, tampering with prescriptions, and reluctance to provide prior medical records or contact information for other treating healthcare provider(s). “Doctor shopping” (visiting multiple prescribers to obtain additional prescriptions) is common among people who abuse drugs and people with substance

use disorder. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with inadequate pain control.

ACTIQ, like other opioids, can be diverted for nonmedical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests, as required by state and federal law, is strongly advised.

Proper assessment of the patient, proper prescribing practices, periodic reevaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Risks Specific to Abuse of ACTIQ

Abuse of ACTIQ poses a risk of overdose and death. The risk is increased with concurrent use of ACTIQ with alcohol and/or other CNS depressants.

ACTIQ is approved for oral transmucosal use only.

9.3 Dependence

Both tolerance and physical dependence can develop during use of opioid therapy.

Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose).

Physical dependence is a state that develops as a result of a physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug.

Withdrawal may be precipitated through the administration of drugs with opioid antagonist activity (e.g., naloxone), mixed agonist/antagonist analgesics (e.g., pentazocine, butorphanol, nalbuphine), or partial agonists (e.g., buprenorphine). Physical dependence may not occur to a clinically significant degree until after several days to weeks of continued use.

Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal signs *[see Use in Specific Populations (8.1)]*.

10 OVERDOSAGE

Clinical Presentation

Acute overdose with fentanyl can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and, in some cases, pulmonary edema, bradycardia, hypotension, hypoglycemia, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations *[see Clinical Pharmacology (12.2)]*.

Treatment of Overdose

In case of overdose, priorities are: removal of the ACTIQ unit, if still in the mouth, the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed. Employ other supportive measures (including oxygen and vasopressors) in

the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life-support measures.

Opioid antagonists, such as naloxone, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression secondary to fentanyl overdose, administer an opioid antagonist.

Because the duration of opioid reversal is expected to be less than the duration of action of fentanyl in ACTIQ, carefully monitor the patient until spontaneous respiration is reliably re-established. If the response to an opioid antagonist is suboptimal or only brief in nature, administer additional antagonist as directed by the product's prescribing information.

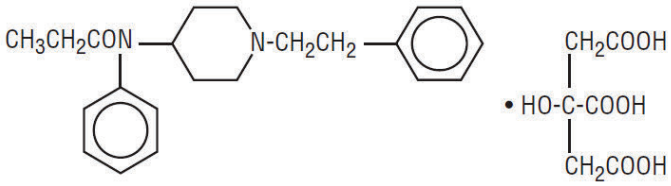
In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be begun with care and by titration with smaller than usual doses of the antagonist.

11 DESCRIPTION

ACTIQ (fentanyl citrate) oral transmucosal lozenge is a solid formulation of fentanyl, an opioid agonist, intended for oral transmucosal administration. ACTIQ is formulated as a white to off-white solid drug matrix on a handle that is fracture resistant (ABS plastic) under normal conditions when used as directed.

ACTIQ is designed to be dissolved slowly in the mouth to facilitate transmucosal absorption. The handle allows the ACTIQ unit to be removed from the mouth if signs of excessive opioid effects appear during administration.

Active Ingredient: Fentanyl citrate, USP is N-(1-Phenethyl-4-piperidyl) propionanilide citrate (1:1). Fentanyl is a highly lipophilic compound (octanol-water partition coefficient at pH 7.4 is 816:1) that is freely soluble in organic solvents and sparingly soluble in water (1:40). The molecular weight of the free base is 336.5 (the citrate salt is 528.6). The pKa of the tertiary nitrogens are 7.3 and 8.4. The compound has the following structural formula:



Inactive Ingredients: Hydrated dextrates, citric acid, dibasic sodium phosphate, artificial berry flavor, magnesium stearate, and edible glue (modified food starch and confectioner's sugar).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fentanyl is an opioid agonist whose principal therapeutic action is analgesia.

12.2 Pharmacodynamics

Effects on the Central Nervous System

The precise mechanism of the analgesic action is unknown although fentanyl is known to be a *mu*-opioid receptor agonist. Specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and play a role in the analgesic effects of this drug.

Fentanyl produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves a reduction in the responsiveness of the brain stem to both increases in carbon dioxide and electrical stimulation.

Fentanyl causes miosis even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of hemorrhagic or ischemic origin may produce similar findings). Marked mydriasis rather than miosis may be seen due to hypoxia in overdose situations.

Effects on the Gastrointestinal Tract and Other Smooth Muscle

Fentanyl causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and in the duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone may be increased to the point of spasm resulting in constipation. Other opioid-induced effects may include a reduction in biliary and pancreatic secretions, spasm of the sphincter of Oddi, and transient elevations in serum amylase.

Effects on the Cardiovascular System

Fentanyl may produce release of histamine with or without associated peripheral vasodilation. Fentanyl produces peripheral vasodilation which may result in orthostatic hypotension or syncope. Manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes, and sweating, and/or orthostatic hypotension.

Effects on the Endocrine System

Opioids inhibit the secretion of adrenocorticotropic hormone (ACTH), cortisol, and luteinizing hormone (LH) in humans *[see Adverse Reactions (6.2)]*. They also stimulate prolactin, growth hormone (GH) secretion, and pancreatic secretion of insulin and glucagon *[see Adverse Reactions (6.2)]*. Thyroid stimulating hormone (TSH) has been shown to be both inhibited and stimulated by opioids.

Use of opioids for an extended period of time may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological

stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date *[see Adverse Reactions (6.2)]*.

Effects on the Immune System

Opioids have been shown to have a variety of effects on components of the immune system in *in vitro* and animal models. The clinical significance of these findings is unknown. Overall, the effects of opioids appear to be modestly immunosuppressive.

Concentration-Efficacy Relationships

The analgesic effects of fentanyl are related to the blood level of the drug, if proper allowance is made for the delay into and out of the CNS (a process with a 3- to 5-minute half-life).

In general, the effective concentration and the concentration at which toxicity occurs increase with increasing tolerance with any and all opioids. The rate of development of tolerance varies widely among individuals.

The minimum effective analgesic concentration of fentanyl for any individual patient may increase over time due to an increase in pain, the development of a new pain syndrome and/or the development of analgesic tolerance.

Concentration-Adverse Reaction Relationships

There is a relationship between increasing fentanyl plasma concentration and increasing frequency of dose-related opioid adverse reactions such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation may be altered by the development of tolerance to opioid-related adverse reactions *[see Dosage and Administration (2.1, 2.3, 2.4, 2.5)]*.

Respiratory System

All opioid *mu*-receptor agonists, including fentanyl, produce dose-dependent respiratory depression. The risk of respiratory depression is less in patients receiving chronic opioid therapy who develop tolerance to respiratory depression and other opioid effects. During the titration phase of the clinical trials, somnolence, which may be a precursor to respiratory depression, did increase in patients who were treated with higher doses of ACTIQ. Peak respiratory depressive effects may be seen as early as 15 to 30 minutes from the start of oral transmucosal fentanyl citrate product administration and may persist for several hours.

Serious or fatal respiratory depression can occur even at recommended doses. Although not observed with oral transmucosal fentanyl products in clinical trials, fentanyl given rapidly by intravenous injection in large doses may interfere with respiration by causing rigidity in the muscles of respiration *[see Warnings and Precautions (5), Overdosage (10)]*.

12.3 Pharmacokinetics

Absorption

The absorption pharmacokinetics of fentanyl from the oral transmucosal dosage form is a combination of an initial rapid absorption from the buccal mucosa and a more prolonged absorption of swallowed fentanyl from the GI tract. Both the blood fentanyl profile and the

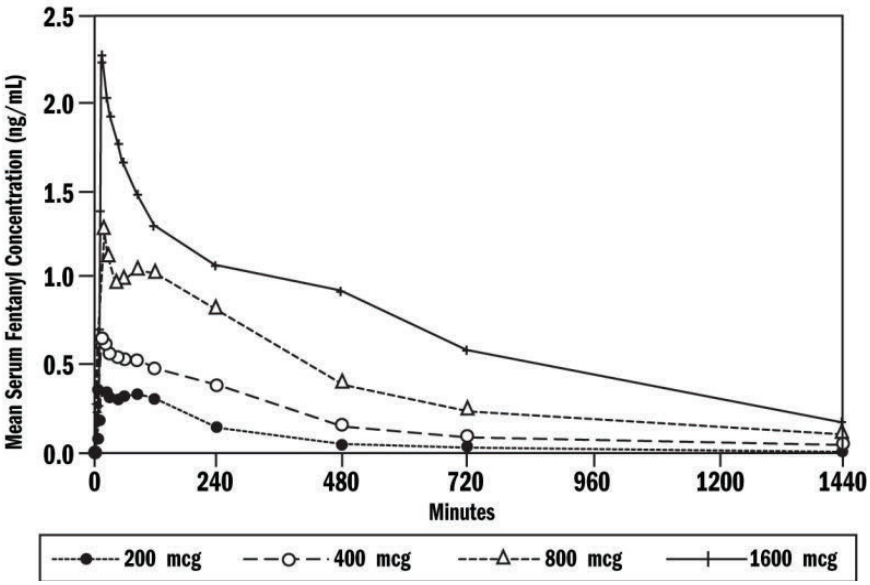
bioavailability of fentanyl will vary depending on the fraction of the dose that is absorbed through the oral mucosa and the fraction swallowed.

Absolute bioavailability, as determined by area under the concentration-time curve, of 15 mcg/kg in 12 adult males was 50% compared to intravenous fentanyl.

Normally, approximately 25% of the total dose of ACTIQ is rapidly absorbed from the buccal mucosa and becomes systemically available. The remaining 75% of the total dose is swallowed with the saliva and then is slowly absorbed from the GI tract. About 1/3 of this amount (25% of the total dose) escapes hepatic and intestinal first-pass elimination and becomes systemically available. Thus, the generally observed 50% bioavailability of ACTIQ is divided equally between rapid transmucosal and slower GI absorption. Therefore, a unit dose of ACTIQ, if chewed and swallowed, might result in lower peak concentrations and lower bioavailability than when consumed as directed.

Dose proportionality among four of the available strengths of ACTIQ (200, 400, 800, and 1600 mcg) has been demonstrated in a balanced crossover design in adult subjects (n=11). Mean serum fentanyl levels following these four doses of ACTIQ are shown in Figure 1. The curves for each dose level are similar in shape with increasing dose levels producing increasing serum fentanyl levels. C_{max} and $AUC_{0\rightarrow\infty}$ increased in a dose-dependent manner that is approximately proportional to the ACTIQ administered.

Figure 1. Mean Serum Fentanyl Concentration (ng/mL) in Adult Subjects Comparing 4 Doses of ACTIQ



The pharmacokinetic parameters of the four strengths of ACTIQ tested in the dose-proportionality study are shown in Table 4. The mean C_{max} ranged from 0.39 - 2.51 ng/mL. The median time of maximum plasma concentration (T_{max}) across these four doses of ACTIQ varied from 20 - 40 minutes (range of 20 – 480 minutes) as measured after the start of administration.

Table 4. Pharmacokinetic Parameters* in Adult Subjects Receiving 200, 400, 800, and 1600 mcg Units of ACTIQ

Pharmacokinetic Parameter	200 mcg	400 mcg	800 mcg	1600 mcg
T_{max}, minute median (range)	40 (20-120)	25 (20-240)	25 (20-120)	20 (20-480)
C_{max}, ng/mL mean (%CV)	0.39 (23)	0.75 (33)	1.55 (30)	2.51 (23)
AUC_{0-1440}, ng/mL minute mean (%CV)	102 (65)	243 (67)	573 (64)	1026 (67)
$t_{1/2}$, minute mean (%CV)	193 (48)	386 (115)	381 (55)	358 (45)

***Based on arterial blood samples.**

Distribution

Fentanyl is highly lipophilic. Animal data showed that following absorption, fentanyl is rapidly distributed to the brain, heart, lungs, kidneys and spleen followed by a slower redistribution to muscles and fat. The plasma protein binding of fentanyl is 80-85%. The main binding protein is alpha-1-acid glycoprotein, but both albumin and lipoproteins contribute to some extent. The free fraction of fentanyl increases with acidosis. The mean volume of distribution at steady state (Vss) was 4 L/kg.

Elimination

The total plasma clearance of fentanyl was 0.5 L/hr/kg (range 0.3 – 0.7 L/hr/kg). The terminal elimination half-life after ACTIQ administration is about 7 hours.

Metabolism

Fentanyl is metabolized in the liver and in the intestinal mucosa to norfentanyl by cytochrome P450 3A4 isoform. Norfentanyl was not found to be pharmacologically active in animal studies *[see Drug Interactions (7)]*.

Excretion

Fentanyl is primarily (more than 90%) eliminated by biotransformation to N-dealkylated and hydroxylated inactive metabolites. Less than 7% of the dose is excreted unchanged in the urine, and only about 1% is excreted unchanged in the feces. The metabolites are mainly excreted in the urine, while fecal excretion is less important.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Fentanyl was evaluated for carcinogenic potential in a 104-week rat study and in a 6-month Tg.AC transgenic mouse study. In rats, doses up to 50 mcg/kg in males and 100 mcg/kg in females were administered subcutaneously and no treatment-related neoplasms were observed (doses are equivalent to 1.13 and 2.7 times the exposure of a single human dose of 1600 mcg per pain episode, respectively, based on an AUC comparison). In a 26-week transgenic mice model (Tg.AC), at topical doses up to 50 mcg/dose/day, no increase in the occurrence of treatment-related neoplasms was observed.

Mutagenesis

Fentanyl citrate was not mutagenic in the in vitro Ames reverse mutation assay in *S. typhimurium* or *E. coli*, or the mouse lymphoma mutagenesis assay, and was not clastogenic in the in vivo mouse micronucleus assay.

Impairment of Fertility

In a fertility study, female rats were administered fentanyl subcutaneously for 14 days prior to mating with untreated males at doses up to 300 mcg/kg and no effects on female fertility were observed. The systemic exposure at the dose of 300 mcg/kg was approximately 4.0-times the exposure of a single human dose of 1600 mcg per pain episode, based on an AUC comparison. Males were administered fentanyl subcutaneously for 28 days prior to mating with untreated females at doses up to 300 mcg/kg. At 300 mcg/kg, adverse effects on sperm parameters, which affected fertility, were observed. These effects included decreased percent mobile sperm, decreased sperm concentrations as well as an increase in the percent abnormal sperm. The dose in males at which no effects on fertility were observed was 100 mcg/kg, which is approximately 2.7 times the exposure of a single human dose of 1600 mcg per pain episode, based on an AUC comparison.

Fentanyl has been shown to impair fertility in rats at doses of 30 mcg/kg IV and 160 mcg/kg subcutaneously. Conversion to the human equivalent doses indicates that this is within the range of the human recommended dosing for ACTIQ.

14 CLINICAL STUDIES

ACTIQ was investigated in clinical trials involving 257 opioid tolerant adult cancer patients experiencing breakthrough cancer pain. Breakthrough cancer pain was defined as a transient flare of moderate-to-severe pain occurring in cancer patients experiencing persistent cancer pain otherwise controlled with maintenance doses of opioid medications including at least 60 mg morphine/day, 50 mcg transdermal fentanyl/hour, or an equianalgesic dose of another opioid for a week or longer.

In two dose titration studies 95 of 127 patients (75%) who were on stable doses of either long-acting oral opioids or transdermal fentanyl for their persistent cancer pain titrated to a successful dose of ACTIQ to treat their breakthrough cancer pain within the dose range offered (200, 400, 600, 800, 1200, and 1600 mcg). A “successful” dose was defined as a dose where one unit of ACTIQ could be used consistently for at least two consecutive days to treat breakthrough cancer pain without unacceptable side effects. In these studies 11% of patients withdrew due to adverse reactions and 14% withdrew due to other reasons.

The successful dose of ACTIQ for breakthrough cancer pain was not predicted from the daily maintenance dose of opioid used to manage the persistent cancer pain and is thus best determined by dose titration.

A double-blind placebo controlled crossover study was performed in cancer patients to evaluate the effectiveness of ACTIQ for the treatment of breakthrough cancer pain. Of 130 patients who entered the study 92 patients (71%) achieved a successful dose during the titration phase. The distribution of successful doses is shown in Table 5.

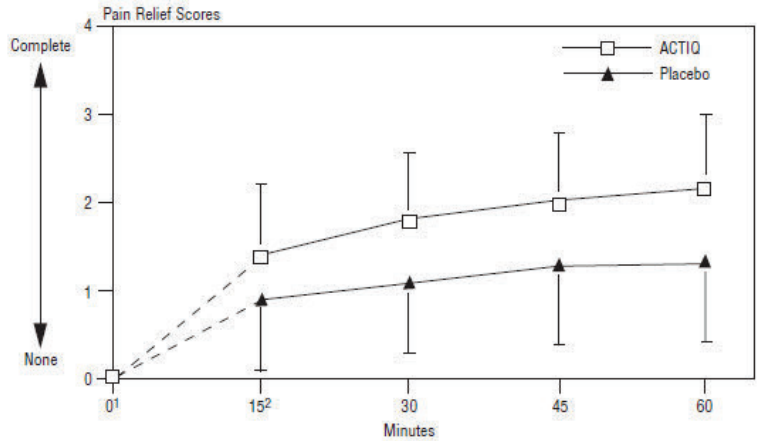
Table 5. Successful Dose of ACTIQ Following Initial Titration

ACTIQ Dose	Total No. (%) (N=92)
200 mcg	13 (14)
400 mcg	19 (21)
600 mcg	14 (15)
800 mcg	18 (20)
1200 mcg	13 (14)
1600 mcg	15 (16)
Mean +/- SD	789 +/- 468 mcg

On average, patients over 65 years of age titrated to a mean dose that was about 200 mcg less than the mean dose to which younger adult patients were titrated.

ACTIQ was administered beginning at Time 0 minutes and produced more pain relief compared with placebo at 15, 30, 45, and 60 minutes as measured after the start of administration (see Figure 2). The differences were statistically significant.

Figure 2. Pain Relief (PR) Scores (Mean±SD) During the Double-Blind Phase – All Patients with Evaluable Episodes on Both ACTIQ and Placebo (N=86)



[1] 0 minutes = Start of administration of ACTIQ
[2] 15 minutes = First time to measure pain relief

16 HOW SUPPLIED/STORAGE AND HANDLING

ACTIQ is supplied in six dosage strengths. Each unit is individually wrapped in a child-resistant, protective blister package. These blister packages are packed 30 per shelf carton for use when patients have been titrated to the appropriate dose.

Each dosage unit has a white to off-white color. Each individual solid drug matrix is marked with "ACTIQ" and the strength of the unit ("200", "400", "600", "800", "1200", or "1600"). The dosage strength is also marked on the handle tag, the blister package and the carton. See blister package and carton for product information.

Dosage Strength (fentanyl base)	**Carton/Blister Package Color**	**NDC Number**
200 mcg	**Gray**	**NDC 63459-502-30**
400 mcg	**Blue**	**NDC 63459-504-30**
600 mcg	**Orange**	**NDC 63459-506-30**
800 mcg	**Purple**	**NDC 63459-508-30**
1200 mcg	**Green**	**NDC 63459-512-30**
1600 mcg	**Burgundy**	**NDC 63459-516-30**

Note: Colors are a secondary aid in product identification. Please be sure to confirm the printed dosage before dispensing.

Store at 20°C to 25°C (68°F to 77°F) with excursions permitted between 15°C and 30°C (59°F to 86°F) until ready to use. (See USP Controlled Room Temperature.) Protect ACTIQ from freezing and moisture. Do not use if the blister package has been opened.

Store ACTIQ securely and dispose of properly.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling *(Medication Guide)*.

Storage and Disposal of Unused and Used ACTIQ *[see Medication Guide / Instructions for Use]*.

Because of the risks associated with accidental ingestion, misuse, and abuse, advise patients to store ACTIQ securely, out of sight and reach of children, and in a location not accessible by others, including visitors to the home. Inform patients that leaving ACTIQ unsecured can pose a deadly risk to others in the home *[see Warnings and Precautions (5.1, 5.2), Drug Abuse and Dependence (9.2)]*.

Advise patients and caregivers that when medicines are no longer needed, they should be disposed of promptly. Inform patients that they can visit www.fda.gov/drugdisposal for a complete list of medicines recommended for disposal by flushing, as well as additional information on disposal of unused medicines.

Disposal of Used ACTIQ Units:
Instruct patients on proper disposal of completely used and partially used ACTIQ units as follows:

1. After consumption of the unit is complete and the matrix is totally dissolved, throw away the handle in a trash container that is out of the reach of children.
2. If any of the drug matrix remains on the handle, place the handle under hot running tap water until all of the drug matrix is dissolved, and then dispose of the handle in a place that is out of the reach of children.
3. Dispose of handles in the child-resistant container (as described in steps 1 and 2) at least once a day.

If the patient does not entirely consume the unit and the remaining drug cannot be immediately dissolved under hot running water, the patient or caregiver must temporarily store the ACTIQ unit in the specially provided child-resistant container out of the reach of children until proper disposal is possible.

Disposal of Unopened ACTIQ Units When No Longer Needed:
Patients and members of their household must be advised to dispose of any unopened units remaining from a prescription as soon as they are no longer needed.

To dispose of the unused ACTIQ units:

- Remove the ACTIQ unit from its blister package using scissors, and hold the ACTIQ by its handle over the toilet bowl.
- Using wire-cutting pliers cut off the drug matrix end so that it falls into the toilet.
- Dispose of the handle in a place that is out of the reach of children.
- Repeat steps 1, 2, and 3 for each ACTIQ unit. Flush the toilet twice after 5 units have been cut and deposited into the toilet.

Do not flush the entire ACTIQ units, ACTIQ handles, blister packages, or cartons down the toilet. Dispose of the handle where children cannot reach it.

Detailed instructions for the proper storage, administration, disposal, and important instructions for managing an overdose of ACTIQ are provided in the ACTIQ *Medication Guide*. Encourage patients to read this information in its entirety and give them an opportunity to have their questions answered.

In the event that a caregiver requires additional assistance in disposing of excess unusable units that remain in the home after a patient has expired, instruct them to call the toll-free number for Teva Pharmaceuticals (1-888-483-8279) or seek assistance from their local DEA office.

Addiction, Abuse, and Misuse

Inform patients that the use of ACTIQ, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose and death *[see Warnings and Precautions (5.1)]*. Instruct patients not to share ACTIQ with others and to take steps to protect ACTIQ from theft or misuse.

Life-Threatening Respiratory Depression

Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting ACTIQ or when the dosage is increased, and that it can occur even at recommended dosages.

Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help right away in the event of a known or suspected overdose *[see Warnings and Precautions (5.2)]*.

Accidental Ingestion

- Healthcare providers and dispensing pharmacists must specifically question patients or caregivers about the presence of children in the home (on a full time or visiting basis) and counsel them regarding the dangers to children from inadvertent exposure *[see Warnings and Precautions (5.3)]*.
- Inform patients that accidental ingestion, especially by children, may result in respiratory depression or death *[see Warnings and Precautions (5.3)]*.
- Instruct patients to take steps to store ACTIQ securely and to dispose of unused ACTIQ *[see Dosage and Administration (2.8), Warnings and Precautions (5.3, 5.7)]*.
- Instruct patients and caregivers to keep both used and unused ACTIQ out of the reach of children *[see Warnings and Precautions (5.3)]*.
- Inform patients and their caregivers that, in the event that a unit is not completely consumed, it must be properly disposed as soon as possible *[see Warnings and Precautions (5.3)]*.

  ACTIQ Child Safety Kit
  Provide patients and their caregivers who have children in the home or visiting with an ACTIQ Child Safety Kit, which contains educational materials and safe interim storage containers to help patients store ACTIQ and other medicines out of the reach of children. To obtain a supply of Child Safety Kits, health care professionals can call 1-888-534-3119.

Interactions with Benzodiazepines and Other CNS Depressants (including Alcohol)

Inform patients and caregivers that potentially fatal additive effects may occur if ACTIQ is used with benzodiazepines or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a healthcare provider *[see Warnings and Precautions (5.4), Drug Interactions (7)]*.

Patient Access to Naloxone for the Emergency Treatment of Opioid Overdose

Discuss with the patient and caregiver the availability of naloxone for the emergency treatment of opioid overdose, both when initiating and renewing treatment with ACTIQ. Inform patients and caregivers about the various ways to obtain naloxone as permitted by individual state naloxone dispensing and prescribing requirements or guidelines (e.g., by prescription, directly from a pharmacist, or as part of a community-based program) *[see Dosage and Administration (2.2), Warnings and Precautions (5.2)]*.

Educate patients and caregivers on how to recognize the signs and symptoms of an overdose.

Explain to patients and caregivers that naloxone's effects are temporary, and that they must call 911 or get emergency medical help right away in all cases of known or suspected opioid overdose, even if naloxone is administered *[see Overdosage (10)]*.

If naloxone is prescribed, also advise patients and caregivers:

- How to treat with naloxone in the event of an opioid overdose
- To tell family and friends about their naloxone and to keep it in a place where family and friends can access it in an emergency
- To read the Patient Information (or other educational material) that will come with their naloxone. Emphasize the importance of doing this before an opioid emergency happens, so the patient and caregiver will know what to do.

Transmucosal Immediate-Release Fentanyl (TIRF) REMS

ACTIQ is available only through a restricted program called the Transmucosal Immediate Release Fentanyl (TIRF) REMS *[see Warnings and Precautions (5.7)]*. Inform the patient of the following notable requirements:

- Outpatients must be enrolled in the REMS program
- Patients must be opioid-tolerant to receive ACTIQ

ACTIQ is available only from certified pharmacies participating in this program. Therefore, provide patients with the telephone number and website for information on how to obtain the product.

Pharmacies, outpatients, and healthcare professionals who prescribe to outpatients are required to enroll in the program. Inpatient pharmacies must develop policies and procedures to verify opioid tolerance in inpatients who require ACTIQ while hospitalized *[see Warnings and Precautions (5.7)]*.

Hyperalgesia and Allodynia

Inform patients and caregivers not to increase opioid dosage without first consulting a clinician. Advise patients to seek medical attention if they experience symptoms of hyperalgesia, including worsening pain, increased sensitivity to pain, or new pain *[see Warnings and Precautions (5.9), Adverse Reactions (6.2)]*.

Serotonin Syndrome

Inform patients that opioids could cause a rare but potentially life-threatening condition called serotonin syndrome resulting from concomitant administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and to seek medical attention right away if symptoms develop. Instruct patients to inform their healthcare providers if they are taking, or plan to take serotonergic medications *[see Warnings and Precautions (5.10), Drug Interactions (7)]*.

MAOI Interaction

Inform patients to avoid taking ACTIQ while using any drugs that inhibit monoamine oxidase. Patients should not start MAOIs while taking ACTIQ *[see Warnings and Precautions (5.10), Drug Interactions (7)]*.

Important Administration Instructions *[see Dosage and Administration (2)]*

- Instruct patients not to take ACTIQ for acute pain, postoperative pain, pain from injuries, headache, migraine or any other short-term pain, even if they have taken other opioid analgesics for these conditions.
- Instruct patients on the meaning of opioid tolerance and that ACTIQ is only to be used as a supplemental pain medication for patients with pain requiring around-the-clock opioids, who have developed tolerance to the opioid medication, and who need additional opioid treatment of breakthrough pain episodes.
- Instruct patients that, if they are not taking an opioid medication on a scheduled basis (around-the-clock), they should not take ACTIQ.
- Instruct patients that, if the breakthrough pain episode is not relieved 15 minutes after finishing the ACTIQ unit, they may take only one additional unit of ACTIQ using the same strength for that episode. Thus, patients should take no more than two units of ACTIQ for any breakthrough pain episode.
- Instruct patients that they MUST wait at least 4 hours before treating another episode of breakthrough pain with ACTIQ.
- Instruct patients NOT to share ACTIQ and that sharing ACTIQ with anyone else could result in the other individual's death due to overdose.
- Make patients aware that ACTIQ contains fentanyl which is a strong pain medication similar to hydromorphone, methadone, morphine, oxycodone, and oxymorphone.
- Caution patients to talk to their healthcare provider if breakthrough pain is not alleviated or worsens after taking ACTIQ.
- Instruct patients to use ACTIQ exactly as prescribed by their healthcare provider and not to take ACTIQ more often than prescribed.

Driving or Operating Heavy Machinery

Inform patients that ACTIQ may impair the ability to perform potentially hazardous activities such as driving a car or operating heavy machinery. Advise patients not to perform such tasks until they know how they will react to the medication *[see Warnings and Precautions (5.17)]*.

Constipation

Advise patients of the potential for severe constipation, including management instructions and when to seek medical attention *[see Adverse Reactions (6), Clinical Pharmacology (12.2)]*.

Dental Decay

Because each ACTIQ unit contains approximately 2 grams of sugar (hydrated dextrates), frequent consumption may increase the risk of dental decay. The occurrence of dry mouth associated with the use of opioid medications (such as fentanyl) may add to this risk.

Post-marketing reports of dental decay have been received in patients taking ACTIQ *[see Adverse Reactions (6.2)]*. In some of these patients, dental decay occurred despite reported routine oral hygiene. As dental decay in cancer patients may be multi-factorial, patients using ACTIQ should consult their dentist to ensure appropriate oral hygiene.

Adrenal Insufficiency

Inform patients that opioids could cause adrenal insufficiency, a potentially life-threatening condition. Adrenal insufficiency may present with non-specific symptoms and signs such as nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. Advise patients to seek medical attention if they experience a constellation of these symptoms *[see Warnings and Precautions (5.12)]*.

Hypotension

Inform patients that ACTIQ may cause orthostatic hypotension and syncope. Instruct patients how to recognize symptoms of low blood pressure and how to reduce the risk of serious consequences should hypotension occur (e.g., sit or lie down, carefully rise from a sitting or lying position) *[see Warnings and Precautions (5.13)]*.

Anaphylaxis

Inform patients that anaphylaxis has been reported with ingredients contained in ACTIQ. Advise patients how to recognize such a reaction and when to seek medical attention *[see Contraindications (4), Adverse Reactions (6)]*.

Pregnancy

Neonatal Opioid Withdrawal Syndrome
Inform patients that use of ACTIQ for an extended period of time during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated *[see Warnings and Precautions (5.8), Use in Specific Populations (8.1)]*.

Embryo-Fetal Toxicity
Inform female patients of reproductive potential that ACTIQ can cause fetal harm and to inform their healthcare provider of a known or suspected pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation

Advise nursing mothers to carefully observe infants for increased sleepiness (more than usual), breathing difficulties, or limpness. Instruct nursing mothers to seek immediate medical care if they notice these signs *[see Use in Specific Populations (8.2)]*.

Infertility

Inform patients that use of opioids for an extended period of time may cause reduced fertility. It is not known whether these effects on fertility are reversible *[see Use in Specific Populations (8.3)]*.

Diabetic Patients

Advise diabetic patients that ACTIQ contains approximately 2 grams of sugar per unit.

Dispense with Medication Guide available at: www.tevausa.com/medguides

ACT-016

Distributed By:
Teva Pharmaceuticals USA, Inc.
Parsippany, NJ 07054

Dispense with Medication Guide available at: www.tevausa.com/medguides

Medication Guide

ACTIQ® (AK-tik)
(fentanyl citrate) oral transmucosal lozenge, CII

IMPORTANT:

Do not use ACTIQ unless you are regularly using another opioid pain medicine around-the-clock for at least one week or longer for your cancer pain and your body is used to these medicines (this means that you are opioid tolerant). You can ask your healthcare provider if you are opioid tolerant.

Keep ACTIQ in a safe place away from children.

Get emergency medical help right away if:

- **a child takes ACTIQ. ACTIQ can cause an overdose and death in any child who takes it.**
- **an adult who has not been prescribed ACTIQ uses it.**
- **an adult who is not already taking opioids around-the-clock, uses ACTIQ.**

These are medical emergencies that can cause death. If possible, remove ACTIQ from the mouth.

ACTIQ is:

- A strong prescription pain medicine that contains an opioid (narcotic) that is used to manage breakthrough pain in adults (16 years of age and older) with cancer who are already routinely taking other opioid pain medicines around-the-clock for cancer pain. ACTIQ is started only after you have been taking other opioid pain medicines and your body has become used to them (you are opioid tolerant). Do not use ACTIQ if you are not opioid tolerant.
- An opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death.

Important information about ACTIQ:

- **Get emergency help or call 911 right away if you take too much ACTIQ (overdose).** When you first start taking ACTIQ, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur. Talk to your healthcare provider about naloxone, a medicine for the emergency treatment of an opioid overdose.
- Taking ACTIQ with other medicines that may make you sleepy, such as other pain medicines, anti-depressants, sleeping pills, anti-anxiety medicines, antihistamines, or tranquilizers, or with alcohol or street drugs can cause severe drowsiness, confusion, breathing problems, coma, and death.
- Never give anyone else your ACTIQ. They could die from taking it. Selling or giving away ACTIQ is against the law.
- Store ACTIQ securely, out of sight and reach of children, and in a location not accessible by others, including visitors to the home.
- If you stop taking your around-the-clock opioid pain medicine for your cancer pain, **you must stop** using ACTIQ. You may no longer be opioid tolerant. Talk to your healthcare provider about how to treat your pain.
- ACTIQ is available only through a program called the **T**ransmucosal **I**mmediate **R**elease **F**entanyl (TIRF) **R**isk **E**valuation and **M**itigation **S**trategy (REMS). To receive ACTIQ, you must:
  - talk to your healthcare provider
  - understand the benefits and risks of ACTIQ
  - agree to all of the instructions
  - sign the Patient Enrollment Form
- ACTIQ is only available at pharmacies that are part of the TIRF REMS. Your healthcare provider can help you locate a pharmacy closest to your home where you can have your ACTIQ prescription filled.
- Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

Do not take ACTIQ if:

- You are not opioid tolerant. Opioid tolerant means that you are already taking other opioid pain medicines around-the-clock for at least one week or longer for your cancer pain, and your body is used to these medicines.
- You have severe asthma, trouble breathing, or other lung problems.
- You have a bowel blockage or have narrowing of the stomach or intestines.
- You are allergic to any of the ingredients in ACTIQ. See the end of this Medication Guide for a complete list of ingredients in ACTIQ.
- You have short-term pain that you would expect to go away in a few days, such as:
  - pain after surgery
  - headache or migraine
  - dental pain

Before taking ACTIQ, tell your healthcare provider if you have a history of:

- troubled breathing or lung problems such as asthma, wheezing, or shortness of breath
- head injury, seizures
- slow heart rate or other heart problems
- low blood pressure
- mental problems [including major depression, schizophrenia or hallucinations (seeing or hearing things that are not there)]
- problems urinating
- liver, kidney, thyroid problems
- pancreas or gallbladder problems
- abuse of street or prescription drugs, alcohol addiction, opioid overdose, or mental health problems
- diabetes. Each ACTIQ unit contains about ½ teaspoon (2 grams) of sugar.

Tell your healthcare provider if you are:

- **noticing your pain getting worse.** If your pain gets worse after you take ACTIQ, do not take more ACTIQ without first talking to your healthcare provider. Talk to your healthcare provider if the pain you have increases, if your feel more sensitive to pain, or if you have new pain after taking ACTIQ.
- **pregnant or planning to become pregnant.** Use of ACTIQ for an extended period of time during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated.
- **breastfeeding.** ACTIQ passes into breast milk and may harm your baby. Carefully observe infants for increased sleepiness (more than usual), breathing difficulties, or limpness. Seek immediate medical care if you notice these signs.
- living in a household where there are small children or someone who has abused street or prescription drugs.
- taking prescription over-the-counter medicines, vitamins, or herbal supplements. Taking ACTIQ with certain other medicines can cause serious side effects that could lead to death.

When taking ACTIQ:

- Do not change your dose. Take ACTIQ exactly as prescribed by your healthcare provider.
- Your healthcare provider will change the dose until you and your healthcare provider find the right dose for you.
- **See the detailed Patient Instructions for Use at the end of this Medication Guide for information about how to use ACTIQ.**
- Finish the unit completely in 15 minutes to get the most relief. If you finish ACTIQ too quickly, you will swallow more of the medicine and get less relief.
- **Do not bite or chew. You will get less relief for your breakthrough cancer pain.**
- You may drink some water before using ACTIQ but you should not drink or eat anything while using ACTIQ.
- You must not use more than 2 units of ACTIQ during each episode of breakthrough cancer pain:
  - Use **1** unit for an episode of breakthrough cancer pain. Finish the unit over 15 minutes.
  - If your breakthrough cancer pain is not relieved 15 minutes after you finished the ACTIQ unit, use **only 1** more unit of ACTIQ at this time.
  - If your breakthrough pain does not get better after the second unit of ACTIQ, call your healthcare provider for instructions. **Do not use another unit of ACTIQ at this time.**
- Wait at least **4** hours before treating a new episode of breakthrough cancer pain with ACTIQ.
- It is important for you to keep taking your around-the-clock opioid pain medicine.
- Talk to your healthcare provider if your dose of ACTIQ does not relieve your breakthrough cancer pain. Your healthcare provider will decide if your dose of ACTIQ needs to be changed.
- Talk to your healthcare provider if you have more than 4 episodes of breakthrough cancer pain per day. The dose of your around-the-clock opioid pain medicine may need to be adjusted.
- If you begin to feel dizzy, sick to your stomach, or very sleepy before ACTIQ is completely dissolved, remove ACTIQ from your mouth.
- Do not stop taking ACTIQ without talking to your healthcare provider. You could become sick with uncomfortable withdrawal symptoms because your body has become used to these medicines. Physical dependency is not the same as drug addiction.
- After you stop taking, or when ACTIQ is no longer needed, see "**How should I dispose of ACTIQ units when they are no longer needed?**" for proper disposal of ACTIQ.
- Dispose of expired, unwanted, or unused ACTIQ by following the "**How should I dispose of ACTIQ units when they are no longer needed?**" sections of this Medication Guide below. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.
- **DO NOT** Drive or operate heavy machinery until you know how ACTIQ affects you. ACTIQ can make you sleepy, dizzy, or lightheaded.
- **DO NOT** Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with ACTIQ may cause you to overdose and die.
- **DO NOT Switch from ACTIQ to other medicines that contain fentanyl without talking to your healthcare provider.** The amount of fentanyl in a dose of ACTIQ is not the same as the amount of fentanyl in other medicines that contain fentanyl. Your healthcare provider will prescribe a starting dose of ACTIQ that may be different than other fentanyl containing medicines you may have been taking.

The possible side effects of ACTIQ:

- constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, abdominal pain, weakness, anxiety, depression, rash, trouble sleeping. Call your healthcare provider if you have any of these symptoms and they are severe.
- Decreased blood pressure. This can make you feel dizzy or lightheaded if you get up too fast from sitting or lying down.
- ACTIQ contains sugar. Cavities and tooth decay can happen in people taking ACTIQ. When taking ACTIQ, you should talk to your dentist about proper care of your teeth.

Get emergency medical help or call 911 right away if you have:

- trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue, or throat, extreme drowsiness, light-headedness when changing positions, feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.
- These symptoms can be a sign that you have used too much ACTIQ or the dose is too high for you. **These symptoms may lead to serious problems or death if not treated right away. If you have any of these symptoms, do not use any more ACTIQ until you have talked to your healthcare provider.**

These are not all the possible side effects of ACTIQ. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. **For more information go to dailymed.nlm.nih.gov**

How should I store ACTIQ?

- **Always keep ACTIQ in a safe place away from children and from anyone for whom it has not been prescribed.** Protect ACTIQ from theft.
  - You can use the ACTIQ Child Safety Kit to help you store ACTIQ and your other medicines out of the reach of children. It is very important that you use the items in the ACTIQ Child Safety Kit to help protect the children in your home or visiting your home.
  - If you were not offered a Child Safety Kit when you received your medicine, call 888-534-3119.

The ACTIQ Child Safety Kit contains important information on the safe storage and handling of ACTIQ.

The Child Safety Kit includes:

- **A child-resistant lock that** you use to secure the storage space where you keep ACTIQ (See Figure 1).

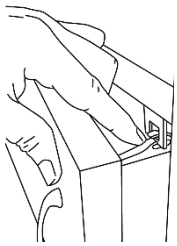


Figure 1

- **A portable locking pouch** for you to keep a small supply of ACTIQ nearby. The rest of your ACTIQ must be kept in a locked storage space.
    - Keep this pouch secured with its lock and keep it out of the reach and sight of children (See Figure 2).

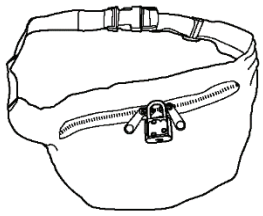


Figure 2

- **A child-resistant temporary storage bottle** (See Figure 3).

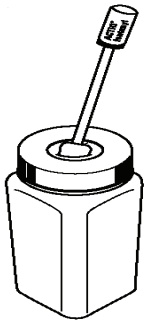


Figure 3

- Store ACTIQ at room temperature, 59°F to 86°F (15°C to 30°C) until ready to use.
- Do not freeze ACTIQ.
- **Keep ACTIQ in the original sealed child-resistant blister package. Do not open the blister package until you are ready to use ACTIQ.**
- Keep ACTIQ dry.

How should I dispose of ACTIQ units when they are no longer needed?

Disposing of ACTIQ units after use:

Partially used ACTIQ units may contain enough medicine to be harmful or fatal to a child or other adults who have not been prescribed ACTIQ. **You must properly dispose of the ACTIQ handle right away after use even if there is little or no medicine left on it.**

After you have finished the ACTIQ unit and the medicine is totally gone, throw the handle away in a place that is out of the reach of children.

If **any** medicine remains on the used ACTIQ unit after you have finished:

- Place the used ACTIQ unit under hot running water until the medicine is gone, and then throw the handle away out of the reach of children and pets (See Figure 4).

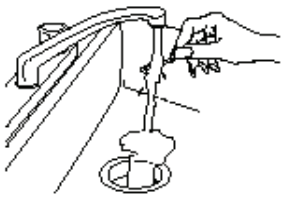


Figure 4

<u>Temporary Storage of Used ACTIQ Units</u>:

- If you did not finish the entire ACTIQ unit and you cannot dissolve the medicine under hot running water right away, put the used ACTIQ unit in the temporary storage bottle that you received in the ACTIQ Child Safety Kit. Push the used ACTIQ unit into the opening on the top until it falls completely into the bottle. **Never leave unused or partially used ACTIQ units where children or pets can get to them** (See Figure 5).

Figure 5

<u>Disposing of Used ACTIQ Units from the Temporary Storage Bottle</u>:

You must dispose of all used ACTIQ units in the temporary storage bottle **at least one time each day**, as follows:

1. To open the temporary storage bottle, push down on the cap until you are able to twist the cap to the left to remove it (See Figure 6).

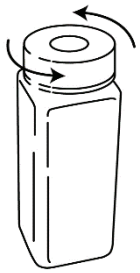


Figure 6

2. Remove one ACTIQ unit from the temporary storage bottle. Hold the ACTIQ by its handle over the toilet bowl.
3. Using wire-cutting pliers, cut the medicine end off so that it falls into the toilet.
4. Throw the handle away in a place that is out of the reach of children.
5. Repeat these 3 steps for each ACTIQ handle that is in the storage bottle. There should not be more than 4 handles in the temporary storage bottle for 1 day.
6. Flush the toilet twice.

Do not flush entire unused ACTIQ units, ACTIQ handles, or blister packages down the toilet.

Disposing of unopened ACTIQ units: Dispose of any unopened ACTIQ units remaining from a prescription as soon as they are no longer needed, as follows:

1. Remove all ACTIQ from the locked storage space (See Figure 7).

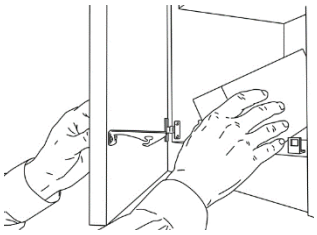


Figure 7

2. Remove one ACTIQ unit from its blister package by using scissors to cut off the marked end and then peel back the blister backing (See Figures 8A and 8B).

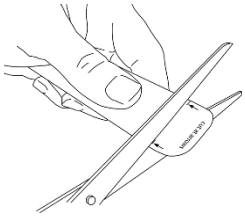


Figure 8A

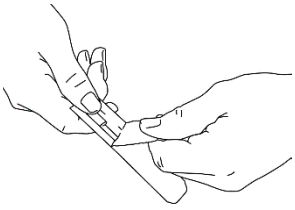


Figure 8B

3. Hold ACTIQ by its handle over the toilet bowl. Use wire-cutting pliers to cut the medicine end off so that it falls into the toilet (See Figures 9A and 9B).

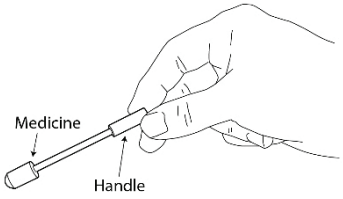


Figure 9A

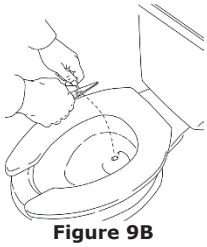


Figure 9B

4. Throw the handle away in a place that is out of the reach of children (See Figure 10).

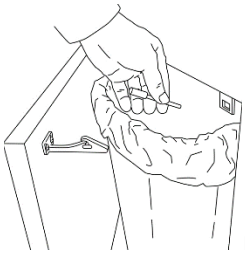


Figure 10

5. Repeat steps 1 through 4 for each ACTIQ unit.
6. Flush the toilet twice after the medicine ends from 5 ACTIQ units have been cut off (See Figure 11). Do not flush more than 5 ACTIQ units at a time.

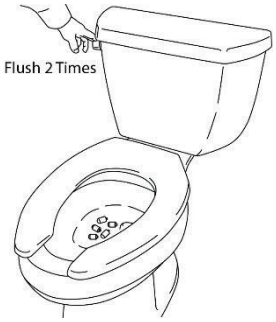


Figure 11

- Do not flush entire unused ACTIQ units, ACTIQ handles, or blister packages down the toilet.

If you need help with disposal of ACTIQ, call Teva Pharmaceuticals at 1-888-483-8279, or call your local Drug Enforcement Agency (DEA) office.

General information about ACTIQ

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. **Use ACTIQ only for the purpose for which it was prescribed. Do not give ACTIQ to other people, even if they have the same symptoms you have**. ACTIQ can harm other people and even cause death. Sharing ACTIQ is against the law.

This Medication Guide summarizes the most important information about ACTIQ. If you would like more information, talk with your healthcare provider or pharmacist. You can ask your pharmacist or healthcare provider for information about ACTIQ that is written for healthcare professionals.

For more information about the TIRF REMS Access program, go to www.TIRFREMSAccess.com or call 1-866-822-1483.

What are the ingredients of ACTIQ?

Active Ingredient: fentanyl citrate

Inactive Ingredients: sugar, citric acid, dibasic sodium phosphate, artificial berry flavor, magnesium stearate, modified food starch and confectioner's sugar.

Patient Instructions for Use

Before you use ACTIQ, it is important that you read the Medication Guide and these Patient Instructions for Use. Be sure that you read, understand, and follow these Patient Instructions for Use so that you use ACTIQ the right way. Ask your healthcare provider or pharmacist if you have any questions about the right way to use ACTIQ.

When you get an episode of breakthrough cancer pain, use the dose of ACTIQ prescribed by your healthcare provider as follows:

- You may drink some water before using ACTIQ but you should not drink or eat anything while using ACTIQ.
- Each unit of ACTIQ is sealed in its own blister package (See Figure 12). **Do not open the blister package until you are ready to use ACTIQ.**

Figure 12

- When you are ready to use ACTIQ, cut open the package using scissors. Peel back the blister backing, and remove the ACTIQ unit (See Figures 13A and 13B). The end of the unit printed with "ACTIQ" and the strength number of the unit ("200", "400", "600", "800", "1200", or "1600") is the medicine end that is to be placed in your mouth. Hold the ACTIQ unit by the handle (See Figure 14).

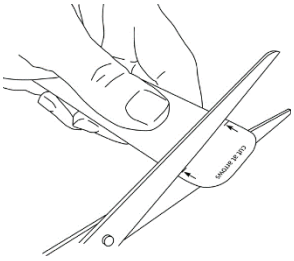


Figure13A

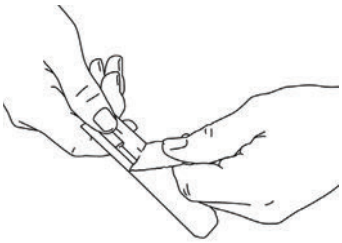


Figure 13B

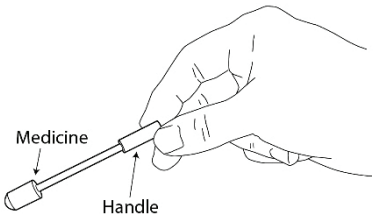


Figure 14

1. Place the medicine end of the ACTIQ unit in your mouth between your cheeks and gums and actively suck on the medicine.
2. Move the medicine end of the ACTIQ unit around in your mouth, especially along the inside of your cheeks (See Figure 15).

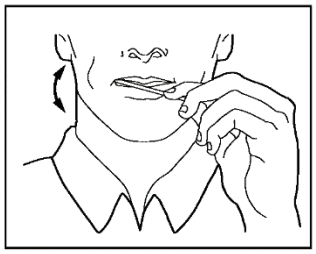


Figure 15

3. Twirl the handle often.
4. Finish the ACTIQ unit completely over 15 minutes to get the most relief. If you finish ACTIQ too quickly, you will swallow more of the medicine and get less relief.
5. **Do not bite or chew ACTIQ. You will get less relief for your breakthrough cancer pain.**

- If you cannot finish all of the medicine on the ACTIQ unit and cannot dissolve the medicine under hot tap water right away, immediately put the ACTIQ unit in the temporary storage bottle for safe keeping (See Figure 16).
    - Push the ACTIQ unit into the opening on the top until it falls completely into the bottle. You must properly dispose of the ACTIQ unit as soon as you can.

Figure 16

See "**How should I dispose of ACTIQ units when they are no longer needed?**" for proper disposal of ACTIQ.

Distributed by:
Teva Pharmaceuticals USA, Inc.
Parsippany, NJ 07054

call 1-888-483-8279

ACTMG-016

Printed in USA

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

020747Orig1s050

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document
Transmucosal Immediate Release Fentanyl (TIRF)
Shared System REMS Program

I. Administrative Information

Initial Shared System REMS Approval: 12/2011
Most Recent REMS Update: 12/2020

II. REMS Goals

The goals of the TIRF REMS are to:

1. Mitigate the risk of overdose by:
   a) Requiring documentation of opioid tolerance with every TIRF prescription for outpatient use.
   b) Requiring inpatient pharmacies to develop policies and procedures to verify opioid tolerance in inpatients who require TIRF medicines while hospitalized.
   c) Educating prescribers, pharmacists and patients that the safe use of TIRF medicines requires patients to be opioid-tolerant throughout treatment.
2. Mitigate the risk of accidental exposure by educating prescribers, pharmacists and patients about proper storage and disposal of TIRF medicines.
3. Monitor for accidental exposure, misuse, abuse, addiction, and overdose by enrolling all patients who receive a TIRF medicine for outpatient use into a registry and using surveillance systems and other data sources.

III. REMS Requirements

TIRF Applicants must ensure that healthcare providers, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare Providers who prescribe TIRF medicines for outpatient use must:

To become certified to prescribe	1. Review each drug's Prescribing Information. 2. Review the following: Prescriber Education. 3. Successfully complete the Prescriber Knowledge Assessment and submit it to the REMS program. 4. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS program.

Before treatment initiation	5. Assess the patient for risk factors of opioid addiction, abuse, and misuse. 6. Counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Provide a copy of the materials to the patient. 7. Assess the patient's opioid tolerance. Document and submit to the REMS program using the Patient Enrollment Form. 8. Enroll the patient by completing and submitting the Patient Enrollment Form to the REMS program.
During treatment, before each prescription	9. Assess the patient's health status for opioid tolerance, appropriateness of dose, misuse, abuse, addiction, and overdose. Document and submit to the REMS program using the Patient Status and Opioid Tolerance Form.
During treatment, every 2 years	10. Counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Provide a copy of the materials to the patient. 11. Re-enroll the patient in the REMS by completing the Patient Enrollment Form and submitting it to the REMS program.
Before treatment re-initiation, lapse in treatment of 6 months or longer	12. Counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Provide a copy of the materials to the patient.
To maintain certification to prescribe, every 2 years	13. Review the Prescribing Information for the TIRF medicines. 14. Review the following: Prescriber Education. 15. Successfully complete the Prescriber Knowledge Assessment and submit it to the REMS program. 16. Re-enroll in the REMS by completing the Prescriber Enrollment Form.
At all times	17. Counsel the patient using the Medication Guide for any new TIRF medicine not previously prescribed. Provide a copy to the patient. 18. Report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose to the REMS program using the Adverse Events of Special Interest Reporting Form. 19. Report treatment discontinuations to the REMS Program using the Patient Discontinuation Form.

2. Patients who are prescribed TIRF medicines for outpatient use:	
Before treatment initiation	1. Receive counseling from the prescriber on the safe use of TIRF medicines using the Medication Guide and the Patient Counseling Guide. 2. Enroll in the REMS program by completing the Patient Enrollment Form with the prescriber. Enrollment information will be provided to the REMS program.
Before treatment re-initiation, lapse in treatment of 6 months or longer	3. Receive counseling from the prescriber on the safe use of TIRF medicines using the Medication Guide and the Patient Counseling Guide.
During treatment, every 2 years	4. Receive counseling from the prescriber on the safe use of TIRF medicines using the Medication Guide and the Patient Counseling Guide. 5. Re-enroll in the REMS program by completing the Patient Enrollment Form with the prescriber. Enrollment information will be provided to the REMS program.
At all times	6. Adhere to safe use conditions: taking around-the-clock opioid pain medicine when using TIRF medicines, not sharing TIRF medicines, properly storing and disposing your TIRF medicines. 7. Inform the prescriber if your TIRF medicine does not relieve your pain. Do not change your dose or take a TIRF medicine more often than your prescriber directed. 8. Receive counseling from the prescriber on the safe use of each new TIRF medicine you are prescribed. 9. Inform the prescriber of serious adverse events of accidental exposure, abuse, misuse, addiction, and overdose.
3. Pharmacies that dispense TIRF medicines for outpatient use must:	
To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS program on behalf of the pharmacy. 2. Have the authorized representative review the Pharmacy Education. 3. Have the authorized representative successfully complete the Pharmacy Knowledge Assessment and submit it to the REMS program. 4. Establish processes and procedures to assess the patient's medication use for a change in opioid tolerance.

	5. Have the authorized representative enroll in the REMS Program by completing and submitting the Outpatient Pharmacy Enrollment Form. 6. Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS program using the Pharmacy Education.
Before dispensing	7. Provide the patient with the product-specific Medication Guide. 8. Assess the patient's medication use for a change in opioid tolerant status. Document and submit the results to the REMS Program. 9. Obtain authorization to dispense each prescription by contacting the REMS program to verify that the prescriber and the patient are enrolled, and the patient is opioid tolerant.
To maintain certification to dispense	10. Have any new authorized representative enroll in the REMS Program by reviewing the Pharmacy Education, successfully completing the Pharmacy Knowledge Assessment and the Outpatient Pharmacy Enrollment Form and submitting both to the REMS Program.
At all times	11. Not distribute, transfer, loan, or sell TIRF medicines. 12. Maintain records of staff training. 13. Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed. 14. Report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose to the REMS program using the Adverse Events of Special Interest Reporting Form.

4. Pharmacies that dispense TIRF medicines for inpatient use must:

To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS program on behalf of the pharmacy. 2. Have the authorized representative review the Pharmacy Education. 3. Have the authorized representative successfully complete the Pharmacy Knowledge Assessment and submit it to the REMS program. 4. Have the authorized representative enroll in the REMS program by completing the Inpatient Pharmacy Enrollment Form and submitting it to the REMS program. 5. Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS program using the Pharmacy Education. 6. Establish processes and procedures to verify that the patient is opioid tolerant.
Before dispensing	7. Verify the patient is opioid tolerant through the processes and procedures established as a requirement of the REMS program.
To maintain certification to dispense	8. Have any new authorized representative enroll in the REMS Program by reviewing Pharmacy Education, successfully completing the Pharmacy Knowledge Assessment and the Inpatient Pharmacy Enrollment Form and submitting both to the REMS Program.
At all times	9. Not distribute, transfer, loan, or sell TIRF medicines. 10. Maintain records of staff training. 11. Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed. 12. Not dispense TIRF medicines for outpatient use.

5. Wholesalers-Distributors that distribute TIRF medicines must:	
To be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies. 2. Train all relevant staff involved in distributing TIRF medicines on the procedures and the REMS program requirements.
At all times	3. Distribute only to certified pharmacies. 4. Maintain records of shipments to certified pharmacies. 5. Comply with audits carried out by TIRF Applicants or a third party acting on behalf of the TIRF Applicants to ensure that all processes and procedures are in place and are being followed.

TIRF Applicants must provide training to healthcare providers who prescribe TIRF medicines. The training includes the following educational material: Prescriber Education. The training must be made available on a website and by calling the REMS program.

TIRF Applicants must provide training to pharmacies that dispense TIRF medicines. The training includes the following educational material: Pharmacy Education. The training must be made available on a website and by calling the REMS program.

To inform healthcare providers about the REMS program and the risks and safe use of TIRF medicines, TIRF Applicants must disseminate REMS communication materials according to the table below:

Target Audience	**Communication Materials & Dissemination Plans**
Inpatient and outpatient pharmacies that dispense Schedule II drugs and may be involved in dispensing TIRF medicines	REMS Letter: Inpatient Pharmacy Letter with attachment Pharmacy Education; Outpatient Pharmacy Letter with attachment Pharmacy Education. a. Email within 30 calendar days of the approval of the REMS modification and again 1 month later. a. Send by mail or fax within 45 calendar days of the date the second email was sent if email was undeliverable or unopened. b. Disseminate through the following professional societies and request the letter or content be provided to their members: b. American Association of Colleges of Pharmacy (AACP), American College of Clinical Pharmacy (ACCP), Accreditation Council for Pharmacy Education (ACPE), Academy of Managed Care Pharmacy (AMCP), American Pharmacists Association (APhA), American Society of Consultant Pharmacists (ASCP), American Society of Health-System Pharmacists (ASHP), Board of Pharmacy Specialties (BPS), Board Certified Oncology Pharmacists (BCOP), National Association of Boards of Pharmacy (NABP), National Community Pharmacists Association (NCPA), National Alliance of State Pharmacy Associations (NASPA)

Inpatient and outpatient pharmacies previously enrolled in the TIRF REMS	REMS Letter: Inpatient Pharmacy Letter with attachment Pharmacy Education; Outpatient Pharmacy Letter with attachment Pharmacy Education 1. Mail or fax within 45 calendar days of approval of the REMS modification (12/23/2020).
Inpatient and outpatient pharmacies, and wholesaler-distributors previously enrolled in the TIRF REMS	REMS Letter: Urgent Notification Regarding TIRF Products Stock Letter Mail or fax within 120 calendar days of approval of the REMS modification (12/23/2020).
Healthcare providers who are likely to prescribe TIRF medicines	REMS Letter: Healthcare Provider Letter with attachment Prescriber Education 1. Email within 30 calendar days of the approval of the REMS modification and again 1 month later. a. Send by mail or fax within 45 calendar days of the date the second email was sent if email was undeliverable or unopened. 2. Disseminate through the following professional societies and request the letter or content be provided to their members: a. American Academy of Hospice and Palliative Medicine, American Academy of Pain Management, American Academy of Pain Medicine, American Association of Poison Control Centers, American College of Physicians, American Chronic Pain Association, American Pain Society, American Society of Pain Educators, National Hospice and Palliative Care Organization
Prescribers previously enrolled in the TIRF REMS	REMS Letter: Healthcare Provider Letter with attachment Prescriber Education 1. Mail or fax within 45 calendar days of approval of the REMS modification (12/23/2020).

To support REMS program operations, TIRF Applicants must:

1. Authorize dispensing for each patient based on receipt of the Patient Status and Opioid Tolerance Form and pharmacy assessment for a change in opioid tolerance. The authorization is valid for one dispensing for up to 30 calendar days from date the prescriber initiates the authorization.
2. Establish and maintain a REMS program website, www.TIRFREMSaccess.com. The REMS program website must include the capability to complete prescriber, pharmacy, and patient enrollment online, document Adverse Events of Special Interest, document opioid tolerance, obtain authorization to dispense, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS program website. The REMS program website must not link back to the promotional product website(s).
3. Make the REMS program website fully operational and all REMS materials available through the website and coordinating center within 180 calendar days of the REMS modification (12/23/2020).
4. Establish and maintain a REMS program coordinating center for REMS participants at 1-866-822-1483.

5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the TIRF REMS program. The database must contain information on their enrollment status.
6. Ensure that prescribers and pharmacies are able to complete enrollment by fax and online.
7. Ensure prescribers are able to document opioid tolerance using the Patient Status and Opioid Tolerance Form by fax and online.
8. Ensure prescribers are able to report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose using the Adverse Events of Special Interest Reporting Form by fax and online.
9. Ensure pharmacies are able to report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose using the Adverse Events of Special Interest Reporting Form by phone, fax, and online.
10. Ensure pharmacies are able to enroll as an inpatient pharmacy (hospitals, in-hospital hospices, and long-term care facilities that dispense for inpatient use) or as an outpatient pharmacy.
11. Ensure outpatient pharmacies are able to document changes in opioid tolerance by phone and online.
12. Ensure outpatient pharmacies are able to obtain authorization to dispense TIRF medicines by phone and online.
13. Provide Prescriber Enrollment Form, Patient Enrollment Form, Outpatient Pharmacy Enrollment Form, Inpatient Pharmacy Enrollment Form, Prescriber Education, Prescriber Knowledge Assessment, Patient Counseling Guide, Pharmacy Education, Pharmacy Knowledge Assessment, and the Prescribing Information to REMS participants who (1) attempt to prescribe/dispense/distribute TIRFs and are not yet certified or (2) inquire about how to become certified.
14. Notify prescribers and pharmacies within three business days after they become certified in the REMS program.
15. Notify REMS participants 30 calendar days before their enrollment expires and of the need to re-enroll.
16. Provide certified prescribers access to the database of certified pharmacies and enrolled patients.
17. Provide certified outpatient pharmacies access to the database of certified prescribers and enrolled patients.
18. Establish and maintain a registry which includes a reporting and collection system for all outpatients to provide information on serious adverse events including accidental exposure, abuse, misuse, addiction, and overdose.
19. Follow up with the healthcare provider to obtain the reason for discontinuation if the patient is not dispensed a TIRF medicine after 2.5 times the days' supply of their last prescription's days' supply.
20. Ensure that once a report suggestive of accidental exposure, abuse, misuse, addiction, or overdose is received, TIRF Applicants follow up with the healthcare provider to obtain all required data for complete adverse event reporting related to accidental exposure, abuse, misuse, addiction, and overdose under the REMS.
21. Report any overdose that results in a death associated with a TIRF medicine, as soon as possible to FDA but no later than 15 calendar days from the initial receipt of the information by the TIRF Applicants. This requirement does not affect the applicants' other reporting and follow-up requirements under FDA regulations.

To ensure REMS participants' compliance with the REMS program, TIRF Applicants must:

22. Ensure a Patient Status and Opioid Tolerance Form is received, and the pharmacy assesses for a change in opioid tolerance for each patient for each dispensing.

23. Verify every two years that the pharmacy's authorized representative's name and information correspond to the designated authorized healthcare for the certified pharmacy, and if different, require the pharmacy to recertify with a new authorized representative.

24. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: TIRF distribution and dispensing; certification of prescribers, pharmacies; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.

25. Establish a plan for addressing noncompliance with REMS program requirements.

26. Monitor prescribers, pharmacies, and wholesalers-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.

27. Annually audit all certified outpatient pharmacies and 10% but no less than 50 certified inpatient pharmacies no later than 90 calendar days after they have become certified/re-certified in the TIRF REMS to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements. Similarly, annually audit all wholesalers-distributors no later than 90 calendar days after they become authorized to distribute TIRFs to ensure that all REMS processes and procedures are in place, functioning, and support the REMS program requirements.

28. Take reasonable steps to improve operations of and compliance with the requirements in the TIRF REMS program based on monitoring and evaluation of the TIRF REMS program.

IV. REMS Assessment Timetable

TIRF NDA Applicants must submit REMS Assessments at 12 months from 12/23/2020, 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 assessment should conclude no earlier than 60 days before the submission date for that assessment. TIRF NDA Applicants must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the TIRF REMS program**:**

Enrollment Forms

Prescriber:

1. Prescriber Enrollment Form

Patient:

2. Patient Enrollment Form

Pharmacy:

3. Outpatient Pharmacy Enrollment Form
4. Inpatient Pharmacy Enrollment Form

Training and Educational Materials

Prescriber:

5. Prescriber Education
6. Prescriber Knowledge Assessment

Patient:

7. Patient Counseling Guide

8. Medication Guides (available at www.TIRFREMSaccess.com)

Pharmacy:

9. Pharmacy Education
10. Pharmacy Knowledge Assessment

Patient Care Forms

11. Patient Status and Opioid Tolerance Form
12. Adverse Events of Special Interest Reporting Form
13. Patient Discontinuation Form

Communication Materials

14. Healthcare Provider Letter
15. Outpatient Pharmacy Letter
16. Inpatient Pharmacy Letter
17. Urgent Notification Regarding TIRF Products Stock Letter

Other Materials

18. Website (www.TIRFREMSaccess.com)

Prescriber Enrollment Form

TIRF REMS

Instructions

To become certified in the TIRF REMS and prescribe TIRF medicines:

1. Review all TIRF medicines Prescribing Information
2. Review the **Prescriber Education**
3. Complete and submit the **Prescriber Knowledge Assessment** to the TIRF REMS
4. Complete and submit this **Prescriber Enrollment Form** to the TIRF REMS

For real time processing of enrollment, visit www.TIRFREMSaccess.com

Or submit completed Prescriber Enrollment Form by fax to 1-866-822-1487.

1 Prescriber Information (PLEASE TYPE OR PRINT)

First Name	Middle Initial	Last Name

Individual NPI #	Clinic / Practice Name

Specialty	Credentials ☐ MD ☐ NP ☐ PA ☐ DO ☐ Other

Address	City	State	Zip

Phone ( )	Ext.	Fax ( )	Email Address

Preferred Time of Contact ☐ Morning ☐ Afternoon ☐ Evening	Preferred Method of Contact ☐ Text to Mobile # ☐ Email ☐ Phone Call

2 Office Contact Information (PLEASE TYPE OR PRINT)

First and Last Name	Phone	Fax

Email Address	Preferred Time of Contact ☐ Morning ☐ Afternoon ☐ Evening	Preferred Method of Contact ☐ Text to Mobile # ☐ Email ☐ Phone Call

3 Prescriber Attestation

By signing below, you attest to the following:

I have:

- Reviewed each drug's **Prescribing Information**.
- Reviewed the **Prescriber Education**.
- Successfully completed the **Prescriber Knowledge Assessment** and submitted it to the REMS.

Before treatment initiation, I must:

- Assess the patient for risk factors of opioid addiction, abuse, and misuse including personal and family history of substance abuse or mental illness.
- Counsel the patient on the safe use of TIRF medicines using the **Medication Guide** for the prescribed TIRF medicine and the **Patient Counseling Guide**.
- Provide a copy of the materials to the patient.
- Assess the patient's opioid tolerance.
- Document the patient's opioid tolerance using the **Patient Enrollment Form** and submit to the REMS.
- Enroll the patient by completing and submitting the **Patient Enrollment Form** to the TIRF REMS.

During treatment, and before each prescription, I must:

- Assess the patient's health status for opioid tolerance, appropriateness of dose, misuse, abuse, addiction, and overdose.
- Document and submit this information to the REMS using the **Patient Status and Opioid Tolerance Form**.

During treatment, every 2 years, I must:

- Counsel the patient on the safe use of TIRF medicines using the **Medication Guide** for the prescribed TIRF medicine, and the **Patient Counseling Guide**.
- Provide a copy of the materials to the patient.
- Re-enroll the patient in the REMS by completing the **Patient Enrollment Form** and submitting it to the REMS.

Before treatment re-initiation, after a lapse in treatment of 6 months or longer, I must:

- Counsel the patient on the safe use of TIRF medicines using the **Medication Guide** for the prescribed TIRF medicine and the **Patient Counseling Guide**.
- Provide a copy of the materials to the patient.

At all times, I must:

- Counsel the patient using the **Medication Guide** for any new TIRF medicine not previously prescribed and provide a copy to the patient.
- Report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose to the REMS using the **Adverse Events of Special Interest Reporting Form**.
- Report treatment discontinuation to the REMS using the **Patient Discontinuation Form**.

To maintain certification to prescribe, every 2 years, I must:

- Review each drug's **Prescribing Information**.
- Review the **Prescriber Education**.
- Successfully complete the **Prescriber Knowledge Assessment** and submit it to the REMS.
- Re-enroll in the REMS by completing the **Prescriber Enrollment Form**.

Required for all prescribers	**Prescriber Signature** **X**	**Date:** / /

If you have additional practice sites that you use when prescribing TIRF medicines, you may provide this information online.

Patient Enrollment Form

TIRF REMS

Instructions

Transmucosal Immediate Release Fentanyl (TIRF) medicines are available only through the TIRF REMS. Prescribers must enroll each patient in the TIRF REMS by submitting this completed form. Patients must review and sign the Patient Attestation section.

For real-time processing of patient enrollment, visit www.TIRFREMSAccess.com.

For fax submission, complete all required fields below and submit all pages to 1-855-474-3062.

Allow one (1) business day for processing before the patient can obtain their prescription fill.

All fields with asterisks (*) are required.

1 Patient Information (PLEASE TYPE OR PRINT)

First Name*	Middle Initial*	Last Name*	Date of Birth*
			mm / dd / yyyy

Sex
□ Male □ Female □ Other

Ethnicity
Are you Hispanic or Latino?
□ Yes □ No

Race (check all that apply)
☐ White ☐ Asian ☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify): _____

Address*	City*	State*	Zip*

Phone*	Email Address*
( )	

Preferred Time of Contact*
□ Morning □ Afternoon □ Evening

Preferred Method of Contact*
□ Text to Mobile # □ Email □ Phone Call □ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
□ Yes □ No

Do you have a safe and secure place to store your medicine?*
□ Yes □ No

2 Patient Representative (if required) (PLEASE TYPE OR PRINT)

First Name*	Last Name*	Relationship to Patient*

Phone*	Email Address*
( )	

3 Patient Attestation

TIRF Medicines can cause your breathing to stop – which can lead to death.

Safety Rules for TIRF Medicines

You have agreed to take a TIRF Medicine and to follow all the safety rules to make it less likely you or others will experience serious harm.

- My healthcare provider has talked to me about the safe use of TIRF medicines using the **Medication Guide** and **Patient Counseling Guide**.
- I will only use this medicine if I am regularly using another opioid, around-the-clock, for constant pain.
- If I stop taking my around-the-clock-opioid pain medicine, I **MUST** stop taking my TIRF medicine.
- I will never share or give my TIRF medicine to anyone else, even if they have the same symptoms.
  - My TIRF medicine could cause harm to others or even death. A dose that is okay for me could cause an overdose and death for someone else.
- I will store my TIRF medicine in a safe and secure place away from children. I understand that accidental use by a child, or anyone for whom the medicine was not prescribed, can cause death.

Continued on next page

- I have been told how to properly dispose of my partially used or unneeded TIRF medicine remaining from my prescription. I will dispose of my TIRF medicine properly as soon as I no longer need it.
- I will contact my healthcare provider if my TIRF medicine does not relieve my pain. I will not change the dose of my TIRF medicine myself or take it more often than my healthcare provider has directed.
- I must enroll in the TIRF REMS and Patient Registry by completing the **Patient Enrollment Form** with my healthcare provider.
- I understand that the TIRF REMS and its agents may use and share my personal information to manage the program, and that information about patients who get TIRF medicines will be stored in a private and secure database. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TIRF REMS. However, my name will not be shared.
- I give permission for the TIRF REMS and its agents or vendors to contact me by phone, mail, or email to support the administration of the TIRF REMS Program.
- I will tell my healthcare provider if I, or anyone else, experience an adverse event of accidental exposure, abuse, misuse, addiction, and overdose.
- I will re-enroll in the TIRF REMS by completing the **Patient Enrollment Form** with my healthcare provider every two years during treatment.

Required for all patients	**Patient or Patient Representative Signature:** X	**Date:** mm / dd / yyyy

The following sections to be completed by the prescriber

4 Prescriber Information (PLEASE PRINT)

First Name*	**Last Name***		
Address*	**City***	**State***	**Zip***
Phone* ( )	**Fax*** ( )	**Individual NPI #***	**Email Address***

5 Medical Information

Prior TIRF Use within the last 6 months*: ☐ Yes ☐ No			
TIRF Product Name*	**Strength***	**Dose***	**Frequency***

Type of Pain*

☐ Cancer

☐ Non-cancer pain

Continued on next page

6 Verify Opioid Tolerance*

Moiety*	Formulation*	Strength*	Route*	Dose*	Frequency*

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply)*:

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ an equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

7 Concomitant Medications

Concomitant Medications (check all that apply)*:

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Required for all prescribers	**Prescriber Signature***	**Date***
	X	mm / dd / yyyy

The following events are of special interest to the TIRF REMS: overdose, addiction, misuse, abuse, and accidental exposure. If the patient experiences any of these events associated with a TIRF medicine, report them on the Adverse Events of Special Interest Reporting Form which is available on the TIRF REMS website at www.TIRFREMSaccess.com or fax the completed form to 1-855-474-3062.

If you have any questions, require additional information, or need copies of any TIRF REMS documents, visit www.TIRFREMSaccess.com or call the TIRF REMS at 1-866-822-1483.

Outpatient Pharmacy Enrollment Form

TIRF REMS

Instructions

To become certified in the TIRF REMS and dispense TIRF medicines, a pharmacy must designate an Authorized Representative to:

1. Review the **Pharmacy Education**
2. Complete and submit the **Pharmacy Knowledge Assessment** to the TIRF REMS
3. Complete and submit this **Pharmacy Enrollment Form** to the TIRF REMS

For real time processing of enrollment, visit www.TIRFREMSaccess.com

Or submit completed Pharmacy Enrollment Form by fax to 1-866-822-1487.

1 Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			**Organizational NPI #**	
Address		**City**	**State**	**Zip**
Phone ( )	**Ext.**	**Fax** ( )	**Chain ID**	

2 Authorized Representative Information (PLEASE TYPE OR PRINT)

First Name	**Last Name**	**Credentials** ☐ RPh ☐ PharmD ☐ BCPS ☐ Other	**Position/Title**
Email Address		**Phone** ( )	**Fax** ( )

Preferred Method of Contact

☐ Text to Mobile # ☐ Email ☐ Phone Call

3 Pharmacy Attestation

As the Authorized Representative, I must:

- Review the **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Establish processes and procedures to check the patient's medication use for a change in opioid tolerance.
- Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS using the **Pharmacy Education**.

Before dispensing, all pharmacy staff must:

- Provide the patient with the product-specific **Medication Guide**.
- Assess the patient's medication use for a change in opioid tolerant status. Document and submit the results to the REMS.
- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber and the patient are enrolled, and the patient is opioid tolerant.

All pharmacy staff must:

- Not distribute, transfer, loan, or sell TIRF medicines.
- Maintain records of staff training.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed.
- Report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose associated with the TIRF medicine to the REMS using the **Adverse Events of Special Interest Reporting Form**.

CONTINUED ON THE NEXT PAGE

To maintain certification to dispense, any new authorized representative must: • Review the **Pharmacy Education**. • Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS. • Enroll in the REMS by completing the **Outpatient Pharmacy Enrollment Form.**
The name, location, and phone number of your pharmacy will be publicly available on www.TIRFREMSaccess.com. If you do not want your information available, please call the TIRF REMS at 1-866-822-1483.

Required	Pharmacy Authorized Representative Signature X	Date: / /

You may add additional pharmacy locations below.

Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			Organizational NPI #	
Address		City	State	Zip
Phone ( )	Ext.	Fax ( )	Chain ID	

Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			Organizational NPI #	
Address		City	State	Zip
Phone ( )	Ext.	Fax ( )	Chain ID	

Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			Organizational NPI #	
Address		City	State	Zip
Phone ( )	Ext.	Fax ( )	Chain ID	

Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			Organizational NPI #	
Address		City	State	Zip
Phone ( )	Ext.	Fax ( )	Chain ID	

Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			Organizational NPI #	
Address		City	State	Zip
Phone ( )	Ext.	Fax ( )	Chain ID	

Inpatient Pharmacy Enrollment Form

TIRF REMS

Instructions

To become certified in the TIRF REMS and dispense TIRF medicines, a pharmacy must designate an Authorized Representative to:

1. Review the **Pharmacy Education**
2. Complete and submit the **Pharmacy Knowledge Assessment** to the TIRF REMS
3. Complete and submit this **Pharmacy Enrollment Form** to the TIRF REMS

For real time processing of enrollment, visit www.TIRFREMSaccess.com

Or submit completed Pharmacy Enrollment Form by fax to 1-866-822-1487.

1 Pharmacy Information (PLEASE TYPE OR PRINT)

Pharmacy Name			Organizational NPI #	
Address		**City**	**State**	**Zip**
Phone ( )	**Ext.**	**Fax** ( )	**Chain ID**	

2 Authorized Representative Information (PLEASE TYPE OR PRINT)

First Name	Last Name	Credentials ☐ RPh ☐ PharmD ☐ BCPS ☐ Other	Position/Title
Email Address		**Phone** ( )	**Fax** ( )

Preferred Method of Contact

☐ Text to Mobile # ☐ Email ☐ Phone Call

3 Pharmacy Attestation

As the Authorized Representative, I must:

- Review the **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS using the **Pharmacy Education**.
- Establish processes and procedures to verify that the patient is opioid tolerant.

All pharmacy staff must:

- Verify the patient is opioid tolerant through the processes and procedures established as a requirement of the REMS.

All pharmacy staff must:

- Not distribute, transfer, loan, or sell TIRF medicines.
- Maintain records of staff training.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed.
- Not dispense TIRF medicines for outpatient use.

To maintain certification to dispense, any new authorized representative must:

- Review the following: **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Enroll in the REMS by completing the **Inpatient Pharmacy Enrollment Form.**

Required	Pharmacy Authorized Representative Signature	Date:
	X	/ /

TIRF REMS

Transmucosal Immediate-Release Fentanyl (TIRF) REMS

Prescriber Education

This education program includes information about:

- **The TIRF REMS requirements**
- **Serious risks of:**
  - **life-threatening and/or fatal respiratory depression**
  - **increased risk of overdose, especially in children, due to accidental ingestion or exposure**
- **Counseling your patient**

The purpose of this educational material is to inform prescribers about the **Risk Evaluation and Mitigation Strategy (REMS)** for transmucosal immediate-release fentanyl (TIRF) medicines. This education presents important safety issues and messages about the TIRF REMS needed to manage and counsel patients about the safe use of TIRF products.

What is the TIRF REMS (Risk Evaluation and Mitigation Strategy)?

The TIRF REMS is a safety program to manage the risk of overdose and accidental exposure by ensuring that patients prescribed a TIRF medicine are opioid tolerant and ensuring that prescribers, pharmacists, and patients are educated about proper storage and disposal of TIRF medicines. The TIRF REMS registry helps to assess safe use and trends in accidental exposure, misuse, abuse, addiction, and overdose by enrolling all patients who receive a TIRF medicine for outpatient use.

The TIRF REMS is required by the U. S. Food and Drug Administration (FDA) to help ensure that the benefits of treatment with transmucosal fentanyl-containing products outweigh the known risks of these products.

Products Covered Under This Program:

- **Actiq®** (fentanyl citrate) oral transmucosal lozenge
- **Fentora®** (fentanyl buccal tablet)
- **Lazanda®** (fentanyl) nasal spray
- **Onsolis®** (fentanyl buccal soluble film)
- **Subsys®** (fentanyl sublingual spray)
- Approved generic equivalents of these products

How Does the TIRF REMS Work?

The TIRF REMS requires prescribers, pharmacies, patients, and wholesaler-distributors to enroll in the program to utilize TIRF medications. Prescribers must verify and document that patients are opioid-tolerant before each prescription.

Steps for Prescriber Enrollment in the TIRF REMS

1. Complete the Training Program:
    - review the **Prescriber Education**
2. Successfully complete the **Knowledge Assessment**; and
3. Complete and submit a signed **Prescriber Enrollment Form**

The enrollment process may be completed online at **www.TIRFREMSaccess.com**

Or

Materials and forms can be downloaded from the website on the Prescriber tab, then completed and faxed to the program at **1-866-822-1487**.

Prescribers must re-enroll in the TIRF REMS every two years. You will receive a reminder to renew your enrollment 30 days before your current enrollment expires.

Prescribing TIRF Medicines for Inpatient Use

Prescribers who prescribe TIRF medications for inpatient use only (e.g., hospitals, in-hospital hospices, and long-term care facilities) **do not need to enroll** in the TIRF REMS.

Patient enrollment in the TIRF REMS is not required for inpatient administration of TIRF medicines.

Prescribing TIRF Medicines for Outpatient Use

What actions must I take as an outpatient prescriber to comply with the TIRF REMS?

1. Enroll each patient
2. Document each patient's opioid tolerance
3. Counsel your patients on the risks
4. Report adverse events of concern

Prescribing Naloxone

Consider prescribing naloxone for the emergency treatment of opioid overdose.

If concomitant use with benzodiazepines, other CNS depressants, or muscle relaxants is warranted, consider prescribing naloxone for the emergency treatment of opioid overdose.

Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help right away in the event of a known or suspected overdose. (See the patient counseling section below.)

Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver both when initiating and renewing treatment with TIRF products.

Inform patients about the various ways to obtain naloxone.

1 - Enroll each patient

Enroll each patient into the TIRF REMS prior to their first prescription for a TIRF medicine. Inform the patient that they will be included in a registry to monitor for serious side effects, including fatal and non-fatal overdose.

- Use the **Patient Enrollment Form**

2 – Document each patient's opioid tolerance

Document patient's opioid tolerance before every prescription.

- Use the **Patient Enrollment Form** to document the patient's opioid tolerance for their first prescription.
- Use the **Patient Status and Opioid Tolerance Form** for documenting opioid tolerance prior to each prescription thereafter.
- Documentation of the patient's opioid tolerance must be on file with the TIRF REMS prior to each prescription being authorized for dispensing at the pharmacy. In addition, the program requires that the TIRF medicine prescriptions be written by the same prescriber listed on the **Patient Status and Opioid Tolerance Form**.
- The **Patient Status and Tolerance Opioid Form** can be submitted online from the Prescriber Dashboard on the TIRF REMS website, or by downloading and faxing to the TIRF REMS.

3 – Counsel your patient on the risks

Counsel each patient

- **Before initiating treatment with a TIRF medicine, review the product-specific Medication Guide with patients and/or caregivers.** Counsel them on the TIRF medicine's risks and conditions of safe use**. Use** the **Patient Counseling Guide** to assist in the discussion and provide the materials to the patient.

Tell the patient:

- You must be opioid tolerant to be able to take a TIRF medicine for your breakthrough cancer pain. Opioid tolerant means that you have been using around-the-clock daily opioid pain medicine for your persistent cancer pain for at least 1 week immediately preceding the start of the TIRF medicine.
- If you stop taking your around-the-clock opioid pain medicine for your persistent cancer pain, you **must stop taking your TIRF medicine for the breakthrough cancer pain because you may no longer be opioid tolerant**.

Note: Patients have had difficulty understanding this concept. Emphasize this requirement to your patients and explain that the risk of life-threatening and/or fatal breathing problems with their TIRF medicine increases if they are not taking around-the-clock opioid pain medicines.

- Inform patients of the risk of life-threatening and/or fatal respiratory depression, including information that the risk is greatest when starting the TIRF medicine, when the dosage is increased, or when changing TIRF medicines, and that it can occur even at recommended dosages.

- Tell patients exactly how to take the TIRF medicine. Instruct them to take the TIRF medicine strictly as prescribed, with special regard to dosage, dose titration, and administration.

Proper storage and disposal

- **Accidental ingestion or exposure, especially in children, may result in life-threatening breathing problems or death.**
- Explain that the TIRF medicine **must** be stored in a secure place safely out of sight and out of reach of all others, especially children. Encourage the use of a lockbox or locked medication bag.

Accidental use by a child, or anyone for whom a TIRF medicine was not prescribed, is a medical emergency and can cause death. Use the child safety kit if one is provided with your TIRF medicine.

TIRF medicines contain fentanyl, which can be a target for people who abuse prescription medications or street drugs. Protect your TIRF medicine from theft.

Properly dispose of partially used or unneeded TIRF medicine remaining from a prescription. Refer to each product's Medication Guide for instructions for disposal.

Naloxone

- Naloxone rapidly reverses the effects of opioid overdose and is the standard treatment for overdose.

- An opioid overdose usually involves unconsciousness and shallow breathing. Other signs and symptoms of an overdose include:

  - Unresponsiveness
  - Limpness
  - Blue lips, gums or fingertips
  - Show or irregular heartbeat or pulse
  - Small pupils

- Advise your patient to be aware of these signs and symptoms in themselves or

if someone around them may be overdosing.

- If there is a suspected overdose, give naloxone immediately. Call 911 or get emergency help right away after administering the first dose of naloxone. Wait 2-3 minutes after the first dose is given to see if the overdose patient wakes up. If they do not wake up, give another dose and continue to give another dose every 2-3 minutes until the person wakes up. Stay with the overdose patient until the ambulance arrives. Give another dose if the overdose patient becomes sleepy again.

Misuse, abuse, addiction and overdose

- Prescribe a limited amount of medication to the patient that will last until the next visit.
- Continually monitor patients for appropriateness of dosing.
- Continually assess whether benefits of treatment outweigh the risks.
- Warn patients that it is dangerous to self-administer benzodiazepines or other CNS depressants including alcohol while taking TIRF medicines. Potentially fatal additive effects may occur if the TIRF medicine is used with benzodiazepines or other CNS depressants, including alcohol. Caution patients who are prescribed benzodiazepines or other CNS depressants to use them only as directed by their prescriber.
- The use of a TIRF medicine, even when taken as recommended, can result in misuse, abuse, addiction, overdose and death.
- Opioids could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs – serotonin syndrome. Seek medical attention right away if you develop the following symptoms of serotonin syndrome: mental status changes such as confusion, agitation, restlessness, and anxiety; high fever, seizures, rapid breathing, profuse sweating, and irregular heartbeat.
- Avoid concomitant use of a TIRF medicine and a monoamine oxidase inhibitor (MAOI).

Frequency of counseling

Counseling is required:

- before treatment initiation,
- after two years of continuous treatment,
- before treatment re-initiation, and
- upon any lapse in treatment of six months or longer

Effective Patient Management and Follow-up

At follow-up visits:

- Assess appropriateness of dose and make any necessary dose adjustments to the TIRF medicine for the breakthrough cancer pain or the around-the-clock opioid medicine for the persistent cancer pain.
- Assess for side effects or adverse effects.
- Assess for signs of misuse, abuse, or addiction.
    - Assessment and reinforcement of patient's compliance with his/her treatment plan.
    - Assessment of appropriateness of TIRF medicine dosage prescribed depending on tolerability and therapeutic response.
    - Assessment of concomitant medications.

Check Your Knowledge - Scenario 1

Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide with the patient. Which of the following counseling statements are FALSE?

Select any statements which are false.

A. TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
B. Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
C. Instruct patients that, if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.
D. Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.
E. Once a patient becomes familiar with the use of their TIRF medicine, if their BTCP is not controlled they can repeat their dose every 20 minutes until their pain is relieved.

See answer on page 17

4 – Report adverse events

Report adverse events, including misuse, abuse, addiction, overdose, and accidental exposure to TIRF medicines.

- Go to **www.TIRFREMSaccess.com** to complete the Patient Status and Opioid Tolerance Form or the Adverse Events of Special Interest Reporting Form online. These forms can also be obtained from the website, completed and faxed to **1-855-474-3062**; or call the TIRF REMS at **1-866-822-1483**.

Report patient's discontinuation of TIRF medicines

- Report discontinuation of a patient's use of TIRF medicines to the TIRF REMS. Go to **www.TIRFREMSaccess.com** to complete the **Patient Discontinuation Form** online. The form can also be obtained from the website, completed and faxed to **1-855-474-3062**; or you can report by calling **1-866-822-1483.**

KEY SAFETY INFORMATION

Risk of Life-threatening Respiratory Depression

Serious, life threatening, or fatal respiratory depression has been reported with the use of opioids even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death.

Indication:

TIRF medicines are indicated only for the management of breakthrough cancer pain (BTCP) in cancer patients 18 years of age or older **who are already receiving and who are tolerant to, around-the-clock opioid therapy for underlying persistent cancer pain**.

- The only exception is for ACTIQ, and its generic equivalents, which are approved for cancer patients **16** years of age or older.

Patients Must be Opioid Tolerant to be Prescribed a TIRF Medicine

Definition of Opioid Tolerance:

Patients are considered **opioid tolerant** if they are currently taking (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and have been on the regimen(s) **for one week or longer**:

- ≥ 60 mg oral morphine/day
- ≥ 25 mcg transdermal fentanyl/hour
- ≥ 30 mg oral oxycodone/day
- ≥ 8 mg oral hydromorphone/day
- ≥ 25 mg oral oxymorphone/day
- ≥ 60 mg oral hydrocodone/day
- an equianalgesic dose of another opioid

Patients must remain opioid tolerant to continue using a TIRF medicine.

TIRF medicines should only be prescribed by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids for the treatment of cancer pain.

Contraindications

TIRF medicines are contraindicated in:

- Patients who are not opioid tolerant. **Life-threatening respiratory depression could occur at any dose in patients who are not opioid tolerant, and deaths have occurred**.
- The management of acute or postoperative pain, including:
    - headache/migraine;
    - dental pain; or
    - acute pain in the emergency department
- Patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
- Patients with known or suspected gastrointestinal obstruction, including paralytic ileus
- Patients with known hypersensitivity to fentanyl or components of the TIRF medicine

Please see the Prescribing Information for each individual TIRF medicine for a complete list of contraindications.

Check Your Knowledge - Scenario 2

The patients described are experiencing breakthrough pain. A TIRF medicine is NOT appropriate for some of them. Which patients should not receive a TIRF medicine?

Select any that apply:

A. Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.
B. 12-year-old sarcoma patient whose underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.
C. Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.
D. Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.
E. Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

See answer on page 17

Accidental Ingestion or Exposure

- **TIRF medicines contain fentanyl, which can put patients at risk for overdose and death, especially in the following circumstances**:
    - Patients who are not opioid tolerant
    - Children who are accidentally exposed
    - Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers)
    - Concomitant use with benzodiazepines or other CNS depressants, including alcohol
- Inform patients that TIRF medicines have a rapid onset of action.
- **Instruct patients to store their TIRF medicines in a safe and secure place, out of the sight and out of reach of all others, especially children.**
- Accidental or deliberate ingestion of a TIRF medicine by a child may cause severe, possibly even fatal, respiratory depression. Advise patients to seek immediate medical attention if a child is exposed to a TIRF medicine. Immediately give the child naloxone if naloxone is available.
- Prescribers must specifically question patients or their caregivers about the presence of children in the home (on a full-time or visiting basis) and counsel them regarding the dangers to children from accidental exposure.
- Talk with your patients about safe and appropriate storage and disposal of TIRF medicines.

Check Your Knowledge - Scenario 3

There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate?

Select one option.

A. TIRF medicines can be fatal if taken by children.
B. TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.
C. TIRF medicines can be fatal if taken by anyone who is not opioid tolerant.
D. All of the above.

See answer on page 17

Dosage and Administration

- The risk of life-threatening or fatal respiratory depression is greatest during the initiation of therapy or following a dosage increase.

- **A TIRF medicine MUST be initiated at the lowest dose available for that specific product, even if the patient is currently or has taken another TIRF medicine in the past. Titration, if needed, starts at the lowest dose available for that specific product.** Carefully review the initial dosing instructions in each product's specific Prescribing Information.

- **Appropriate Conversion Rules:**

    - TIRF medicines are **not interchangeable**, regardless of route of administration. Significant differences exist in the pharmacokinetic profiles of fentanyl products that result in clinically important differences in the extent of absorption of fentanyl that could result in a fatal overdose.

    - TIRF medicines are **not equivalent** on a microgram-per-microgram basis to any other fentanyl product, including another TIRF medicine. The only exception is for substitution of a generic equivalent for a branded TIRF medicine.

    - **Because of these differences, conversion of a TIRF medicine to another TIRF medicine on a microgram-per-microgram basis may result in fatal overdose.**

    - Therefore, converting from one TIRF medicine to a different TIRF medicine **must not be done on a microgram-per-microgram basis**. The new TIRF medicine must be titrated according to the labeled dosing instructions for each new TIRF medicine the patient begins.

        - The only exception is for substitutions between a branded TIRF medicine and its generic **equivalents**.

Check Your Knowledge - Scenario 4

A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed?

Select any correct option:

A. The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.
B. The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.
C. Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.
D. The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.
E. The dose that the prescriber believes is appropriate based on their clinical experience.

See answer on page 17

- **Drug Interactions**
    - Fentanyl is metabolized mainly by the cytochrome P450 (CYP3A4) isoenzyme system; therefore, potential drug interactions may occur when TIRF medicines are administered concurrently with agents that affect CYP3A4 activity.
        - Concomitant use of TIRF medicines with CYP3A4 inhibitors (e.g., certain protease inhibitors, ketoconazole, fluconazole, diltiazem, erythromycin, verapamil) may increase plasma concentrations of fentanyl and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression.
            - Patients receiving TIRF medicines who begin therapy with or increase the dose of CYP3A4 inhibitors must be carefully monitored for signs of opioid toxicity over an extended period. Dosage increases should be done conservatively.
        - Concomitant use of TIRF medicines with CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin), can decrease the plasma concentration of fentanyl, resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to fentanyl.

- If concomitant use with a CYP3A4 inducer is necessary, consider increasing the dose of the TIRF medicine until stable drug effects are achieved. Monitor for signs of opioid withdrawal. If a CYP3A4 inducer is discontinued, consider reducing the dose of the TIRF medicine and monitor for signs of respiratory depression.

Note: This list does not include a complete list of drug interactions with TIRF medications. Check each drug's PI for a complete list.

Maintenance/Dose Adjustments for all TIRF Medicines

- Once a dose that provides adequate analgesia and minimizes adverse reactions is found, that dose should be prescribed for each subsequent episode of breakthrough cancer pain (BTCP).
- Patients must wait at least 2 or 4 hours before treating another episode of breakthrough pain with their TIRF medicine. Please refer to the specific TIRF medicine's Prescribing Information to determine the appropriate dosing interval.
- Limit the use of TIRF medicines to no more than 4 doses per day.
- If the prescribed dose no longer adequately manages the BTCP for several consecutive episodes, increase the dose as described in the titration section of the Prescribing Information.
- Consider re-evaluating the dose of the around-the-clock opioid medicine used for persistent cancer pain in patients experiencing more than 4 BTCP episodes per day.

REPORTING ADVERSE EVENTS

Serious adverse events and adverse events of special interest, including misuse, abuse, addiction, overdose, death or accidental exposure associated with a TIRF medicine, can be reported online at **www.TIRFREMSaccess.com** by use of the:

- **Patient Status and Opioid Tolerance Form**, or
- **Events of Special Interest Reporting Form**

Adverse events may also be reported by contacting the TIRF REMS at **1-866-822-1483**.

Products* Covered Under this Program:

Product	Dosage and Administration			
	Initial dose	Maximum Dose Per Episode	Frequency	Titration
Actiq® (fentanyl citrate) oral transmucosal lozenge	Always 200 mcg.	If the breakthrough pain episode is not relieved after 30 minutes, patients may take one (1) additional dose using the same strength. Patients should not take more than two (2) doses of ACTIQ per breakthrough pain episode.	Patients must wait at least Four (4) hours before treating another breakthrough pain episode with ACTIQ.	Closely follow patients and change the dosage level until adequate analgesia with tolerable side effects is achieved with angle unit.
FENTORA® (fentanyl buccal tablet)	Always 100 mcg (unless the patient is being converted from ≥600 mcg ACTIQ - please see Prescribing Information)	If the breakthrough pain episode is not relieved after 30 minutes, patients may take one (1) additional dose using the same strength. Patients should not take more than two (2) doses of FENTORA per breakthrough pain episode. Patients must wait at least four (4) hours before treating another breakthrough pain episode with FENTORA.	For patients being converted from ACTIQ, prescribers must use the Initial Dosing Recommendations for Patients on ACTIQ found in Table 1 of the Prescribing Information. The doses of FENTORA in the table are starting doses and not intended to represent equip-analgesic doses to ACTIQ.	Closely follow patients and change the dosage level until adequate analgesia is achieved with a single tablet. During titration, patients can be instructed to use multiple tablets (one on each side of the mouth in the upper/lower buccal cavity) until a maintenance dose is achieved.

Product	Dosage and Administration			
	Initial dose	Maximum Dose Per Episode	Frequency	Titration
Lazanda® (fentanyl) nasal spray	Always 100 mcg	Only use LAZANDA once (1 time) per cancer breakthrough pain episode; i.e., do not re-dose LAZANDA within an episode. Patients must wait at least two (2) hours before treating another episode of breakthrough pain with LAZANDA.	Limit LAZANDA use to four (4) or fewer doses per day.	If adequate analgesia was not obtained with the first 100 mcg dose, continue dose escalation in a stepwise manner over consecutive breakthrough pain episodes until adequate analgesia with tolerable side effects is achieved. Patients should confirm the dose of LAZANDA that works for them with a second episode of breakthrough pain.
Subsys® (fentanyl sublingual spray)	Always 100 mcg (unless the patient is being converted from >600 mcg ACTIQ – please see Prescribing Information.	If the breakthrough pain episode is not relieved after 30 minutes, patients may take one (1) additional dose using the same strength. Patients should not take more than 2 doses of SUBSYS per episode of breakthrough pain.	Patients must wait at least four (4) hours before treating another episode of breakthrough pain with SUBSYS.	Closely follow patients and change the dosage level until adequate analgesia is achieved using a single dose per episode of breakthrough cancer pain.

Note: This table is also available to print for use as a quick reference guide. Please visit www.TIRFREMSaccess.com for further information and resources.

* This includes approved generic equivalents of these products.

For more information about TIRF medicines, see the Prescribing Information, including the BOXED WARNING, for each product.

Resources for More Information

If you have any questions and/or need additional information or copies of any TIRF REMS documents, please visit the program website at www.TIRFREMSaccess.com or call the TIRF REMS at 1-866-822-1483.

ANSWER KEY

Scenarios: Answers and Rationales

Scenario 1: Patient Counseling on use of ATC Opioids

Item A, B, and D Response. This statement is correct.

Item C Response: This statement is incorrect. Patients should be instructed that, if they stop taking their around-the-clock opioid medicine, they must discontinue taking their TIRF medicine.

Item E Response: This statement is incorrect. Individual TIRF medicines have different and product-specific number of times they may be repeated per BTCP occurrence. Patients should be counseled that: they must never use more doses of their TIRF medicine than directed per instance of BTCP occurrence due to the toxicity of fentanyl; and, when their breakthrough pain is not controlled by their TIRF medicine, they should call their prescriber for evaluation.

Scenario 2: Patient Selection/Opioid Tolerance:

Item A, D, and E Response: This patient is appropriate for treatment with a TIRF medicine.

Item B Response: This patient is not appropriate for treatment with a TIRF medicine. TIRF medicines are indicated for use in treatment of BTCP in patients who are 18 years of age or older (or 16 years of age and older in the case of ACTIQ use.)

Item C Response: This patient is not appropriate for treatment with a TIRF medicine. This patient does not meet the definition of “opioid-tolerant” which in the case of oral morphine use as her opioid background regimen would require daily use for at least one previous week of 60 mg or more of morphine.

Scenario 3: Accidental Ingestion or Exposure

Item D: Correct, TIRF medicines can be fatal if taken by children, by anyone for whom it is not prescribed, or by anyone who is opioid non-tolerant.

Items A, B, C: This answer is correct however Answer D most accurate. TIRF medicines can be fatal if taken by children, by anyone for whom it is not prescribed, or by anyone who is opioid non-tolerant.

Scenario 4: Dosage and Administration General

Item B and D Response: Correct. Conversions must not occur on a microgram-for-microgram basis due to the difference in the absorption and bioavailability profiles of the different TIRF products.

Item A or C or E Response: Incorrect. The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose, a simple ½ reduction of the microgram dosage or estimates based on prior clinical experience. Because TIRF medicines have different absorption and bioavailability profiles, conversion to an alternate TIRF product must be done at the newly prescribed TIRF medicine’s lowest available dose. Conversions must be based on individual product provided product-specific guidance obtained from the Prescribing Information.

Prescriber Knowledge Assessment

TIRF REMS

Instructions

To submit this form via fax, please fill in the prescriber information below, answer all questions below, and fax all pages to 1-866-822-1487. You will receive enrollment confirmation via email or fax.

For real-time processing of this Knowledge Assessment, please go to www.TIRFREMSaccess.com.

1 Prescriber Information (PLEASE TYPE OR PRINT)

First Name	Middle Initial	Last Name

Individual NPI #

Address	City	State	Zip

Phone	Ext.	Fax	Email Address
( )		( )	

2 Knowledge Assessment

Question 1

The patients described are all experiencing breakthrough cancer pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine?

Select one option

A. 12-year-old sarcoma patient, using transdermal fentanyl for her underlying persistent cancer pain.
B. Adult female with advanced breast cancer; on 60 mg of oral morphine daily for the past 4 weeks.
C. Adult male with advanced lung cancer, his underlying persistent pain is managed with 25 mcg/hour transdermal fentanyl patches for the past 3 months.
D. Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.

Question 2

The patients described are experiencing breakthrough cancer pain. A TIRF medicine is NOT appropriate for one of them. Which patient should not receive a TIRF medicine?

Select one option.

A. Adult male with advanced lung cancer; underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.
B. Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.
C. Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.
D. Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

Continued on next page

Question 3

Certain factors may increase the risk of abuse and/or diversion of opioid medications. Which of the following is most accurate?

Select one option.

A. A history of alcohol abuse with the patient or close family members.
B. The patient has a household member with a street drug abuse problem.
C. The patient has a history of prescription drug misuse.
D. All of the above.

Question 4

A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed?

Select one option.

A. The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.
B. The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.
C. Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.
D. The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.

Question 5

A patient is starting titration with a TIRF medicine. What dose must they start with?

Select one option.

A. An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
B. The dose that the prescriber believes is appropriate based on their clinical experience.
C. The lowest available dose, unless individual product Prescribing Information provides product-specific guidance.
D. The median available dose.

Question 6

A prescriber has started titrating a patient with the lowest dose of a TIRF medicine. However, after 30 minutes, the breakthrough cancer pain has not been sufficiently relieved. What should they advise the patient to do?

Select one option.

A. Take another (identical) dose of the TIRF medicine immediately.
B. Take a dose of an alternative rescue medicine.
C. Provide guidance based on the product-specific Prescribing Information because the instructions are not the same for all TIRF medicines.
D. Double the dose and take immediately.

Continued on next page

Question 7

A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Which of the following statements is TRUE?

Select one option.

A. The patient can't be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.
B. Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment of the TIRF medicine; carefully monitor the patient for opioid toxicity, otherwise such use may cause serious life threatening, and/or fatal respiratory depression.
C. There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.
D. The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.

Question 8

Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide and Patient Counseling Guide with the patient. Which of the following counseling statements is FALSE?

Select one option.

A. TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
B. Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
C. Instruct patients that, if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.
D. Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.

Question 9

There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate?

Select one option.

A. TIRF medicines can be fatal if taken by children.
B. TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.
C. TIRF medicines can be fatal if taken by anyone who is not opioid-tolerant.
D. All of the above.

Question 10

Which one of the following statements is most accurate regarding the safe storage and disposal of TIRF medicines?

Select one option.

A. TIRF medicines should be kept in in a safe and secure place, out of sight and out of reach of all others, especially children.
B. TIRF medicines should be protected from theft.
C. Dispose of partially used or unneeded TIRF medicine by following the TIRF medicine-specific procedure specified in the Medication Guide.
D. All of the above.

Continued on next page

Question 11:

Which of the following statements is FALSE?

Select one option.

The TIRF REMS mitigates the risk of overdose by:

A. Educating prescribers, pharmacist and patients that respiratory depression is more common in patients who are not opioid tolerant.
B. Requiring that patients remain opioid-tolerant throughout their treatment with TIRF medicines.
C. Requiring inpatient pharmacies to verify opioid tolerance in inpatients who require TIRF medicine while hospitalized.
D. Requiring documentation of opioid tolerance with only the initial prescription of a TIRF medicine

Required for all prescribers	**Prescriber Signature** **X**	**Date:** / /

Prescriber Knowledge Assessment Key

Question #	Answer
1	A
2	B
3	D
4	B
5	C
6	C
7	B
8	C
9	D
10	D
11	D

Patient Counseling Guide

TIRF REMS

What You need to Know about Your TIRF Medicine

Read and keep this guide and the Medication Guide that was given to you by your pharmacy with your medicine.

Go over this information with your healthcare provider and ask about anything you do not understand.

What are TIRF Medicines?

- A transmucosal immediate-release fentanyl (TIRF) medicine is a prescription medicine that contains fentanyl, a very strong opioid pain reliever.
- TIRF medicines are used to manage breakthrough cancer pain in patients who are already routinely taking another opioid pain medicine around-the-clock, for at least one week or longer.
- TIRF medicines are started only after you have been taking other opioid pain medicines and your body has become use to them (meaning you are opioid tolerant).
- You must stop taking your TIRF medicine if you stop taking your around-the-clock opioid pain medicine.

What are the serious risks of using TIRF Medicines?

- Too much TIRF medicine in your body can cause your breathing to stop—which could lead to death.
- Accidental use of a TIRF medicine by a child, or anyone else can cause death.
- Avoid accidental exposure by storing your TIRF medicine in a place where it cannot be reached by children, and where it cannot be stolen by other family members or visitors to your home. Use a lockbox or locking medication bag to keep your TIRF medicine safe and secure.
- TIRF medicines, like other opioids, have serious risks of misuse, abuse and addiction that can lead to death.
- These serious risks can occur even when you use your TIRF medicine as recommended.

The risk of life-threatening breathing problems is greatest:

- if you are not opioid-tolerant
- when you start your TIRF medicine,
- when the dose is increased or
- when changing TIRF medicines

The risk is also greater for people taking other medicines that make them feel sleepy or people with sleep apnea.

How can I take a TIRF Medicine Safely?

- Take your TIRF medicine exactly as your healthcare provider has directed.
- Call your healthcare provider if the TIRF medicine is not controlling your breakthrough cancer pain. Do not increase the dose on your own or take the TIRF medicine more frequently than was directed.

Unless prescribed by your healthcare provider, do not take any of the following with a TIRF medicine. The combination can cause severe drowsiness, confusion, breathing problems, coma and death.

- Alcohol, including any prescription or over-the-counter medicines containing alcohol
- Benzodiazepines, tranquilizers, and anti-anxiety medicines (like Valium or Xanax)
- Muscle relaxants (like Soma or Flexeril)
- Sleep medicines (like Ambien or Lunesta)

Patient Counseling Guide

TIRF REMS

- Do not switch from your TIRF medicine to another medicine containing fentanyl without talking to your healthcare provider first.
- It is against the law to share your TIRF medicine or give it to anyone else even if they have the same symptoms.
- If you become aware that a child or anyone else takes your TIRF medicine, get emergency medical help immediately. These are medical emergencies that can cause death. A dose that is okay for you could cause an overdose and death in someone else.

How can I dispose of my TIRF Medicine safely?

- When you no longer need your TIRF medicine, dispose of it properly and as quickly as possible.
- NEVER dispose of an unused TIRF medicine in an open trash bin where children, family or pets may accidentally come into contact with the TIRF medicine. Accidental exposure to a TIRF medicine by anyone who is not opioid tolerant is a medical emergency.

The Medication Guide received from your pharmacy with your TIRF medicine, tells the proper way to dispose of the unused portion of your TIRF medicine. Follow the disposal instructions provided in the Medication Guide exactly.

What is Naloxone and When should I use it?

- Naloxone is a medicine that helps reverse an opioid overdose. It is sprayed inside your nose or injected into your body. Some naloxone products are designed for people to use in their home.
- If either of the following occurs, immediately use naloxone:
  - You or someone else has taken an opioid medicine, including a TIRF medicine, and is having trouble breathing, is short of breath, or is unusually sleepy
- A child has accidentally taken an opioid medicine, including a TIRF medicine, or you think they might have.
- Giving naloxone to a person, even a child, who has not taken an opioid medicine will not hurt them.
- Naloxone is never a substitute for emergency medical care. Always call 911 and go to the emergency room if the patient or someone else has used or been given naloxone. This is because they may have had an opioid overdose.
- Ask your healthcare provider how you can get naloxone. Naloxone is available in pharmacies, and in some states, you may not need a prescription.
- Keep naloxone in a place where you, your family, or friends can quickly get to it in an emergency.

Patient Counseling Guide

TIRF REMS

What should I know about the specific TIRF Medicine I am taking?

- Read the Medication Guide that comes with your TIRF medicine prescription for specific information about your medicine.
- You or your healthcare provider can write notes below about things you should know about your TIRF medicine. (This might include dosing instructions, other medicines that you should avoid when taking your specific TIRF medicine, or anything else that you or your healthcare provider want to write down.)

NOTES:

_____
_____
_____
_____
_____
_____

What if I have more questions?

- Talk to your healthcare provider or pharmacist and ask them any questions you may have.
- Visit www.fda.gov/opioids for more information about opioid medicines.

For information about the TIRF REMS call 1-866-822-1453 or visit www.TIRFREMSAccess.com

TIRF REMS

Transmucosal Immediate-Release Fentanyl (TIRF) REMS

Pharmacy Education

This education program includes information about:

- **The TIRF REMS requirements**
- **Serious risks of:**
  - **life-threatening and/or fatal respiratory depression**
  - **increased risk of overdose, especially in children, due to accidental ingestion or exposure**
- **Patient Counseling**

Reference ID: 4721749

The purpose of this educational material is to inform pharmacies about the **Risk Evaluation and Mitigation Strategy (REMS)** for transmucosal immediate-release fentanyl (TIRF) medicines. This education provides important safety issues and messages about the TIRF REMS required to dispense and counsel patients about the safe use of these products.

What is the TIRF REMS (Risk Evaluation and Mitigation Strategy)?

The TIRF REMS is a safety program to manage the risk of life-threatening and/or fatal respiratory depression and increased risk of overdose, especially in children, due to accidental ingestion or exposure.

The TIRF REMS is required by the U. S. Food and Drug Administration (FDA) to help ensure that the benefits of treatment with transmucosal immediate-release fentanyl-containing products outweigh the known risks of these products.

Products Covered Under This Program:

- **Actiq®** (fentanyl citrate) oral transmucosal lozenge
- **Fentora®** (fentanyl buccal tablet)
- **Lazanda®** (fentanyl) nasal spray
- **Onsolis®** (fentanyl buccal soluble film)
- **Subsys®** (fentanyl sublingual spray)
- Approved generic equivalents of these products

How Does the TIRF REMS Work for Pharmacies?

The TIRF REMS requires prescribers, pharmacies, patients, and wholesaler-distributors to enroll in the program in order to utilize TIRF medications.

- The outpatient pharmacy must establish policies and procedures to assess the patient's medication use for a change in opioid tolerance. This could include reviewing data from various sources (e.g. - available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.) The pharmacist will document and submit results to the REMS for any discrepancies.
- The outpatient pharmacy is required to obtain authorization to dispense each prescription online or by contacting the TIRF REMS Call Center at **1-866-822-1453** to verify that the prescriber and the patient are enrolled, and the patient is opioid tolerant.
- Enrolled wholesaler-distributors will verify the current enrollment status of the pharmacy prior to shipment of TIRF medicines.
- Inpatient hospital pharmacies are required to develop policies and procedures to verify the patient's opioid tolerance prior to dispensing. This could include reviewing data from various sources (e.g. - available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.)

What Actions Must Be Taken in an Outpatient Pharmacy to Comply with the TIRF REMS?

- Pharmacies must be enrolled in the program to be able to dispense TIRF medicines

Steps for Pharmacy Enrollment in the TIRF REMS

1. Designate an authorized representative to carry out the enrollment process and oversee the implementation and compliance with the TIRF REMS on behalf of the pharmacy.
2. Complete the Training Program:
   - review the **Pharmacy Education**
3. Successfully complete the **Pharmacy Knowledge Assessment**; and
4. Complete and submit a signed **Outpatient Pharmacy Enrollment Form**
5. Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS.

The enrollment process may be completed online at **www.TIRFREMSaccess.com**

Or

Materials and forms can be downloaded from the website on the Pharmacy tab, then completed, and faxed to the program at **1-866-822-1487**.

Requirements for Dispensing TIRFs

- Pharmacies must establish policies and procedures to assess **the patient's opioid tolerance** prior to dispensing. This could include reviewing data from available various sources (e.g. state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.)
  - Data found during this review must be compared against the opioid tolerance verification data provided by the prescriber. This can be done online while obtaining a REMS Dispense Authorization or by calling the TIRF REMS Call Center at **1-866-822-1453**.
  - Contact the prescriber if there is a discrepancy in data or if the data indicates that the patient is not opioid tolerant.
- For each outpatient prescription, obtain a REMS Dispense Authorization number from the TIRF REMS prior to dispensing each TIRF medicine prescription. This verifies that the patient, prescriber, and pharmacy are enrolled, and the prescriber has confirmed that the patient is opioid tolerant.
  - A REMS Dispense Authorization can be obtained online or by calling the TIRF REMS Call Center at **1-866-822-1453**.

To obtain a REMS Dispense Authorization online at **www.TIRFREMSaccess.com**:

1. Log in to the TIRF REMS website
2. Select the Obtain a Patient RDA option
3. Enter the patient's name and date of birth; the patient's phone or email address, the prescriber's name and NPI number; and the NDC code and the number of days' supply being dispensed
4. Select the Obtain RDA button

If any requirements are not satisfied when obtaining an RDA, the system will generate a rejection and the prescription must not be dispensed.

- Provide a Medication Guide with every refill of a TIRF medicine and discuss the risks and side effects associated with fentanyl-containing products, including what to do if patients experience side effects.

Other TIRF REMS Requirements

- Pharmacies must obtain TIRF medicine product stock only from an enrolled wholesaler-distributor.
- If the pharmacy's authorized representative changes, the new authorized representative must enroll in the TIRF REMS by reviewing the **Pharmacy Education**, successfully completing the **Pharmacy Knowledge Assessment** and the **Outpatient Pharmacy Enrollment Form** and submitting both to the TIRF REMS.
- Outpatient pharmacies must comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed. Outpatient pharmacies must maintain records of staff training and records of opioid tolerance verification data for each dispensing including moiety, formulation, strength, route, dose, and frequency of around-the-clock opioids for the patient. These records must be available for audits.

What Actions Must be Taken in an Inpatient Pharmacy to Comply with the TIRF REMS?

- Pharmacies must be enrolled in the program to be able to dispense TIRF medicines

Steps for Pharmacy Enrollment in the TIRF REMS

1. Designate an authorized representative to carry out the enrollment process and oversee the implementation and compliance with the TIRF REMS on behalf of the pharmacy.
2. Complete the Training Program:
   - review the **Pharmacy Education**
3. Successfully complete the **Knowledge Assessment**; and
4. Complete and submit a signed **Inpatient Pharmacy Enrollment Form**

5. Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS using the Pharmacy Education.

The enrollment process may be completed online at **www.TIRFREMSaccess.com**

Or

Materials and forms can be downloaded from the website on the Resources tab, then completed, and faxed to the program at **1-866-822-1487**.

- Pharmacies must obtain TIRF medicine product stock only from an enrolled distributor.
- Inpatient pharmacies are required to develop policies and procedures to verify the patient's opioid tolerance in patients who require TIRF medicines while hospitalized prior to dispensing. This could include reviewing data from various sources (e.g. - available state Prescription Drug Monitoring Programs (PDMPs) the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.) Inpatient pharmacies do not need to obtain a REMS Dispense Authorization to dispense a TIRF medicine within the inpatient setting.
- If the pharmacy's authorized representative changes, the new authorized representative must enroll in the TIRF REMS by reviewing the **Pharmacy Education**, successfully completing the **Pharmacy Knowledge Assessment** and the **Inpatient Pharmacy Enrollment Form** and submitting both to the TIRF REMS.
- Inpatient pharmacies must comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed. Inpatient pharmacies must maintain records of staff training. These records must be available for audits.

KEY SAFETY INFORMATION

Risk of Life-threatening Respiratory Depression

Serious, life threatening, or fatal respiratory depression has been reported with the use of opioids even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death.

Indication:

TIRF medicines are indicated only for the management of breakthrough cancer pain (BTCP) in cancer patients 18 years of age or older **who are already receiving and who are tolerant to, around-the-clock opioid therapy for underlying persistent cancer pain**.

- The only exception is for ACTIQ, and its generic equivalents, which are approved for cancer patients **16** years of age or older.

Patients Must be Opioid Tolerant to be Prescribed a TIRF Medicine

Definition of Opioid Tolerance:

Patients are considered **opioid tolerant** if they are currently taking (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and have been on the regimen(s) **for one week or longer**:

- ≥ 60 mg oral morphine/day
- ≥ 25 mcg transdermal fentanyl/hour
- ≥ 30 mg oral oxycodone/day
- ≥ 8 mg oral hydromorphone/day
- ≥ 25 mg oral oxymorphone/day
- ≥ 60 mg oral hydrocodone/day
- an equianalgesic dose of another opioid

- Patients must remain opioid tolerant to continue using a TIRF medicine.
- TIRF medicines are intended for use only by opioid-tolerant patients with cancer. They should only be prescribed by healthcare professionals who are knowledgeable of and skilled in the use of Schedule II opioids for the treatment of breakthrough cancer pain.

Check Your Knowledge - Scenario 1

The patients described are experiencing breakthrough pain. A TIRF medicine is NOT appropriate for some of them. Which patients should NOT receive a TIRF medicine?

Select any that apply:

A. Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.

B. 12-year-old sarcoma patient whose underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.

C. Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.

D. Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.

E. Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

See answer on page 18

Contraindications

TIRF medicines are contraindicated in:

- Patients who are not opioid tolerant. **Life-threatening respiratory depression could occur at any dose in patients who are not opioid tolerant, and deaths have occurred**.
- The management of acute or postoperative pain, including:
  - headache/migraine;
  - dental pain; or
  - acute pain in the emergency department
- Patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
- Patients with known or suspected gastrointestinal obstruction, including paralytic ileus
- Patients with known hypersensitivity to fentanyl or components of the TIRF medicine

Please see the Prescribing Information for each individual TIRF medicine for a complete list of contraindications.

Accidental Ingestion or Exposure

- **TIRF medicines contain fentanyl, which can put patients at risk for overdose and death, especially in the following circumstances**:
  - Patients who are not opioid tolerant
  - Children who are accidentally exposed
  - Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers)
  - Concomitant use with benzodiazepines or other CNS depressants, including alcohol
- TIRF medicines have a rapid onset of action.
- **Instruct patients to store their TIRF medicines in a safe and secure place, out of the sight and out of reach of all others, especially children.**
- **Accidental or deliberate ingestion of a TIRF medicine by a child may cause severe, possibly even fatal, respiratory depression. Advise patients to seek immediate medical attention if a child is exposed to a TIRF medicine.**

- Prescribers must specifically question patients or their caregivers about the presence of children in the home (on a full-time or visiting basis) and counsel them regarding the dangers to children from accidental exposure.

- Talk with your patients about safe and appropriate storage and disposal of TIRF medicines.

Check Your Knowledge - Scenario 2

There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate?

Select one option.

A. TIRF medicines can be fatal if taken by children.
B. TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.
C. TIRF medicines can be fatal if taken by anyone who is not opioid tolerant.
D. All of the above.

See answer on page 18

Dosage and Administration

- The risk of life-threatening or fatal respiratory depression is greatest during the initiation of therapy or following a dosage increase.

- **A TIRF medicine MUST be initiated at the lowest dose available for that specific product, even if the patient is currently taking a TIRF medicine or has taken another TIRF medicine in the past. Titration, if needed, starts at the lowest dose available for that specific product.** Carefully review the initial dosing instructions in each product's specific Prescribing Information.

- **Appropriate Conversion Rules:**

    - TIRF medicines are **not interchangeable**, regardless of route of administration. Significant differences exist in the pharmacokinetic profiles of fentanyl products that result in clinically important differences in the extent of absorption of fentanyl that could result in a fatal overdose.

    - TIRF medicines are **not equivalent** on a microgram-per-microgram basis to any other fentanyl product, including another TIRF medicine. The only exception is for substitution of a generic equivalent for a branded TIRF medicine.

    - **Because of these differences, conversion of a TIRF medicine to another TIRF medicine on a microgram-per-microgram basis may result in fatal overdose.**

    - Therefore, converting from one TIRF medicine to a different TIRF medicine **must not be done on a microgram-per-microgram basis**. The new TIRF medicine must be titrated according to the labeled dosing instructions for each new TIRF medicine the patient begins.

    - The only exception is for substitutions between a branded TIRF medicine and its generic **equivalents**.

Check Your Knowledge - Scenario 3

A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed?

Select any correct option:

A. The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.
B. The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.
C. Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.
D. The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.
E. The dose that the prescriber believes is appropriate based on their clinical experience.

See answer on page 18

Drug Interactions

- Fentanyl is metabolized mainly by the cytochrome P450 (CYP3A4) isoenzyme system; therefore, potential drug interactions may occur when TIRF medicines are administered concurrently with agents that affect CYP3A4 activity.
  - Concomitant use of TIRF medicines with CYP3A4 inhibitors (e.g., certain protease inhibitors, ketoconazole, fluconazole, diltiazem, erythromycin, verapamil) may increase plasma concentrations of fentanyl and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression.
    - Patients receiving TIRF medicines who begin therapy with or increase the dose of CYP3A4 inhibitors must be carefully monitored for signs of opioid toxicity over an extended period. Dosage increases should be done conservatively.
  - Concomitant use of TIRF medicines with CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin) can decrease the plasma concentration of fentanyl, resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to fentanyl.
    - If concomitant use with a CYP3A4 inducer is necessary, consider increasing the dose of the TIRF medicine until stable drug effects are achieved. Monitor for signs of opioid withdrawal. If a CYP3A4 inducer is discontinued, consider reducing the dose of the TIRF medicine and monitor for signs of respiratory depression.

Note: This list does not include a complete list of drug interactions with TIRF medications. Check each drug's Prescribing Information for a complete list.

Maintenance/Dose Adjustments for all TIRF Medicines

- Once a dose that provides adequate analgesia and minimizes adverse reactions is found, that dose should be prescribed for each subsequent episode of breakthrough cancer pain (BTCP).
- Patients must wait at least 2 or 4 hours before treating another episode of breakthrough pain with their TIRF medicine. Please refer to the specific TIRF medicine's Prescribing Information to determine the appropriate dosing interval.
- Limit the use of TIRF medicines to no more than 4 doses per day.
- If the prescribed dose no longer adequately manages the BTCP for several consecutive episodes, increase the dose as described in the titration section of the Prescribing Information.
- Consider increasing the dose of the around-the-clock opioid medicine used for persistent cancer pain in patients experiencing more than 4 BTCP episodes per day.

Naloxone

- Prescribers should consider prescribing naloxone for the emergency treatment of opioid overdose.
- If concomitant use with benzodiazepines, other CNS depressants, or muscle relaxants is warranted, prescribers should consider prescribing naloxone for the emergency treatment of opioid overdose.
- Educate patients and caregivers on how to recognize respiratory depression and emphasize the importance of calling 911 or getting emergency medical help right away in the event of a known or suspected overdose. *(See patient counseling section below).*
- Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver both when initiating and renewing treatment with TIRF products.
- Inform patients about the various ways to obtain naloxone.

Counsel Patients Concerning Risks of TIRF Medicines

- Tell patients exactly how to take the TIRF medicine. Instruct them to take the TIRF medicine strictly as prescribed, with special regard to dosage, dose titration, administration and proper disposal of partially used or unneeded TIRF medicine.
- Remind patients they **must be** opioid tolerant to be able to take a TIRF medicine for their breakthrough cancer pain. Opioid tolerant means that the patient is

already using around-the-clock daily opioid pain medicine for constant pain for 1 week or longer.

- If the patient stops taking around-the-clock opioid pain medicine for their constant pain, the patient **must stop taking their TIRF medicine because they may no longer be opioid tolerant**.
    - **Note:** Patients have had difficulty understanding this concept. Emphasize this requirement to your patients and explain that the risk of life-threatening and/or fatal breathing problems with their TIRF medicine increases if they are not taking around-the-clock opioid pain medicines.
- TIRF medicines can cause serious side effects, including life-threatening breathing problems that can lead to death. The patient must take the TIRF medicine exactly as prescribed.
- Instruct patients to store their TIRF medicines in a safe and secure place, out of the sight and reach of all others, especially children. Accidental or deliberate ingestion of a TIRF medicine by a child may cause severe, possibly even fatal, respiratory depression. Advise patients to seek immediate medical attention if a child is exposed to a TIRF medicine.
- Talk with patients about Naloxone.
    - Naloxone is a medicine that helps reverse opioid overdose. It is sprayed inside the nose or injected into the body. Some naloxone products are designed for people to use in their home.
    - The patient should immediately use naloxone if they have it and call 911 and wait for emergency medical services if:
        - The patient or someone else has taken an opioid medicine, including a TIRF medicine, and is having trouble breathing, is short of breath, or is unusually sleepy.
        - A child has accidentally taken an opioid medicine, including a TIRF medicine, or if it is suspected that they might have.
    - Giving naloxone to a person, even a child, who has not taken an opioid medicine will not hurt them.
    - Naloxone is never a substitute for emergency medical care. Always call 911 and go to the emergency room if the patient or someone else has used or been given naloxone.
    - Ask your healthcare provider how you can get naloxone. Naloxone is available in pharmacies, and in some states, you may not need a prescription.
    - Keep naloxone in a place where the patient, the patient's family or friends can get to it in an emergency.
- Talk with patients about safe and appropriate disposal of TIRF medicines.

- Inform patients that TIRF medicines have a rapid onset of action.
- Pharmacists and prescribers must specifically question patients or their caregivers about the presence of children in the home (on a full-time or visiting basis) and counsel them regarding the dangers to children from inadvertent exposure.
- Refer patients to their prescribing healthcare provider if they have additional questions about their regimen(s) or dosing.
- Inform patients that TIRF medicines have significant risks for drug-drug interactions:
    - Fentanyl is metabolized mainly by the cytochrome P450 (CYP3A4) isoenzyme system; therefore, potential drug interactions may occur when TIRF medicines are administered concurrently with agents that affect CYP3A4 activity. Concurrent use of TIRF medicines with CYP3A4 inhibitors such as certain protease inhibitors, ketoconazole, fluconazole, diltiazem, erythromycin, verapamil may increase plasma concentrations of fentanyl and prolong opioid adverse reactions, which could lead to potentially fatal respiratory depression. Concomitant use of TIRF medicines with CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin) can decrease the plasma concentration of fentanyl, resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to fentanyl.
    - Due to the additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants, including alcohol, increases the risk of respiratory depression, profound sedation, coma, and death. Warn patients that it is extremely dangerous to self-administer non-prescribed benzodiazepines or other CNS depressants including alcohol while taking TIRF medicines. Caution patients who are prescribed benzodiazepines or other CNS depressants to use them only as directed by their prescriber.
    - The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system can induce serotonin syndrome.
    - Monoamine oxidase inhibitors (MAOIs) interactions with opioids may manifest as serotonin syndrome.
    - Mixed agonist/antagonist and partial agonist opioid analgesics may reduce the analgesic effect of TIRF medicines and/or precipitate withdrawal symptoms.
    - Fentanyl may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.

Check Your Knowledge - Scenario 4

Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide with the patient. Which of the following counseling statements are FALSE?

Select any statements which are false.

A. TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
B. Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
C. Instruct patients that, if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.
D. Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.
E. Once a patient becomes familiar with the use of their TIRF medicine, if their BTCP is not controlled they can repeat their dose every 20 minutes until their pain is relieved.

See answer on page 18

REPORTING ADVERSE EVENTS

Serious Adverse events, **including adverse events** of special interest, including the misuse, abuse, addiction, overdose, death or accidental exposure of a TIRF medicine, **should** be reported online at **www.TIRFREMSaccess.com** by use of the:

- **Patient Status and Opioid Tolerance Form**, or
- **Adverse Events of Special Interest Reporting Form**

Adverse events may also be reported by contacting the TIRF REMS at **1-866-822-1483.**

Products* Covered Under this Program:

Product	Dosage and Administration			
	Initial dose	Maximum Dose Per Episode	Frequency	Titration
Actiq® (fentanyl citrate) oral transmucosal lozenge	Always 200 mcg.	If the breakthrough pain episode is not relieved after 30 minutes, patients may take one (1) additional dose using the same strength. Patients should not take more than two (2) doses of ACTIQ per breakthrough pain episode.	Patients must wait at least Four (4) hours before treating another breakthrough pain episode with ACTIQ.	Closely follow patients and change the dosage level until adequate analgesia with tolerable side effects is achieved with angle unit.
FENTORA® (fentanyl buccal tablet)	Always 100 mcg (unless the patient is being converted from ≥600 mcg ACTIQ - please see Prescribing Information)	If the breakthrough pain episode is not relieved after 30 minutes, patients may take one (1) additional dose using the same strength. Patients should not take more than two (2) doses of FENTORA per breakthrough pain episode. Patients must wait at least four (4) hours before treating another breakthrough pain episode with FENTORA.	For patients being converted from ACTIQ, prescribers must use the Initial Dosing Recommendations for Patients on ACTIQ found in Table 1 of the Prescribing Information. The doses of FENTORA in the table are starting doses and not intended to represent equip-analgesic doses to ACTIQ.	Closely follow patients and change the dosage level until adequate analgesia is achieved with a single tablet. During titration, patients can be instructed to use multiple tablets (one on each side of the mouth in the upper/lower buccal cavity) until a maintenance dose is achieved.

Product	Dosage and Administration			
	Initial dose	Maximum Dose Per Episode	Frequency	Titration
Lazanda® (fentanyl) nasal spray	Always 100 mcg	Only use LAZANDA once (1 time) per cancer breakthrough pain episode; i.e., do not re-dose LAZANDA within an episode. Patients must wait at least two (2) hours before treating another episode of breakthrough pain with LAZANDA.	Limit LAZANDA use to four (4) or fewer doses per day.	If adequate analgesia was not obtained with the first 100 mcg dose, continue dose escalation in a stepwise manner over consecutive breakthrough pain episodes until adequate analgesia with tolerable side effects is achieved. Patients should confirm the dose of LAZANDA that works for them with a second episode of breakthrough pain.
Subsys® (fentanyl sublingual spray)	Always 100 mcg (unless the patient is being converted from >600 mcg ACTIQ – please see Prescribing Information.	If the breakthrough pain episode is not relieved after 30 minutes, patients may take one (1) additional dose using the same strength. Patients should not take more than 2 doses of SUBSYS per episode of breakthrough pain.	Patients must wait at least four (4) hours before treating another episode of breakthrough pain with SUBSYS.	Closely follow patients and change the dosage level until adequate analgesia is achieved using a single dose per episode of breakthrough cancer pain.

Note: This table is also available to print for use as a quick reference guide. Please visit www.TIRFREMSaccess.com for further information and resources.

* This includes approved generic equivalents of these products.

For more information about TIRF medicines, see the Prescribing Information, including the BOXED WARNING, for each product.

Resources for More Information

If you have any questions and/or need additional information or copies of any TIRF REMS documents, please visit the program website at www.TIRFREMSaccess.com or call the TIRF REMS at 1-866-822-1483.

ANSWER KEY

Scenarios: Answers and Rationales

Scenario 1: Patient Counseling on use of ATC Opioids

Item A, B, and D Response. This statement is correct.

Item C Response: This statement is incorrect. Patients should be instructed that, if they stop taking their around-the-clock opioid medicine, they must discontinue taking their TIRF medicine.

Item E Response: This statement is incorrect. Individual TIRF medicines have different and product-specific number of times they may be repeated per BTCP occurrence. Patients should be counseled that: they must never use more doses of their TIRF medicine than directed per instance of BTCP occurrence due to the toxicity of fentanyl; and, when their breakthrough pain is not controlled by their TIRF medicine, they should call their prescriber for evaluation.

Scenario 2: Patient Selection/Opioid Tolerance:

Item A, D, and E Response: This patient is appropriate for treatment with a TIRF medicine.

Item B Response: This patient is not appropriate for treatment with a TIRF medicine. TIRF medicines are indicated for use in treatment of BTCP in patients who are 18 years of age or older (or 16 years of age and older in the case of ACTIQ use.)

Item C Response: This patient is not appropriate for treatment with a TIRF medicine. This patient does not meet the definition of “opioid-tolerant” which in the case of oral morphine use as her opioid background regimen would require daily use for at least one previous week of 60 mg or more of morphine.

Scenario 3: Accidental Ingestion or Exposure

Item D: Correct, TIRF medicines can be fatal if taken by children, by anyone for whom it is not prescribed, or by anyone who is opioid non-tolerant.

Items A, B, C: This answer is correct however Answer D most accurate. TIRF medicines can be fatal if taken by children, by anyone for whom it is not prescribed, or by anyone who is opioid non-tolerant.

Scenario 4: Dosage and Administration General

Item B and D Response: Correct. Conversions must not occur on a microgram-for-microgram basis due to the difference in the absorption and bioavailability profiles of the different TIRF products.

Item A or C or E Response: Incorrect. The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose, a simple ½ reduction of the microgram dosage or estimates based on prior clinical experience. Because TIRF medicines have different absorption and bioavailability profiles, conversion to an alternate TIRF product must be done at the newly prescribed TIRF medicine’s lowest available dose. Conversions must be based on individual product provided product-specific guidance obtain from the Prescribing Information.

Pharmacy Knowledge Assessment

TIRF REMS

Instructions

To submit this form via fax, please fill in the authorized representative information, answer all questions, and fax all pages to 1-866-822-1487. You will receive enrollment confirmation via email or fax.

For real-time processing of this Knowledge Assessment, please go to www.TIRFREMSaccess.com.

1 Authorized Representative Information (PLEASE TYPE OR PRINT)

First Name	Last Name	Credentials
		☐ RPh ☐ PharmD ☐ BCPS ☐ Other

Email Address	Phone	Fax	Position/Title
	( )	( )	

2 Knowledge Assessment

Question 1

The patients described are all experiencing breakthrough cancer pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine?

Select one option

A. 12-year-old sarcoma patient, using 25 mcg/hour transdermal fentanyl patches for her underlying persistent cancer pain.
B. Adult female with advanced breast cancer; on 60 mg of oral morphine daily for the past 4 weeks.
C. Adult male with advanced lung cancer, his underlying persistent pain is managed with transdermal fentanyl patches for the past 3 months.
D. Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.
E. Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

Question 2

Pharmacists can assist in prevention of diversion or accidental exposure of TIRF medicines by people for whom they are not prescribed. Which of the following statements is TRUE?

Select one option.

A. Pharmacists should counsel TIRF medicine users to keep their TIRF medicine out of reach of children and pets.
B. Pharmacists should counsel TIRF medicine users to refer to safe disposal guidelines in the TIRF product-specific Medication Guide.
C. Pharmacists should counsel patients not to share their TIRF medicine with anyone else even if their symptoms are the same as it could result in serious life threatening and/or fatal respiratory depression.
D. Remind patients to call their prescriber if they have questions about usage of their TIRF medicine.
E. All of the above.

Continued on next page

Question 3

A patient's prescriber has ordered a new TIRF medicine for the patient. What dose must they start with?

Select one option.

A. An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
B. The dose the prescriber believes is appropriate based on the previous clinical history of TIRF medicine use.
C. The lowest available dose, unless individual product Prescribing Information provides product-specific guidance.
D. The median available dose.
E. The dose the prescriber believes is appropriate based on their clinical experience.

Question 4

Select the following statement which is FALSE.

Select one option.

A. Before dispensing, the pharmacy must check the patient's medication use for a change in opioid tolerance. This could include reviewing data from various sources (e.g. -available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.)
B. When a patient's breakthrough cancer pain is not relieved by their TIRF medicine, he/she may repeat their dose of TIRF medicine every 20 minutes until they achieve pain relief.
C. TIRF medicines are not interchangeable on a microgram-per-microgram basis.
D. The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.

Question 5

Which of the following is not a pharmacy requirement in the TIRF REMS?

Select one option.

A. The authorized representative must train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the TIRF REMS using the Pharmacy Education.
B. The authorized representative must re-enroll in the TIRF REMS by completing the Outpatient Pharmacy Enrollment Form.
C. Before dispensing, the pharmacy must check the patient's medication use for a change in opioid tolerance. This could include reviewing data from various sources (e.g. - available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.)
D. The pharmacy may dispense the first prescription to the patient before the patient is enrolled in the TIRF REMS as long as the patient is enrolled before the next dispensing.

Question 6

A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Which of the following statements is TRUE?

Select one option.

A. The patient cannot be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.
B. Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment of the TIRF medicine; carefully monitor the patient for opioid toxicity, otherwise such use may cause potentially fatal respiratory depression.
C. There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.
D. The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.

Continued on next page

Question 7

Before dispensing a TIRF medicine, pharmacists must provide a patient with the Medication Guide. Which of the following counseling statements is FALSE?

Select one option.

A. TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
B. Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
C. Instruct patients that, if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.
D. Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.

Question 8

There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate?

Select one option.

A. TIRF medicines can be fatal if taken by children.
B. TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.
C. TIRF medicines can be fatal if taken by anyone who is not opioid-tolerant.
D. All of the above.

Question 9

Which of the following statements is FALSE?

Select one option.

A. A REMS Dispense Authorization is required before dispensing TIRF medicines at all outpatient pharmacies.
B. A REMS Dispense Authorization is not required when the patient is paying by cash rather than submitting a traditional pharmacy benefit claim.
C. A REMS Dispense Authorization is not required prior to dispensing TIRF medicines to hospital inpatients.
D. A REMS Dispense Authorization at an outpatient pharmacy confirms that the required opioid tolerance verification is on file with the TIRF REMS prior to dispensing.

Question 10

Which one of the following statements is most accurate regarding the safe storage and disposal of TIRF medicines?

Select one option.

A. TIRF medicines should be stored in a safe and secure place, out of sight and out of reach of all others, especially children.
B. TIRF medicines should be protected from theft.
C. Dispose of partially used or unneeded TIRF medicine by following the TIRF medicine-specific procedure specified in the Medication Guide.
D. All of the above.

Continued on next page

Question 11:

As an authorized representative for my pharmacy, which of the following is <u>not</u> my responsibility?

Select one option.

A. Make sure that my staff and I confirm pharmacy, patient and prescriber enrollment in the TIRF REMS and patient opioid tolerance by obtaining a REMS Dispense Authorization prior to every outpatient dispensing of a TIRF medicine.
B. Enroll and train all sub-stores if my pharmacy acts as a chain headquarters pharmacy in the TIRF REMS.
C. Provide a Patient Status and Opioid Tolerance Form to the TIRF REMS for every prescription prior to dispensing.
D. My pharmacy must not sell, loan or transfer TIRF medicine inventory to any other pharmacy, institution, distributor, or prescriber.

Required	**Pharmacy Authorized Representative Signature** **X**	**Date:** / /

Pharmacy Knowledge Assessment Key

Question #	Answer
1	A
2	E
3	C
4	B
5	D
6	B
7	C
8	D
9	B
10	D
11	C

TIRF REMS

Patient Status and Opioid Tolerance Form

INSTRUCTIONS:

- Patients receiving TIRF medicines for outpatient use must be enrolled in the TIRF REMS prior to receiving their first TIRF prescription.
- This form must be completed by the prescriber and submitted to the TIRF REMS prior to each subsequent prescription for outpatient use.
- All fields with asterisks (*) are required.
- For real time processing, complete this form online at TIRFREMSaccess.com.
- The form may also be faxed to the program at 1-855-474-3062. If faxed, allow one (1) business day for processing.
- **Prescriptions will not be authorized for dispensing until this continuation form is on file at the TIRF REMS.**

1 Patient Information (please type or print)

First Name*	M.I.*	Last Name*	Date of Birth* (MM/DD/YYYY)	Zip Code*

TIRF Product Name*	Strength*	Dose*	Frequency*

2 Concomitant Medications

Check all that apply*:

☐ Benzodiazepines	☐ Barbiturates	☐ Prescription Insomnia Medications
☐ Gabapentinoids	☐ Antipsychotics	☐ Other CNS depressant
☐ Sedative Hypnotics	☐ Sodium Oxybate	☐ None
☐ Tranquilizers	☐ Alcohol	
☐ Muscle Relaxants	☐ Prescription Cannabinoids	

3 Medical Information

Type of Pain*:

- ☐ Cancer pain
- ☐ Non-cancer pain

4 Prescriber Information (please type or print)

First Name*	MI.	Last Name*	Individual NPI #*

Phone*	Extension*	Fax*

Email Address*

Continued on next page

5 Adverse Events of Special Interest

Adverse events that MUST be reported to the TIRF REMS:

- Accidental exposure
- Overdose
- Addiction
- Abuse
- Misuse
- Other serious adverse events

To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine? *

☐ **NO** ➡ Continue to section 6 (Verify Opioid Tolerance)

☐ **YES –** Complete and submit the **Adverse Events of Special Interest Reporting Form.** This form is available via www.TIRFREMSaccess.com or by contacting 1-866-822-1483.

If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.

6 Verify Opioid Tolerance*

Moiety*	Formulation*	Strength*	Route*	Dose*	Frequency*

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply)*:

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

7 Prescriber Signature

Prescriber Signature*:	Date*:

Complete this form online at TIRFREMSaccess.com or fax the completed form to 1-855-474-3062.

Please visit TIRFREMSaccess.com or call 1-866-822-1483 for more information about the TIRF REMS.

TIRF REMS

Adverse Events of Special Interest Reporting Form

INSTRUCTIONS:

- **Adverse events related to accidental exposure, misuse, abuse, addiction, overdose or other serious adverse events must be reported to the TIRF REMS.**
- This form must be completed to report an adverse event of special interest to the TIRF REMS for any patient taking a TIRF medicine.
- For real-time processing, complete this form online at www.TIRFREMSaccess.com by logging on, selecting the patient, and reporting the Adverse Event of Special Interest.
- The form may also be faxed to the program at 1-855-474-3062. If faxed, allow one (1) business day for processing.

*Indicates required field

1 Patient Information (please print)

First Name*	M.I.	Last Name*	Date of Birth* (MM/DD/YYYY)	Zip Code*

TIRF Product Name (if known)	Strength (if known)	Dose (if known)	Frequency (if known)

2 Reporter Information (please print)

First Name*	MI.	Last Name*	Individual NPI # (if applicable)

Phone*	Extension*	Fax*

Email Address*	Best Time to Contact: ☐ Morning ☐ Afternoon ☐ Evening

3 Adverse Events of Special Interest

Adverse events related to accidental exposure, misuse, abuse, addiction, overdose or other serious adverse events must be reported to the TIRF REMS.
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.

Check all that apply below

- ☐ **Experienced an overdose of their TIRF medicine (Overdose** - ingestion of an excessive amount of drug that is considered lethal or toxic, either intentionally or accidentally)
- ☐ **Shown signs or symptoms of addiction to their TIRF medicine (Addiction** – a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance. Signs and symptoms include: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal)
- ☐ **Misused or been suspected of misusing their TIRF medicine (Misuse** - the use of a medicinal product without a prescription or in a manner other than as directed by a physician, including use without a prescription of one's own; use in greater amounts to feel euphoria (i.e. to get high), more often, or for a period longer than prescribed; or use in any other way not directed by the prescribing physician)
- ☐ **Abused or been suspected of abusing their TIRF medicine (Abuse** - intentional non-therapeutic use of a medicinal product, even once, for its rewarding psychological or physiological or euphoric effect, and often associated with physical dependence)
- ☐ **Someone else has been accidentally exposed to the patient's TIRF medicine (Accidental exposure** - unintended exposure of a medicinal product to someone other than to whom it was prescribed)
- ☐ **Another serious adverse event (Serious Adverse Event** – any adverse event at any dose that results in death, is life-threatening, requires inpatient hospitalization, or causes prolongation of existing hospitalization)

4 Reporter Signature

Reporter Signature*:	Date*:

Complete this form online at www.TIRFREMSaccess.com or fax the completed form to 1-855-474-3062.

Please visit TIRFREMSaccess.com or call 1-866-822-1483 for more information about the TIRF REMS.

TIRF REMS

Patient Discontinuation Form

INSTRUCTIONS:

- This form must be completed and submitted to the TIRF REMS by the prescriber when a patient discontinues treatment with TIRF medicines for any reason.
- For real time processing, complete this form online at TIRFREMSaccess.com.
- The form may also be faxed to the program at 1-855-474-3062. If faxed, allow one (1) business day for processing.
- **Adverse events related to accidental exposure, misuse, abuse, addiction, overdose or other serious adverse events must be reported to the TIRF REMS by the Adverse Events of Special Interest Reporting Form.**

*Indicates required field

1 Patient Information (please type or print)

First Name*	M.I.	Last Name*	Date of Birth* (MM/DD/YYYY)	Zip Code*

2 Prescriber Information (please type or print)

First Name*	MI.	Last Name*	Individual NPI #*

Phone*	Extension*	Fax*

Email Address*

3 Discontinuation of a TIRF Medicine

Was the TIRF medicine discontinued? ☐ **YES** ☐ **NO**

Date TIRF medicine was discontinued: _____

Reason for discontinuation (check all that apply):

- ☐ **No longer required to manage pain**
- ☐ **No longer on around-the-clock Opioid**
- ☐ **Death** ➡ **Date:** _____ **Cause of Death:** _____
- ☐ **Adverse event** ➡ Complete Section 4
- ☐ **Other (financial reasons, patient preference, etc.)**

4 Adverse Events of Special Interest

Adverse events related to accidental exposure, misuse, abuse, addiction, overdose or other serious adverse events must be reported to the TIRF REMS.

Has this patient experienced one or more of the following adverse events of special interest associated with the use of their TIRF medicine? *

☐ **NO ➡ Continue to Section 5 Prescriber Signature**

☐ **YES – Check all that apply below** (Adverse Events of Special Interest)

- ☐ **Experienced an overdose of their TIRF medicine** (**Overdose** - ingestion of an excessive amount of drug that is considered lethal or toxic, either intentionally or accidentally)
- ☐ **Shown signs or symptoms of addiction to their TIRF medicine** (**Addiction** – a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance. Signs and symptoms include: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal)
- ☐ **Misused or been suspected of misusing their TIRF medicine** (**Misuse** - the use of a medicinal product without a prescription or in a manner other than as directed by a physician, including use without a prescription of one's own; use in greater amounts to feel euphoria (i.e. to get high), more often, or for a period longer than prescribed; or use in any other way not directed by the prescribing physician)
- ☐ **Abused or been suspected of abusing their TIRF medicine** (**Abuse** - intentional non-therapeutic use of a medicinal product, even once, for its rewarding psychological or physiological or euphoric effect, and often associated with physical dependence)
- ☐ **Someone else has been accidentally exposed to the patient's TIRF medicine** (**Accidental exposure** - unintended exposure of a medicinal product to someone other than to whom it was prescribed)
- ☐ **Another serious adverse event** (**Serious Adverse Event** – any adverse event at any dose that results in death, is life-threatening, requires inpatient hospitalization, or causes prolongation of existing hospitalization)

If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.

5 Prescriber Signature

Prescriber Signature*:	Date*:

Complete this form online at TIRFREMSaccess.com or fax the completed form to 1-855-474-3062.

Please visit TIRFREMSaccess.com or call 1-866-822-1483 for more information about the TIRF REMS.

<Date>

Changes to Requirements of the TIRF REMS

Subject: - Program changes effective (DATE)
- Current prescribers must re-enroll in TIRF REMS
- Prescribers must document that patients are opioid-tolerant
- Patients who are not opioid-tolerant must be transitioned to alternate therapy

Dear Healthcare Provider:

The TIRF REMS Access Program, now called the TIRF REMS, has been modified and the requirements of the program have changed. You will need to take action within the TIRF REMS system in order to continue to prescribe TIRF medicines.

You will need to re-certify in order to continue dispensing TIRF medicines. Only patients who are opioid-tolerant (see definition below) will be able to receive a TIRF medicine.

Key Modifications:
Only prescribers enrolled and certified in the modified TIRF REMS, effective <DATE>, will be able to prescribe TIRF medicines for outpatient use.

- The prescriber must document and provide verification of the patient's opioid tolerance, per the product labeling, to the TIRF REMS prior to each prescription being authorized for dispense at an outpatient pharmacy every time a TIRF medicine is prescribed.
- As of <DATE>, patients who are not opioid-tolerant will not be able to obtain a TIRF medicine; they must be transitioned off of their TIRF medicine, and to an alternate therapy if appropriate.
- All patients in the outpatient setting must be enrolled into the new TIRF REMS registry to assess safe use and trends in accidental exposure, misuse, abuse, addiction, and overdose.

Starting (DATE), prescriptions will only be filled when:

1. The prescriber is enrolled in the new TIRF REMS,
2. The patient has been enrolled in the new TIRF REMS, and
3. The patient's opioid tolerance has been documented.

What must I do to participate in the modified TIRF REMS?

All current prescribers must re-enroll and re-certify into the modified program

Prescribers must review the modified **Prescriber Education**, complete the **Knowledge Assessment** and sign the **Prescriber Enrollment Form**.

Go to www.TIRFREMSAccess.com to re-enroll and become certified online. You can also find all the materials you need to download and fax to the TIRF REMS to become certified.

Prescribers must enroll all OUTPATIENTS prior to prescribing a TIRF medicine

All outpatients must be enrolled, including those currently receiving a TIRF medicine, starting on <Date>.

Prescribers must complete and submit a **Patient Enrollment Form** before prescribing a TIRF medicine for every patient in an outpatient setting. This will automatically enroll the patient into the TIRF REMS registry.

Prescribers must document Patient's Opioid Tolerance per the labeling definition
Patients are considered opioid-tolerant if they are currently taking (exclusive of the TIRF medicine) one or more of the following opioid regimens daily and they have been on the regimen(s) for one week or longer:

- ≥ 60 mg oral morphine/day
- ≥ 30 mg oral oxycodone/day
- ≥ 25 mg oral oxymorphone/day
- an equianalgesic dose of another opioid
- ≥ 25 mcg transdermal fentanyl/hour
- ≥ 8 mg oral hydromorphone/day
- ≥ 60 mg oral hydrocodone/day

What if my patient is not opioid-tolerant?

You must transition a patient who is not opioid-tolerant from a TIRF medicine to another treatment if needed.

Under the modified program as of <DATE>, the patient will no longer be able to receive a TIRF medicine at the pharmacy.

All materials can be found at www.TIRFREMSAccess.com

For additional information related to the TIRF REMS and recent program modifications, please call **1-866-822-1483**.

Sincerely,

TIRF REMS

<Date>

Changes to Requirements of the TIRF REMS

Subject: - Current outpatient pharmacies must re-certify in TIRF REMS
- Currently stocked TIRF medicines must be returned if you do not re-certify
- Program changes effective (DATE).

Dear Outpatient Pharmacy:

The TIRF REMS Access Program, now called the TIRF REMS, has been modified and the requirements of the program have changed. You will need to take action in order to continue dispensing TIRF medicines.

You will need to re-certify in order to continue dispensing TIRF medicines if you remain as a qualified dispenser.

Key Modifications:
Only pharmacies certified in the modified TIRF REMS, effective <DATE>, will be able to dispense TIRF medicines to patients.

- All pharmacies will be required to obtain an authorization to dispense from the TIRF REMS, online or over the phone, for every prescription for a TIRF medicine.
- As of <DATE>, pharmacies that are not certified in the TIRF REMS will not be able to dispense TIRF medicines and will be required to return all currently stocked TIRF products to the distributor or manufacturer.
- TIRF medicines can only be obtained from qualified wholesalers/distributors that are enrolled in the TIRF REMS.

Starting (DATE), you may only fill prescriptions when:

1. Your pharmacy has re-certified in the modified TIRF REMS,
2. You obtain stock of TIRF medicines from a qualified and enrolled wholesale distributor, and
3. You obtain a TIRF REMS dispense authorization issued by the TIRF REMS prior to dispensing a prescription for a TIRF medicine.

What must I do to participate in the modified TIRF REMS?

All current pharmacies must re-certify in the modified program.
The pharmacy must designate an authorized representative to complete the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy. To re-certify the pharmacy, the authorized representative must review the modified **Education Program**, successfully complete the **Knowledge Assessment**, and complete the **Outpatient Pharmacy Enrollment Form** through the TIRF REMS website, or complete and fax the signed **Knowledge Assessment** and enrollment form to the TIRF REMS.

Go to www.TIRFREMSAccess.com to re-enroll and become certified online. You can also find all the materials you need to download and fax to the TIRF REMS to become certified.

Pharmacies must re-certify prior to dispensing a TIRF medicine
Pharmacies must complete and submit an **Outpatient Pharmacy Enrollment Form** before dispensing a TIRF medicine.

Pharmacies must check the Patient's Opioid Tolerance
Before obtaining a dispense authorization, the pharmacy must check the patient's opioid tolerance. This could include reviewing data from various sources, for example:

- available state Prescription Drug Monitoring Programs (PDMPs),
- the patient's records in the pharmacy's management system, and
- information provided by the TIRF REMS.

Talk to Patients who are Not Opioid-tolerant

- Tell patients who are not opioid-tolerant to work with their doctors to transition off of their TIRF medicine.

What if the Pharmacy does not re-certify in the modified TIRF REMS?

- The pharmacy will not be able to dispense TIRF medicines and will be required to return all currently stocked TIRF products to the distributor or manufacturer by (date).
- You may need to assist patients in finding a pharmacy certified in the TIRF REMS.

All materials can be found at www.TIRFREMSAccess.com

For additional information related to the TIRF REMS and recent program modifications, please call **1-866-822-1483**.

Sincerely,

TIRF REMS

<Date>

Changes to Requirements of the TIRF REMS

Subject: - Current inpatient pharmacies must re-certify in TIRF REMS
- Currently stocked TIRF medicines must be returned if you do not re-certify
- Program changes effective (DATE).

Dear Inpatient Pharmacy:

The TIRF REMS Access Program, now called the TIRF REMS, has been modified and the requirements of the program have changed. You will need to take action in order to continue dispensing TIRF medicines.

You will need to re-certify in order to continue dispensing TIRF medicines if you remain as a qualified dispenser.

Key Modifications:
Only pharmacies certified in the modified TIRF REMS, effective <DATE>, will be able to dispense TIRF medicines to patients.

- All pharmacies will be required to verify the patient is opioid tolerant through the processes and procedures established as a requirement of the TIRF REMS.
- As of <DATE>, pharmacies that are not certified in the TIRF REMS will not be able to dispense TIRF medicines and will be required to return all currently stocked TIRF products to the distributor or manufacturer.
- TIRF medicines can only be obtained from qualified wholesalers/distributors that are enrolled in the TIRF REMS.

Starting (DATE), you may only fill prescriptions when:

1. your pharmacy has re-certified in the modified TIRF REMS,
2. you obtain stock of TIRF medicines from a qualified and enrolled wholesale distributor and
3. you verify the patient is opioid tolerant through the processes and procedures established as a requirement of the REMS.

What must I do to participate in the modified TIRF REMS?

All current pharmacies must re-certify in the modified program.
All currently enrolled pharmacies must re-certify in the TIRF REMS and attest to the modified program requirements to be eligible to dispense TIRF medicines to patients.

The pharmacy must designate an authorized representative to complete the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy. To re-certify the pharmacy, the authorized representative must review the modified

Education Program, successfully complete the **Knowledge Assessment**, and complete the **Inpatient Pharmacy Enrollment Form** through the TIRF REMS website, or complete and fax the signed **Knowledge Assessment** and enrollment form to the TIRF REMS

Go to www.TIRFREMSAccess.com to re-enroll and become certified online. You can also find all the materials you need to download and fax to the TIRF REMS to become certified.

Pharmacies must re-certify prior to dispensing a TIRF medicine
Pharmacies must complete and submit an **Inpatient Pharmacy Enrollment Form** before dispensing a TIRF medicine.

Pharmacies must verify the Patient's Opioid Tolerance
Inpatient pharmacies are required to develop policies and procedures to verify the patient's opioid tolerance prior to dispensing. This could include reviewing data from various sources, for example:

- available state Prescription Drug Monitoring Programs (PDMPs),
- the patient's records in the pharmacy's management system, and
- information provided by the TIRF REMS.

What if the Pharmacy does not re-certify in the modified TIRF REMS?

- The pharmacy will not be able to dispense TIRF medicines and will be required to return all currently stocked TIRF products to the distributor or manufacturer.

All materials can be found at www.TIRFREMSAccess.com

For additional information related to the TIRF REMS and recent program modifications, please call **1-866-822-1483**.

Sincerely,

TIRF REMS

<Date>

Urgent Notification Regarding TIRF Products Stock

Subject:	**Returning TIRF products from wholesaler-distributor or pharmacy stock to the manufacturer for wholesalers-distributors not enrolled in the modified TIRF REMS or pharmacies not certified in the modified TIRF REMS.**

Dear Wholesaler-Distributor or Pharmacy:

The purpose of this letter is to inform wholesalers-distributors not enrolled in the modified TIRF REMS and pharmacies not certified in the modified TIRF REMS to immediately return TIRF products from stock to the manufacturer.

You have been identified as a previously enrolled wholesaler-distributor or certified pharmacy in the TIRF REMS.

If you plan to re-enroll/re-certify:

If you are planning on re-enrolling/re-certifying, please visit the TIRF REMS website at www.TIRFREMSaccess.com for information about enrollment in the modified REMS, including Frequently Asked Questions.

If you do not plan to re-enroll/re-certify:

Wholesalers-Distributors must be enrolled in the modified TIRF REMS to purchase and distribute TIRF products. Wholesalers-Distributors not enrolled in the modified TIRF REMS must immediately return TIRF products from stock to the manufacturer. **Only enrolled Wholesalers-Distributors can purchase and distribute TIRF products.**

Pharmacies must be certified in the modified TIRF REMS to dispense TIRF products. Pharmacies not certified in the modified TIRF REMS must immediately return TIRF products from stock to the manufacturer. **Only certified pharmacies can dispense TIRF products.** Patients will no longer be able to fill prescriptions at pharmacies not certified in the modified TIRF REMS.

TIRF medicines are sold in the following presentation:

Product Description	NDC	Package Size
Actiq® (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 200 mcg	63459-0502-30	30 lozenge per box
Actiq® (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 400 mcg	63459-0504-30	30 lozenge per box
Actiq® (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 600 mcg	63459-0506-30	30 lozenge per box
Actiq® (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 800 mcg	63459-0508-30	30 lozenge per box
Actiq® (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 1200 mcg	63459-0512-30	30 lozenge per box

<Date>

Product Description	NDC	Package Size
Actiq® (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 1600 mcg	63459-0516-30	30 lozenge per box
Authorized generic (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 200 mcg	00093-7865-65	30 lozenge per box
Authorized generic (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 400 mcg	00093-7866-65	30 lozenge per box
Authorized generic (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 600 mcg	00093-7867-65	30 lozenge per box
Authorized generic (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 800 mcg	00093-7868-65	30 lozenge per box
Authorized generic (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 1200 mcg	00093-7869-65	30 lozenge per box
Authorized generic (fentanyl citrate) oral transmucosal lozenge (NDA 20747) 1600 mcg	00093-7870-65	30 lozenge per box
Fentora® fentanyl buccal tablet (NDA 021947) 100 mcg	63459-0541-28	28 tablets per box
Fentora® fentanyl buccal tablet (NDA 021947) 200 mcg	63459-0542-28	28 tablets per box
Fentora® fentanyl buccal tablet (NDA 021947) 400 mcg	63459-0544-28	28 tablets per box
Fentora® fentanyl buccal tablet (NDA 021947) 600 mcg	63459-0546-28	28 tablets per box
Fentora® fentanyl buccal tablet (NDA 021947) 800 mcg	63459-0548-28	28 tablets per box
Authorized generic fentanyl buccal tablet (NDA 021947) 100 mcg	51862-634-28	28 tablets per box
Authorized generic fentanyl buccal tablet (NDA 021947) 200 mcg	51862-635-28	28 tablets per box
Authorized generic fentanyl buccal tablet (NDA 021947) 400 mcg	51862-636-28	28 tablets per box
Authorized generic fentanyl buccal tablet (NDA 021947) 600 mcg	51862-637-28	28 tablets per box
Authorized generic fentanyl buccal tablet (NDA 021947) 800 mcg	51862-638-28	28 tablets per box
Lazanda (fentanyl nasal spray), 100 mcg	71500-110-01	1 unit in 1 carton
Lazanda (fentanyl nasal spray), 400 mcg	71500-140-01	1 unit in 1 carton
Onsolis, fentanyl buccal soluble film, 200 mcg strength	0037-5200-30	30 units per carton
Onsolis, fentanyl buccal soluble film, 400 mcg strength	0037-5400-30	30 units per carton
Onsolis, fentanyl buccal soluble film, 600 mcg strength	0037-5600-30	30 units per carton
Onsolis, fentanyl buccal soluble film, 800 mcg strength	0037-5800-30	30 units per carton
Onsolis, fentanyl buccal soluble film, 1200 mcg strength	0037-5120-30	30 units per carton
Subsys (fentanyl) sublingual spray, 100 mcg	71500-001-10	10 units in 1 carton
Subsys (fentanyl) sublingual spray, 200 mcg	71500-002-30	30 units in 1 carton
Subsys (fentanyl) sublingual spray, 400 mcg	71500-004-30	30 units in 1 carton
Subsys (fentanyl) sublingual spray, 600 mcg	71500-006-30	30 units in 1 carton
Subsys (fentanyl) sublingual spray, 800 mcg	71500-008-30	30 units in 1 carton
Subsys (fentanyl) sublingual spray, 1200 mcg	71500-012-15	15 count (15 blisters of 2x 600 mcg)
Subsys (fentanyl) sublingual spray, 1600 mcg	71500-016-15	15 count (15 blisters of 2x 800 mcg)
Oral Transmucosal Fentanyl Citrate 200 mcg	0406-9202-30	30 units
Oral Transmucosal Fentanyl Citrate 400 mcg	0406-9204-30	30 units
Oral Transmucosal Fentanyl Citrate 600 mcg	0406-9206-30	30 units
Oral Transmucosal Fentanyl Citrate 800 mcg	0406-9208-30	30 units

<Date>

Product Description	NDC	Package Size
Oral Transmucosal Fentanyl Citrate 1200 mcg	0406-9212-30	30 units
Oral Transmucosal Fentanyl Citrate 1600 mcg	0406-9216-30	30 units

If you are not enrolled or certified in the modified TIRF REMS, you need to **stop** distributing and immediately quarantine all listed TIRF medicines. Please examine your inventory and return all units of the listed TIRF medicines to your wholesaler within 21 days.

If you have any questions or require additional information, please call the TIRF REMS Call Center at 1-866-822-1483.

Sincerely,

TIRF REMS

What is the Transmucosal Immediate-Release Fentanyl (TIRF) REMS?

The Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Program is an FDA-required program designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are treated to ensure appropriate use of TIRF medicines. The purpose of the REMS is to mitigate the misuse, abuse, addiction, overdose, and serious complications due to medication errors with the use of TIRF medicines.

You must enroll in the TIRF REMS to prescribe, dispense, or distribute TIRF medicines.

Patient

To receive treatment, a patient must be enrolled in the TIRF REMS by a certified doctor.

Enrollment Information

Pharmacy

Pharmacies must be certified in the TIRF REMS to receive and dispense TIRF medicines.

If you are the designated authorized representative of a pharmacy, you can certify below.

Certify Pharmacy

Prescriber

Prescribers must be certified in the TIRF REMS to prescribe TIRF medicines for outpatient use.

If you are a TIRF medicines prescriber, you can certify below.

Certify Prescriber

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

What is the Transmucosal Immediate-Release Fentanyl (TIRF) REMS?

The Transmucosal Immediate Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Program is an FDA-required program designed to ensure informed risk-benefit decisions before initiating treatment, and while patients are treated to ensure appropriate use of TIRF medicines. The purpose of the REMS is to mitigate the misuse, abuse, addiction, overdose, and serious complications due to medication errors with the use of TIRF medicines.

You must enroll in the TIRF REMS to prescribe, dispense, or distribute TIRF medicines.

Patient

To receive treatment, a patient must be enrolled in the TIRF REMS by a certified doctor.

Enrollment Information

Pharmacy

Pharmacies must be certified in the TIRF REMS to receive and dispense TIRF medicines.

If you are the designated authorized representative of a pharmacy, you can certify below.

Certify Pharmacy

Prescriber

Prescribers must be certified in the TIRF REMS to prescribe TIRF medicines for outpatient use.

If you are a TIRF medicines prescriber, you can certify below.

Certify Prescriber

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Contact the TIRF REMS Call Center

Phone
1-866-822-1483

Fax
1-866-822-1487

Hours of Operation

MONDAY - FRIDAY	8:00-8:00 ET
SATURDAY - SUNDAY	Closed

Or

Contact a participating company about a specific product

Branded Products

Trade Name	Generic Name	Company	Links
Product1®	Oral Transmucosal Fentanyl Citrate Lozenge	Company1	U.S. Prescribing Information and Medication Guide
Product3®	Oral Transmucosal Fentanyl nasal spray	Company2	U.S. Prescribing Information and Medication Guide
Product4®	Oral Transmucosal Fentanyl sublingual spray	Company3	U.S. Prescribing Information and Medication Guide
Product8®	Oral Transmucosal Fentanyl sublingual tabletsL	Company7	U.S. Prescribing Information and Medication Guide

Generic Products

Trade Name	Generic Name	Company	Links
Product5	Oral Transmucosal Fentanyl Citrate Lozenge	Company4	U.S. Prescribing Information and Medication Guide
Product6	Oral Transmucosal Fentanyl Citrate Lozenge	Company5	U.S. Prescribing Information and Medication Guide
Product7	Oral Transmucosal Fentanyl Citrate Buccal Tablets	Company6	U.S. Prescribing Information and Medication Guide

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Find Speciality Pharmacies

Specialty pharmacies certified to dispense TIRF medicines.

OutPat Test Pharmacy
538 Deanna Forks
Filibertobury, VA 10726-7773
826-644-0463

XM Test Screen Shot Pharmacy
575 Lonly Forks
Johnstown, TN 54543-7773
628-987-6364

XM Test Sub01 Pharmacy
815 Daisy Gate
West Palls, ME 40254-1274
377-720-7654

XM Test Pharmacy
358 Gorgia Forks
Filbury, MA 10726-7773
628-644-6364

OutPat Test Sub01 Pharmacy
815 Enos Lock
East Dannie, DE 40254-1274
367-720-5767

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

___Localization_Version

Find Retail Pharmacies

Locate a retail pharmacy certified to dispense TIRF medicines near you.

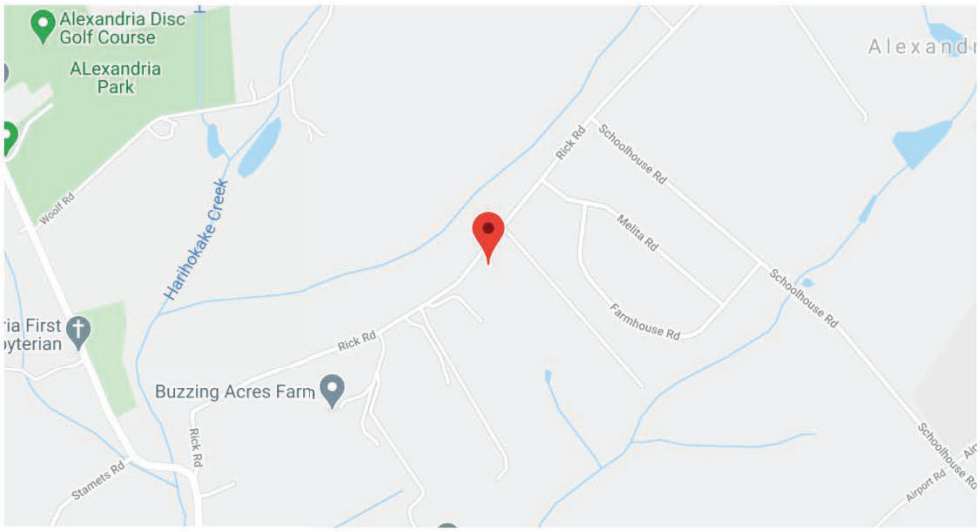
Philadelphia

Find Retail Pharmacies

OutPat Test Sub02 Pharmacy
22333 Jammie Squares
Philadelphia, PA 19002

XM Test Sub02 Pharmacy
22 Rittenhouse Square
Philadelphia, PA 19002

Locations



To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

____Localization_Version

Verify Shipping Address

Generate receipts for proof of shipping destination verification

Wholesaler DEA

Your wholesaler's DEA Number

Destination Organizational NPI

NPI Number

Destination Name, Address

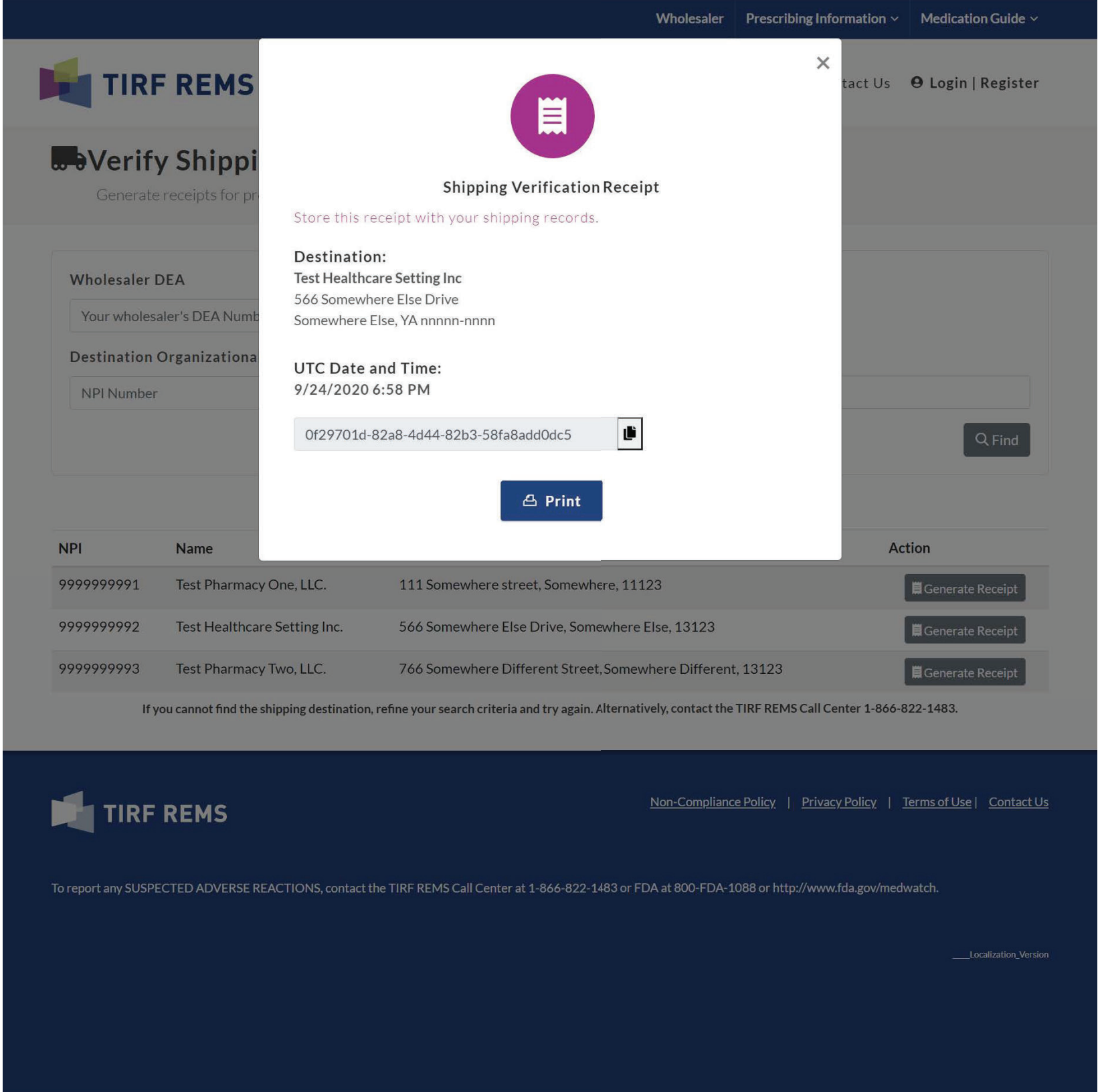
Search Healthcare Settings or Pharmacy...

Find

Certified Shipping Endpoints

NPI	Name	Address	Action
9999999991	Test Pharmacy One, LLC.	111 Somewhere street, Somewhere, 11123	Generate Receipt
9999999992	Test Healthcare Setting Inc.	566 Somewhere Else Drive, Somewhere Else, 13123	Generate Receipt
9999999993	Test Pharmacy Two, LLC.	766 Somewhere Different Street,Somewhere Different, 13123	Generate Receipt

If you cannot find the shipping destination, refine your search criteria and try again. Alternatively, contact the TIRF REMS Call Center 1-866-822-1483.


Wholesaler
Prescribing Information
Medication Guide
TIRF REMS
tact Us
Login | Register
Verify Shippi
Generate receipts for pr
Wholesaler DEA
Your wholesaler's DEA Numb
Destination Organizationa
NPI Number
Find
Shipping Verification Receipt
Store this receipt with your shipping records.
Destination:
Test Healthcare Setting Inc
566 Somewhere Else Drive
Somewhere Else, YA nnnnn-nnnn
UTC Date and Time:
9/24/2020 6:58 PM
0f29701d-82a8-4d44-82b3-58fa8add0dc5
Print
NPI
Name
Action
9999999991
Test Pharmacy One, LLC.
111 Somewhere street, Somewhere, 11123
Generate Receipt
9999999992
Test Healthcare Setting Inc.
566 Somewhere Else Drive, Somewhere Else, 13123
Generate Receipt
9999999993
Test Pharmacy Two, LLC.
766 Somewhere Different Street,Somewhere Different, 13123
Generate Receipt
If you cannot find the shipping destination, refine your search criteria and try again. Alternatively, contact the TIRF REMS Call Center 1-866-822-1483.
TIRF REMS
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To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.
___Localization_Version

Prescriber

Prescribers must be certified in the TIRF REMS to prescribe TIRF medicines for outpatient use.

To certify as a prescriber:

1 Review the Prescribing Information

Review each drug's Prescribing Information

- CompanyPI1
- CompanyPI2
- CompanyPI3
- CompanyPI4
- CompanyPI5
- CompanyPI6

2 Review the Prescriber Materials

Review the Prescriber Education.

3 Complete the Prescriber Knowledge Assessment

Successfully complete the Prescriber Knowledge Assessment and submit it to the TIRF REMS.

Online or Print

4 Complete the Prescriber Enrollment Form

Enroll in the TIRF REMS by completing the Prescriber Enrollment Form and submitting it to the TIRF REMS.

Online or Print

Prescriber Materials

- Prescriber Education
- Prescriber Knowledge Assessment
- Prescriber Enrollment Form
- Patient Counseling Guide
- Patient Status and Opioid Tolerance Form
- Patient Discontinuation Form
- Adverse Events of Special Interest Reporting Form
- Prescriber FAQs

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Pharmacy

Pharmacies must be certified in the TIRF REMS to receive and dispense TIRF medicines.

To certify your pharmacy:

1 Designate an Authorized Representative

Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the TIRF REMS on behalf of the pharmacy.

2 Review the Pharmacy Information

Have the authorized representative review the Pharmacy Education.

3 Complete the Pharmacy Knowledge Assessment

Have the authorized representative successfully complete the Pharmacy Knowledge Assessment and submit it to the TIRF REMS.

Online or Print

4 Enroll Pharmacy

Have the authorized representative enroll in the TIRF REMS by completing the Pharmacy Enrollment Form and submitting it to the TIRF REMS.

Online or Print Inpatient or Print Outpatient

Pharmacy Materials

- Pharmacy Education
- Pharmacy Knowledge Assessment
- Inpatient Pharmacy Enrollment Form
- Outpatient Pharmacy Enrollment Form
- Pharmacy FAQ

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Patient

To receive treatment, a patient must be enrolled in the TIRF REMS by a certified doctor.

How do patients enroll in the TIRF REMS?

1 Talk with your TIRF REMS Certified doctor

Receive counseling from your doctor on the safe use of TIRF medicines using the Patient Counseling Guide and the appropriate Medication Guide.

- Company1MG
- Company2MG
- Company3MG
- Company4MG
- Company5MG
- Company6MG

2 Make sure you understand

You **must** do the following:

- Take around-the-clock opioid pain medicine when using TIRF medicines
- Do **not** share TIRF medicines
- Properly store and dispose of your TIRF medicines

You **must** inform the doctor of serious adverse events

- Accidental exposure
- Abuse
- Misuse
- Addiction
- Overdose

You **must** receive counseling from the doctor on the safe use of each new TIRF medicine you are prescribed.

3 Enroll

Together with your doctor, complete and sign the Patient Enrollment Form. Your doctor or their staff can assist you in completing the enrollment either online or by using the paper form.

Patient Materials

- Patient Counseling Guide
- Patient Enrollment Form
- Patient FAQs

Important Terms

- What is a REMS?
- What are TIRF medicines?
- What is Opioid Tolerant?
- What is Naloxone?

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Patient

To receive treatment, a p

How do pa

1 **Talk with your TI**

Receive counseling fr
Counseling Guide an

- Company1MG
- Company2MG
- Company3MG
- Company4MG
- Company5MG
- Company6MG

2 **Make sure you understand**

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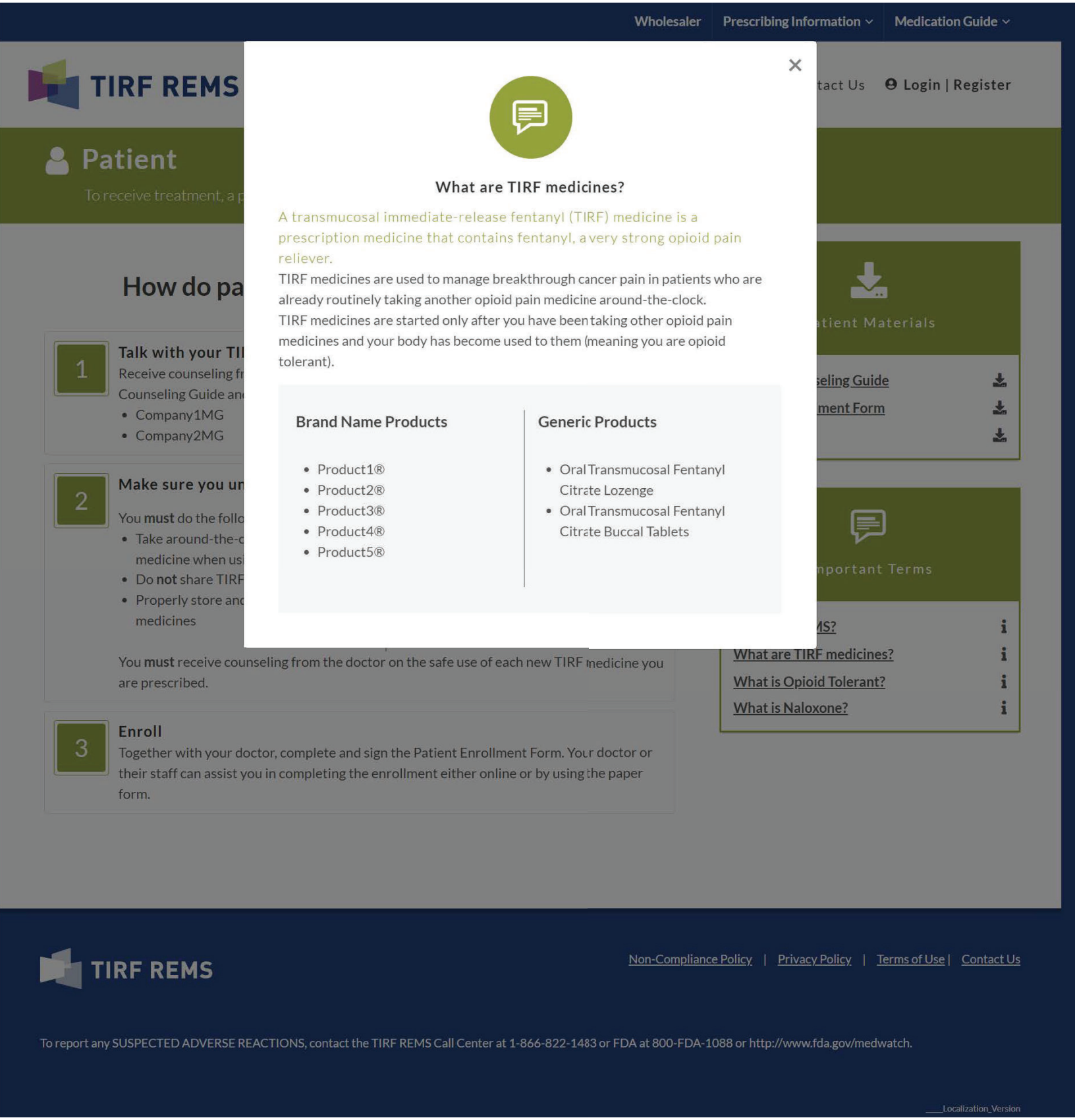
Patient FAQs

Important Terms

What is a REMS?
What are TIRF medicines?
What is Opioid Tolerant?
What is Naloxone?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Patient
To receive treatment, a p
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Talk with your TI
Receive counseling fr
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medicine when usi
Do not share TIRF
Properly store and
medicines
You must receive counseling from the doctor on the safe use of each new TIRF medicine you are prescribed.
3
Enroll
Together with your doctor, complete and sign the Patient Enrollment Form. Your doctor or their staff can assist you in completing the enrollment either online or by using the paper form.
What are TIRF medicines?
A transmucosal immediate-release fentanyl (TIRF) medicine is a prescription medicine that contains fentanyl, a very strong opioid pain reliever.
TIRF medicines are used to manage breakthrough cancer pain in patients who are already routinely taking another opioid pain medicine around-the-clock.
TIRF medicines are started only after you have been taking other opioid pain medicines and your body has become used to them (meaning you are opioid tolerant).
Brand Name Products
Product1®
Product2®
Product3®
Product4®
Product5®
Generic Products
Oral Transmucosal Fentanyl Citrate Lozenge
Oral Transmucosal Fentanyl Citrate Buccal Tablets
atient Materials
seling Guide
ment Form
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MS?
What are TIRF medicines?
What is Opioid Tolerant?
What is Naloxone?
TIRF REMS
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To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.
____Localization_Version

Patient

To receive treatment, a p

What is Opioid Tolerant?

Patients considered opioid tolerant are those who are taking around-the-clock medicine consisting of at least 60 mg of oral morphine per day, or at least 25 mcg per hour of transdermal fentanyl, or at least 30 mg of oral oxycodone per day, or at least 8 mg of oral hydromorphone per day, or at least 25 mg oral oxymorphone per day, or at least 60 mg oral hydrocodone per day or an equianalgesic dose of another opioid medication daily for a week or longer. Patients must remain on around-the- clock opioids when taking a TIRF medicine.

How do pa

1 Talk with your TI

Receive counseling fr
Counseling Guide an

- Company1MG
- Company2MG
- Company3MG
- Company4MG
- Company5MG
- Company6MG

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- Abuse
- Misuse
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- Overdose

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atient Materials

seling Guide
Patient Enrollment Form
Patient FAQs

Important Terms

What is a REMS?
What are TIRF medicines?
What is Opioid Tolerant?
What is Naloxone?

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

What is Naloxone?

Naloxone is a medicine that helps reverse an opioid overdose.
Naloxone is sprayed inside your nose or injected into your body. Some naloxone products are designed for people to use in their home.

Naloxone is never a substitute for emergency medical care. Get emergency help or call 911 right away if you take too much of your TIRF medicine, because you may have had an opioid overdose.
See the Patient Counseling Guide for more information.

Patient

To receive treatment, a p

How do pa

1 Talk with your TI

Receive counseling fr
Counseling Guide an

- Company1MG
- Company2MG
- Company3MG
- Company4MG
- Company5MG
- Company6MG

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Patient FAQs

Important Terms

What is a REMS?
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What is Opioid Tolerant?
What is Naloxone?

TIRF REMS

SITE IS UNDER MAINTENANCE

Please check back soon.

Why is the site down?

The site is under maintenance because we are working on improving it.

What is the expected downtime?

We are usually back within 10-15 minutes, but it depends on the issue.

Do you need support?

You may call the TIRF REMS Call Center at 866-822-1483 if you need support.

TIRF REMS

Create Account

User Type Selection

REMS User Types

- (●) **Pharmacy Authorized Representative**
  A pharmacy authorized representative is an individual designated for each pharmacy location to carry out the certification process and oversee implementation and compliance with the TIRF REMS.

- ( ) **Prescriber**
  A prescriber is an individual who may prescribe Transmucosal Immediate-Release Fentanyl medicines in compliance with the TIRF REMS.

Cancel Next

To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

TIRF REMS

Create Account

Pharmacy Authorized Representative

Username and Password

Username

testr18306@examoto.net

First Name

RxAuth

Last Name

Represenative

Password

••••••••••••

Confirm Password

••••••••••••

Cancel

Next

TIRF REMS

Create Account

Prescriber

Username and Password

Individual National Provider ID (NPI) Number

1310000086

☑ I am Test Prescriber86

If the name above is incorrect, please re-enter your NPI number.

Password

••••••••••••

Confirm Password

••••••••••••

Cancel Next

TIRF REMS

Create Account

Verify Identity

Choose verification method

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

Email me the code

verifytest6726@examoto.net

After logging in, use preferences to add password reset options and/or enable multi-factor authentication.

Cancel Next

Create Account

Verify Identity

Enter Verification Code

Please enter your code.

670194

Cancel | Next

To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

V0_01

TIRF REMS

Create Account

Complete

testr18306@examoto.net, your account has been created.

You may now login to perform REMS functions online.

Login

To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Login

Username

Username

Password

Password

Remember my login

Cancel | Login

Forgot your password?

Sign in with Examoto Corporate AD

Or

Register

To perform REMS functions online, you must have an account. Creating an account involves creating unique login credentials (username and password). Register to create an account.

Register

To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

TIRF REMS

Reset Password

Username

User ID | NPI number

Cancel Next

TIRF REMS

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To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

V0_01

TIRF REMS

Reset Password

Verify Identity

Choose verification method

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

- ( ) Email Txxxxxxxxxx@EXAMOTO.NET
- ( ) Text (SMS) xxx-xxx-7766
- ( ) Call xxx-xxx-7766
- (•) Approve request on my Authenticator App

After logging in, use preferences to add password reset options and/or enable multi-factor authentication.

Cancel Next

TIRF REMS

Reset Password

Verify Code

We sent you a code to verify your identity; please enter it here.

Code

367132

Password

••••••••••••

Confirm password

••••••••••••

Cancel Next

TIRF REMS

Reset Password

Completed

Your password has been reset.

Continue

My Account

Preferences

Identity

Username: 1310000000

You may only change your username by calling the coordinating center at 1-866-822-1483.

Password: Change Account Information

Verification Methods

Email: testr56420@examoto.net Change my Email

Phone: 610-248-8636 Change my Phone Number

Authenticator App: Configured Reset my App

Two-Factor Authentication

Two-factor authentication (2FA) improves security. 2FA adds a second level of authentication to an account login. With 2FA enabled, the user is required to enter their username, password and a code. The code can be provided via several methods.

Use Two-Factor Authentication to improve security

Two-Factor Authentication: Disabled Enable

TIRF REMS

Change Account Information

Verify and Update

Current Password

Current Password

New Password

Password

Confirm Password

Password

Cancel Next

TIRF REMS

Change Account Information

Completed

Your password has been changed.

Continue

TIRF REMS

Change Account Information

Email Address

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

Enter Email

Email

Cancel Next

TIRF REMS

Change Account Information

Phone Number

We will send you a code to verify your identity. The code may only be used once and is time sensitive.

Phone

nnn-nnn-nnnn

(•) Text (SMS) me with the code ( ) Call me with the code

Cancel Next

To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Change Account Information

Verify Email Address

We sent you a code to verify your identity; please enter it here.

Code

301620

I didn't receive the code

Next

To report any SUSPECTED ADVERSE REACTIONS, contact TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

V0_01

TIRF REMS

Change Account Information

Verify Phone Phone Number

We sent you a code to verify your identity; please enter it here.

Code

917381

I didn't receive the code | Next

Account Options

Configure Authenticator App

Follow these steps to use an authenticator app:

1. Download a two-factor authenticator app, like Microsoft Authenticator or Google Authenticator for Android or iOS .
2. Scan the QR Code or enter this key into your two-factor authenticator app:

   YXJ7 FNTY GWRB 45QA OMIC CCKU DRPQ 2XHW

   The spaces are not required, and the code is not case-sensitive.

3. Once you have scanned the QR code or input the key above, your two-factor authentication app will provide you with a unique code. Enter the code in the confirmation box below and select VERIFY.

Code

nnnnnn

Cancel Verify

TIRF REMS

Logged Out

You are now logged out.

Click here to return to the TIRF REMS application.

Enroll Patient

Complete this form to enroll in the TIRF REMS. **A patient must be enrolled in the TIRF REMS** to receive treatment.

Confirm your Date of Birth

Date of Birth

MM/DD/YYYY

Confirm

Patient / Guardian Agreement

TIRF Medicines can cause your breathing to stop – which can lead to death.

Safety Rules for TIRF Medicines

You have agreed to take a TIRF Medicine and follow all the safety rules to make it less likely you or others will experience serious harm.

- My healthcare provider has talked to me about the safe use of TIRF medicines using the **Medication Guide** and **Patient Counseling Guide**.
- I will only use this medicine if I am regularly using another opioid, around-the-clock, for constant pain.
- If I stop taking my around-the-clock-opioid pain medicine, I **MUST** stop taking my TIRF medicine.
- I will never share or give my TIRF medicine to anyone else, even if they have the same symptoms.
  - My TIRF medicine could cause harm to others or even death. A dose that is okay for me could cause an overdose and death for someone else.
- I will store my TIRF medicine in a safe and secure place away from children. I understand that accidental use by a child, or anyone for whom the medicine was not prescribed, can cause death.
- I have been told how to properly dispose of my partially used or unneeded TIRF medicine remaining from my prescription. I will dispose of my TIRF medicine properly as soon as I no longer need it.
- I will contact my healthcare provider if my TIRF medicine does not relieve my pain. I will not change the dose of my TIRF medicine myself or take it more often than my healthcare provider has directed.
- I must enroll in the TIRF REMS and Patient Registry by completing the **Patient Enrollment Form** with my healthcare provider.
- I understand that the TIRF REMS and its agents may use and share my personal information to manage the program, and information all about patients who get TIRF medicines will be stored in a private and secure database. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TIRF REMS. However, my name will not be shared.
- I give permission for the TIRF REMS and its agents or vendors to contact me by phone, mail, or email to support the administration of the TIRF REMS Program.
- I will tell my healthcare provider if I, or anyone else, experience any adverse event of accidental exposure, abuse, misuse, addiction, and overdose.
- I will re-enroll in the TIRF REMS by completing the **Patient Enrollment Form** with my healthcare provider every two years during treatment.

Sign | Type Signature

Please use your mouse or stylus to sign below

Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature.

Sign and Submit

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

« July 1965 »

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11	12	13	14	15	16	17
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25	26	27	28	29	30	31
1	2	3	4	5	6	7

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in the TIRF REMS. **A patient must be enrolled in the TIRF REMS** to receive treatment.

07/15/1965

Confirm

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- I will only use this medicine if I am regularly using another opioid, around-the-clock, for constant pain.
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- I will never share or give my TIRF medicine to anyone else, even if they have the same symptoms.
  - My TIRF medicine could cause harm to others or even death. A dose that is okay for me could cause an overdose and death for someone else.
- I will store my TIRF medicine in a safe and secure place away from children. I understand that accidental use by a child, or anyone for whom the medicine was not prescribed, can cause death.
- I have been told how to properly dispose of my partially used or unneeded TIRF medicine remaining from my prescription. I will dispose of my TIRF medicine properly as soon as I no longer need it.
- I will contact my healthcare provider if my TIRF medicine does not relieve my pain. I will not change the dose of my TIRF medicine myself or take it more often than my healthcare provider has directed.
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- I understand that the TIRF REMS and its agents may use and share my personal information to manage the program, and information all about patients who get TIRF medicines will be stored in a private and secure database. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TIRF REMS. However, my name will not be shared.
- I give permission for the TIRF REMS and its agents or vendors to contact me by phone, mail, or email to support the administration of the TIRF REMS Program.
- I will tell my healthcare provider if I, or anyone else, experience any adverse event of accidental exposure, abuse, misuse, addiction, and overdose.
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Sign | Type Signature

Please use your mouse or stylus to sign below

Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature.

Sign and Submit

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Enroll Patient

Complete this form to enroll in the TIRF REMS. **A patient must be enrolled in the TIRF REMS** to receive treatment.

Confirm your Date of Birth

Date of Birth

07/15/1965

Confirm

Patient / Guardian Agreement

TIRF Medicines can cause your breathing to stop – which can lead to death.

Safety Rules for TIRF Medicines

You have agreed to take a TIRF Medicine and follow all the safety rules to make it less likely you or others will experience serious harm.

- My healthcare provider has talked to me about the safe use of TIRF medicines using the **Medication Guide** and **Patient Counseling Guide**.
- I will only use this medicine if I am regularly using another opioid, around-the-clock, for constant pain.
- If I stop taking my around-the-clock-opioid pain medicine, I **MUST** stop taking my TIRF medicine.
- I will never share or give my TIRF medicine to anyone else, even if they have the same symptoms.
  - My TIRF medicine could cause harm to others or even death. A dose that is okay for me could cause an overdose and death for someone else.
- I will store my TIRF medicine in a safe and secure place away from children. I understand that accidental use by a child, or anyone for whom the medicine was not prescribed, can cause death.
- I have been told how to properly dispose of my partially used or unneeded TIRF medicine remaining from my prescription. I will dispose of my TIRF medicine properly as soon as I no longer need it.
- I will contact my healthcare provider if my TIRF medicine does not relieve my pain. I will not change the dose of my TIRF medicine myself or take it more often than my healthcare provider has directed.
- I must enroll in the TIRF REMS and Patient Registry by completing the **Patient Enrollment Form** with my healthcare provider.
- I understand that the TIRF REMS and its agents may use and share my personal information to manage the program, and information all about patients who get TIRF medicines will be stored in a private and secure database. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TIRF REMS. However, my name will not be shared.
- I give permission for the TIRF REMS and its agents or vendors to contact me by phone, mail, or email to support the administration of the TIRF REMS Program.
- I will tell my healthcare provider if I, or anyone else, experience any adverse event of accidental exposure, abuse, misuse, addiction, and overdose.
- I will re-enroll in the TIRF REMS by completing the **Patient Enrollment Form** with my healthcare provider every two years during treatment.

Sign | Type Signature

Please use your mouse or stylus to sign below

Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature.

Sign and Submit

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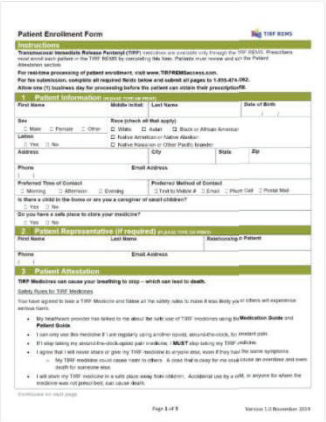
Patient Information Complete

Patient Enrollment Complete

Your enrollment is complete. You may download your copy below.



Patient Enrollment Form

TIRF REMS

Download Form

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Prescriber - Knowledge Assessment

TIRF Prescriber KA

You may leave and return to the Knowledge Assessment at any time, your progress will be saved.

1. The patients described are all experiencing breakthrough pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine? Select one option

- 12-year-old sarcoma patient, using transdermal fentanyl for her underlying persistent cancer pain.
- Adult female with advanced breast cancer; on 60 mg of oral morphine daily for the past 4 weeks.
- Adult male with advanced lung cancer, his underlying persistent pain is managed with 25 mcg/hour transdermal fentanyl patches for the past 3 months.
- Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.

2. The patients described are experiencing breakthrough cancer pain. A TIRF medicine is NOT appropriate for one of them. Which patient should not receive a TIRF medicine? Select one option.

- Adult male with advanced lung cancer; underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.
- Adult female with localized breast cancer; just completed a mastectomy and reconstructive surgery; persistent cancer pain managed with 30 mg oral morphine daily for the past 6 weeks.
- Adult male patient with advanced prostate cancer who, over the last 2 weeks, has been prescribed 100 mg oral morphine daily for pain due to bone metastasis.
- Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

3. Certain factors may increase the risk of abuse and/or diversion of opioid medications. Which of the following is most accurate?

- A history of alcohol abuse with the patient or close family members.
- The patient has a household member with a street drug abuse problem.
- The patient has a history of prescription drug misuse.
- All of the above.

4. A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed? Select one option.

- The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.
- The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.
- Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.
- The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.

5. A patient is starting titration with a TIRF medicine. What dose must they start with? Select one option.

- An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
- The dose that the prescriber believes is appropriate based on their clinical experience.
- The lowest available dose, unless individual product Prescribing Information provides product-specific guidance.
- The median available dose.

6. A prescriber has started titrating a patient with the lowest dose of a TIRF medicine. However, after 30 minutes, the breakthrough cancer pain has not been sufficiently relieved. What should they advise the patient to do? Select one option.

- Take another (identical) dose of the TIRF medicine immediately.
- Take a dose of an alternative rescue medicine.
- Provide guidance based on the product-specific Prescribing Information because the instructions are not the same for all TIRF medicines.
- Double the dose and take immediately.

7. A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Which of the following statements is TRUE? Select one option.

- The patient can't be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.
- Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment of the TIRF medicine; carefully monitor the patient for opioid toxicity, otherwise such use may cause serious life threatening, and/or fatal respiratory depression.
- There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.
- The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.

8. Before initiating treatment with a TIRF medicine, prescribers must review the Medication Guide and Patient Counseling Guide with the patient. Which of the following counseling statements is FALSE? Select one option.

- TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
- Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
- Instruct patients that, if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.
- Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.

9. There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate? Select one option.

- TIRF medicines can be fatal if taken by children.
- TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.
- TIRF medicines can be fatal if taken by anyone who is not opioid-tolerant.
- All of the above.

10. Which one of the following statements is most accurate regarding the safe storage and disposal of TIRF medicines? Select one option.

- TIRF medicines should be kept in in a safe and secure place, out of sight and out of reach of all others, especially children.
- TIRF medicines should be protected from theft.
- Dispose of partially used or unneeded TIRF medicine by following the TIRF medicine-specific procedure specified in the Medication Guide.
- All of the above.

11. Which of the following statements is FALSE? Select one option.

- Educating prescribers, pharmacist and patients that respiratory depression is more common in patients who are not opioid tolerant.
- Requiring that patients remain opioid-tolerant throughout their treatment with TIRF medicines.
- Requiring inpatient pharmacies to verify opioid tolerance in inpatients who require TIRF medicine while hospitalized.
- Requiring documentation of opioid tolerance with only the initial prescription of a TIRF medicine.

Submit KA

Prescriber - Knowledge Assessment

TIRF Prescriber KA

You may leave and return to the Knowledge Assessment at any time, your progress will be saved.

Knowledge Assessment Incomplete

10 correct answers out of 11 (Failed)

1. The patients described are all experiencing breakthrough pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine? Select one option. ✓

- (•) 12-year-old sarcoma patient, using transdermal fentanyl for her underlying persistent cancer pain.
- ( ) Adult female with advanced breast cancer; on 60 mg of oral morphine daily for the past 4 weeks.
- ( ) Adult male with advanced lung cancer, his underlying persistent pain is managed with 25 mcg/hour transdermal fentanyl patches for the past 3 months.
- ( ) Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.

2. The patients described are experiencing breakthrough cancer pain. A TIRF medicine is NOT appropriate for one of them. Which patient should not receive a TIRF medicine? Select one option. ✓

- ( ) Adult male with advanced lung cancer; underlying persistent cancer pain managed with 25 mcg/hour transdermal fentanyl patches for the past 2 months.
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- ( ) Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

3. Certain factors may increase the risk of abuse and/or diversion of opioid medications. Which of the following is most accurate? ✓

- ( ) A history of alcohol abuse with the patient or close family members.
- ( ) The patient has a household member with a street drug abuse problem.
- ( ) The patient has a history of prescription drug misuse.
- (•) All of the above.

4. A patient is already taking a TIRF medicine but wants to change their medicine. His/her doctor decides to prescribe a different TIRF medicine (that is not a bioequivalent generic version of a branded product) in its place. How should the prescriber proceed? Select one option. ✓

- ( ) The prescriber can safely convert to the equivalent dosage of the new TIRF medicine as it has the same effect as other TIRF medicines.
- (•) The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.
- ( ) Convert from the other TIRF medicine to the new TIRF medicine at half of the dose.
- ( ) The prescriber should base the starting dose of the newly prescribed TIRF medicine on the dose of the opioid medicine used for their underlying persistent cancer pain.

5. A patient is starting titration with a TIRF medicine. What dose must they start with? Select one option. ✓

- ( ) An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
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6. A prescriber has started titrating a patient with the lowest dose of a TIRF medicine. However, after 30 minutes, the breakthrough cancer pain has not been sufficiently relieved. What should they advise the patient to do? Select one option. ✓

- ( ) Take another (identical) dose of the TIRF medicine immediately.
- ( ) Take a dose of an alternative rescue medicine.
- (•) Provide guidance based on the product-specific Prescribing Information because the instructions are not the same for all TIRF medicines.
- ( ) Double the dose and take immediately.

7. A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Which of the following statements is TRUE? Select one option. ✓

- ( ) The patient can't be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.
- (•) Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment of the TIRF medicine; carefully monitor the patient for opioid toxicity, otherwise such use may cause serious life threatening and/or fatal respiratory depression.
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- ( ) TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
- ( ) Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
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9. There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate? Select one option. ✓

- ( ) TIRF medicines can be fatal if taken by children.
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- ( ) TIRF medicines should be kept in in a safe and secure place, out of sight and out of reach of all others, especially children.
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- ( ) Dispose of partially used or unneeded TIRF medicine by following the TIRF medicine-specific procedure specified in the Medication Guide.
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Try Again | Home

Prescriber - Knowledge Assessment

There are errors, please correct the items below:

- You have exceeded the maximum number of allowed attempts to pass the knowledge assessment
- To reattempt the knowledge assessment you must first review the Prescriber Education and then call the TIRF REMS Call Center at 1-866-822-1483 to reset your account
- You will be denied enrollment into the TIRF REMS after six failed attempts to complete the knowledge assessment

Home

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___Localization_Version

Prescriber - Knowledge Assessment

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____Localization_Version

Prescriber - Knowledge Assessment

TIRF Prescriber KA

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Knowledge Assessment Complete

11 correct answers out of 11 (Passed)

1. The patients described are all experiencing breakthrough pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine? Select one option. ✓

- (•) 12-year-old sarcoma patient, using transdermal fentanyl for her underlying persistent cancer pain.
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- (•) Requiring documentation of opioid tolerance with only the initial prescription of a TIRF medicine.

Home

Prescriber Enrollment

PRJane PRDoe

To be completed by the prescriber to enroll in the TIRF REMS. Transmucosal Immediate-Release Fentanyl medicines are only available through the TIRF REMS, a restricted distribution program. Only prescribers, pharmacies, and patients enrolled in the program can prescribe, dispense, and/or receive Transmucosal Immediate-Release Fentanyl medicines

Prescriber Information

Individual NPI Number

Use individual NPI to poplute form: 1310000000

(Select address type to populate form)

(•) Office Address ( ) Mailing Address

First Name*: Test

M.I.: A

Last Name*: Prescriber000000

Specialty*: Internal Medicine

Credentials*: ( ) MD ( ) NP ( ) PA ( ) DO ( ) Other

Clinic / Practice Name*: Clinic / Practice Name

Address Line 1*: 1111 LION ROAD

Address Line 2: Address Line 2

City*: SomeWhere

State*: Pennsylvania

Zip Code*: 11111

Number*: 111-111-1111

Extension: nnn...

Fax: 111-111-1111

Email Address*: PR1310000000@examoto.net

Preferred Time of Contact*: ( ) Morning ( ) Afternoon ( ) Evening

Preferred Method of Contact*: (•) Email ( ) Text to Mobile# ( ) Phone Call

Office Contact

First Name*: PRSally

Last Name*: StaffJones

Number*: 378-407-4338

Fax: Fax

Email Address*: PRStaff@examoto.net

Preferred Time of Contact*: ( ) Morning ( ) Afternoon ( ) Evening

Preferred Method of Contact*: ( ) Email ( ) Text to Mobile# (•) Phone Call

Prescriber Agreement

By signing below, you attest to the following:

I have:

- Reviewed each drug's **Prescribing Information.**
- Reviewed the **Prescriber Education.**
- Successfully completed the **Prescriber Knowledge Assessment** and submitted it to the REMS.

Before treatment initiation, I must:

- Assess the patient for risk factors of opioid addiction, abuse, and misuse including personal and family history of substance abuse or mental illness.
- Counsel the patient on the safe use of TIRF medicines using the **Medication Guide** for the prescribed TIRF medicine and the **Patient Counseling Guide.**
- Provide a copy of the materials to the patient.
- Assess the patient's opioid tolerance.
- Document the patient's opioid tolerance using the **Patient Enrollment Form** and submit to the REMS.
- Enroll the patient by completing and submitting the **Patient Enrollment Form** to the REMS.

During treatment, and before each prescription, I must:

- Assess the patient's health status for opioid tolerance, appropriateness of dose, misuse, abuse, addiction, and overdose.
- Document and submit to the REMS using the **Patient Status and Opioid Tolerance Form.**

During treatment, every 2 years, I must:

- Counsel the patient on the safe use of TIRF medicines using the **Medication Guide** for the prescribed TIRF medicine, and the **Patient Counseling Guide.**
- Provide a copy of the materials to the patient.
- Re-enroll the patient in the REMS by completing the **Patient Enrollment Form** and submitting it to the REMS.

Before treatment re-initiation, after a lapse in treatment of 6 months or longer, I must:

- Counsel the patient on the safe use of TIRF medicines using the **Medication Guide** for the prescribed TIRF medicine and the **Patient Counseling Guide.**
- Provide a copy of the materials to the patient.

At all times, I must:

- Counsel the patient using the **Medication Guide** for any new TIRF medicine not previously prescribed, and provide a copy to the patient.
- Report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose to the REMS using the **Adverse Events of Special Interest Reporting Form.**
- Report treatment discontinuation to the REMS using the **Patient Discontinuation Form.**

To maintain certification to prescribe, every 2 years, I must:

- Review each drug's **Prescribing Information.**
- Review the **Prescriber Education**
- Successfully complete the **Prescriber Knowledge Assessment** and submit it to the REMS.
- Re-enroll in the REMS by completing the **Prescriber Enrollment Form.**

Sign | Type Signature

Clear

PRJane PRDoe: Please use your mouse or stylus to sign below

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Prescriber

1310000000

Prescriber Certification

You are currently certified.

PRJane PRDoe

Certified as of 4/20/2020

Edit

Counsel Patient

Before you enroll, counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Remember to provide a copy of these materials to the patient.

- Company1MG
- Company2MG
- Company3MG
- Company4MG
- Company5MG
- Company6MG

Print Patient Counseling Guide

Enroll Patients in the TIRF REMS

Complete this form with your patient to enroll them in the TIRF REMS. **A patient must be enrolled in the TIRF REMS** to receive treatment.

→ Enroll Patient

Manage Patients

Manage your patients. Enter Patient Status and Opioid Tolerance, Discontinuation, and Adverse Events of Special Interest Reporting Forms.

→ Manage Patients

Prescriber Materials

- Prescriber Education
- Prescriber Knowledge Assessment
- Prescriber Enrollment Form
- Patient Counseling Guide
- Patient Status and Opioid Tolerance Form
- Patient Discontinuation Form
- Adverse Events of Special Interest Reporting Form
- Prescriber FAQs

Upload Enrollment Form

Uploads must be in PDF format.

Browse

Or drop files here

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Prescriber

1310000001

Prescriber Certification

You must certify in the TIRF REMS to prescribe Transmucosal Immediate-Release Fentanyl medicines. To certify please complete the following:

1 Review the Prescriber Materials

Review each drug's Prescribing Information

- CompanyPI1
- CompanyPI2
- CompanyPI3
- CompanyPI4
- CompanyPI5
- CompanyPI6

Review the Prescriber Education.

2 Complete the Prescriber Knowledge Assessment

Successfully complete the Prescriber Knowledge Assessment and submit it to the TIRF REMS.

Online or Print

3 Complete the Prescriber Enrollment Form

Enroll in the TIRF REMS by completing the Prescriber Enrollment Form and submitting it to the TIRF REMS.

PRPat PRDoe

Enrolled as of 4/20/2020

Edit

Counsel Patient

Before you enroll, counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Remember to provide a copy of these materials to the patient.

- Company1MG
- Company2MG
- Company3MG
- Company4MG
- Company5MG
- Company6MG

Print Patient Counseling Guide

Enroll Patients in the TIRF REMS

Complete this form with your patient to enroll them in the TIRF REMS. A patient must be enrolled in the TIRF REMS to receive treatment.

→ Enroll Patient

Manage Patients

Manage your patients. Enter Patient Status and Opioid Tolerance, Discontinuation, and Adverse Events of Special Interest Reporting Forms.

→ Manage Patients

Prescriber Materials

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- Prescriber FAQs

Upload Enrollment Form

Uploads must be in PDF format.

Browse Or drop files here

Prescriber

1310000001

Prescriber Certification

You must certify in the TIRF REMS to prescribe Transmucosal Immediate-Release Fentanyl medicines. To certify please complete the following:

1 Review the Prescriber Materials

Review each drug's Prescribing Information

- CompanyPI1
- CompanyPI2
- CompanyPI3
- CompanyPI4
- CompanyPI5
- CompanyPI6

Review the Prescriber Education.

2 Complete the Prescriber Knowledge Assessment

Successfully complete the Prescriber Knowledge Assessment and submit it to the TIRF REMS.

3 Complete the Prescriber Enrollment Form

Enroll in the TIRF REMS by completing the Prescriber Enrollment Form and submitting it to the TIRF REMS.

Online or Print

PRPat PRDoe

Enrolled as of 4/20/2020

Edit

Counsel Patient

Before you enroll, counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Remember to provide a copy of these materials to the patient.

- Company1MG
- Company2MG
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To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Prescriber

1310000000

Re-Certify Notice

Your TIRF REMS certification will soon expire. To dispense Transmucosal Immediate-Release Fentanyl medicines you must:

1 **Review the Prescriber Materials**

Review each drug's Prescribing Information

- CompanyPI1
- CompanyPI2
- CompanyPI3
- CompanyPI4
- CompanyPI5
- CompanyPI6

Review the Prescriber Education.

2 **Complete the Prescriber Knowledge Assessment**

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Online or Print

3 Complete the Prescriber Enrollment Form

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PRJane PRDoe

Certified as of 4/20/2020

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Prescriber

1310000002

Re-Certify Notice

Your TIRF REMS certification has expired. To dispense Transmucosal Immediate-Release Fentanyl medicines you must:

1 Review the Prescriber Materials

Review each drug's Prescribing Information

- CompanyPI1
- CompanyPI2
- CompanyPI3
- CompanyPI4
- CompanyPI5
- CompanyPI6

Review the Prescriber Education.

2 Complete the Prescriber Knowledge Assessment

Successfully complete the Prescriber Knowledge Assessment and submit it to the TIRF REMS.

Online or Print

3 Complete the Prescriber Enrollment Form

Enroll in the TIRF REMS by completing the Prescriber Enrollment Form and submitting it to the TIRF REMS.

PRTom PRSmith

Decertified

Edit

Counsel Patient

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Prescriber

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PRPat PRDoe

Enrolled as of 4/20/2020

Edit

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→ Manage Patients

Prescriber

PRJane PRDoe

Prescriber

Individual NPI Number*

1310000000

First Name* PRJane

Middle Initial Middle Initial

Last Name* PRDoe

Clinic / Practice Name*

Test Prescriber Practice

Specialty* Specialty

Credentials* ○ MD ○ NP ○ PA ○ DO ○ Other

Address Line 1* 12 Parker Avenue

Address Line 2 Address Line 2

City* Chambersburg

State* Pennsylvania

Zip Code* 17201

Number* 420-689-9443

Extension nnn...

Fax 209-772-0961

Email Address* PR1310000000@examoto.net

Preferred Time of Contact*

○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*

◉ Email ○ Text to Mobile# ○ Phone Call

Office Contact

First Name* PRSally

Last Name* StaffJones

Number* 378-407-4338

Fax Fax

Email Address* PRStaff@examoto.net

Preferred Time of Contact*

○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*

○ Email ○ Text to Mobile# ◉ Phone Call

Cancel Save

Manage Patients

PRJane PRDoe
Certified Prescriber
Certified: 15th July, 2014

Find Patient

You can search for a patient already registered in the TIRF REMS and transfer them to your care.

1 **Find a patient by entering the patient's information below:**

First Name: First Name

Last Name: NotFound

Date of Birth: mm/dd/yyyy

Phone Or Email: Phone Or Email

There are errors, please correct the items below:

- Patient cannot be found, please contact the TIRF REMS Call Center or enroll the patient.

Clear | Find

Manage Patients

Manage your patients. Enter Patient Status and Opioid Tolerance, Discontinuation, and Adverse Events of Special Interest Reporting Forms.

Enroll Patient

Show 10 entries

Search My Patient List:

Edit	Name	Date of Birth	Phone	Action
	PatientJulie Williams	6/13/1970		Continuation | Discontinuation | Report AESI
	PatientTerry Smith	9/22/1989		Continuation | Discontinuation | Report AESI
	PatientPat Smith	7/15/1965		Continuation | Discontinuation | Report AESI
	PatientPat Smith	6/27/1954		Continuation | Discontinuation | Report AESI
	PatientAli Smith	4/4/1962		Continuation | Discontinuation | Report AESI

Edit

Showing 1 to 5 of 5 entries

Previous 1 Next

Return

Manage Patients

PRJane PRDoe
Certified Prescriber
Certified: 15th July, 2014

Find Patient

You can search for a patient already registered in the TIRF REMS and transfer them to your care.

1 **Find a patient by entering the patient's information below:**

First Name: First Name

Last Name: Miller

Date of Birth: mm/dd/yyyy

Phone Or Email: Phone Or Email

Match Found

PatientJenn Miller (DOB:10/31/1985)

2 **You may now add this patient to your Managed Patients. To reset search, hit Clear.** Add Patient | Clear

Manage Patients

Manage your patients. Enter Patient Status and Opioid Tolerance, Discontinuation, and Adverse Events of Special Interest Reporting Forms.

Enroll Patient

Show 10 entries

Search My Patient List:

Edit	Name	Date of Birth	Phone	Action
	PatientJulie Williams	6/13/1970		Continuation | Discontinuation | Report AESI
	PatientTerry Smith	9/22/1989		Continuation | Discontinuation | Report AESI
	PatientPat Smith	7/15/1965		Continuation | Discontinuation | Report AESI
	PatientPat Smith	6/27/1954		Continuation | Discontinuation | Report AESI
	PatientAli Smith	4/4/1962		Continuation | Discontinuation | Report AESI

Edit

Showing 1 to 5 of 5 entries

Previous 1 Next

Return

Manage Patients

PRJane PRDoe
Certified Prescriber
Certified: 15th July, 2014

Find Patient

You can search for a patient already registered in the TIRF REMS and transfer them to your care.

1 **Find a patient by entering the patient's information below:**

First Name	Last Name	Date of Birth
First Name	Last Name	mm/dd/yyyy

Phone Or Email

Phone Or Email

Clear | Find

Manage Patients

Manage your patients. Enter Patient Status and Opioid Tolerance, Discontinuation, and Adverse Events of Special Interest Reporting Forms.

Enroll Patient

Show 10 entries

Search My Patient List:

Edit	Name	Date of Birth	Phone	Action
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Edit

Showing 1 to 5 of 5 entries

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Return

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Patient Discontinuation Form

Patient Discontinuation Form

This form must be completed and submitted to the TIRF REMS by the prescriber when a patient discontinues treatment with TIRF REMS for any reason.

PatientTerry Smith — Enrolled as of 6/26/2019

Date of Birth:	9/22/1989	Mobile Phone:	920-727-3214
Address:	273 New Saddle Lane Hickory, NC 28601	Home Phone:	

Discontinuation of a TIRF Medicine

Date TIRF medicine was discontinued:

MM/DD/YYYY

Reason for discontinuation (check all that apply):

- [ ] No longer required to manage pain
- [ ] No longer on around-the-clock Opioid
- [ ] Death
  - Date of Death: N/A Cause of Death: N/A
- [ ] Adverse event (if AESI, list below)
- [ ] Other (financial reasons, patient preference, etc.)

Adverse Events of Special Interest (AESI)

Adverse events that MUST be reported to the TIRF medicines REMS:

- Accidental exposure
- Addiction
- Misuse
- Overdose
- Abuse
- Other serious adverse event

To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*

○ Yes ○ No

If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Patient Discontinuation Form

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Date TIRF medicine was discontinued:

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- ☐ No longer required to manage pain
- ☐ No longer on around-the-clock Opioid
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  - Date of Death: N/A Cause of Death: N/A
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To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*

◉ Yes ○ No

Check all that apply

- ☐ Experienced an overdose of their TIRF medicines medicine (**Overdose** - ingestion of an excessive amount of drug that is considered lethal or toxic, either intentionally or accidentally)
- ☐ Shown signs or symptoms of addiction to their TIRF medicines medicine (**Addiction** – a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance. Signs and symptoms include: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal)
- ☐ Misused or been suspected of misusing their TIRF medicines medicine (**Misuse** - the use of a medicinal product without a prescription or in a manner other than as directed by a physician, including use without a prescription of one's own; use in greater amounts to feel euphoria (i.e. to get high), more often, or for a period longer than prescribed; or use in any other way not directed by the prescribing physician)
- ☐ Abused or been suspected of abusing their TIRF medicines medicine (**Abuse** - intentional non-therapeutic use of a medicinal product, even once, for its rewarding psychological or physiological or euphoric effect, and often associated with physical dependence)
- ☐ Someone else has been accidentally exposed to the patient's TIRF medicines medicine (**Accidental exposure** - unintended exposure of a medicinal product to someone other than to whom it was prescribed)
- ☐ Another serious adverse event (**Other serious adverse event** – any adverse event at any dose that results in death, is lifethreatening, requires inpatient hospitalization, or causes prolongation of existing hospitalization)

If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.

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Adverse Events of Special Interest Reporting Form

Adverse Events of Special Interest Reporting Form

Adverse events related to accidental exposure, misuse, abuse, addiction, overdose or other serious adverse events must be reported to the TIRF REMS. This form must be completed to report an adverse event of special interest to the TIRF REMS for any patient taking a TIRF medicine.

PatientTerry Smith — Enrolled as of 6/26/2019

Date of Birth:	9/22/1989	Mobile Phone:	920-727-3214
Address:	273 New Saddle Lane Hickory, NC 28601	Home Phone:	

Product Name	Product Strength	Dose*	Frequency*
-- Select Product --		Dose	Frequency

Adverse Events of Special Interest (AESI)

Adverse events that MUST be reported to the TIRF medicines REMS:

- Accidental exposure
- Addiction
- Misuse
- Overdose
- Abuse
- Other serious adverse event

To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*

○ Yes ○ No

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Sign | Type Signature

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Patient Status and Opioid Tolerance Form

Patient Status and Opioid Tolerance Form

You must complete and submit this form to the TIRF REMS prior to each subsequent prescription for outpatient use.

Prescriptions will not be authorized for dispensing until this continuation form is on file at the TIRF REMS.

Patient Terry Smith — Enrolled as of 6/26/2019

Date of Birth: 9/22/1989
Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:

Product Name* -- Select Product --
Product Strength*
Dose* Dose
Frequency* Frequency

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Medical Information

Type of Pain:*

○ Cancer Pain ○ Non-Cancer Pain

Adverse Events of Special Interest (AESI)

Adverse events that MUST be reported to the TIRF medicines REMS:

- Accidental exposure
- Addiction
- Misuse
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- Abuse
- Other serious adverse event

To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*

○ Yes ○ No

If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.

Verify Opioid Tolerance

Opioid Moiety* --Moiety--

Moiety/Strength/Route/Formulation*

Quantity* **Units*** **Frequency***

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately

Sign | Type Signature

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Product Name*	Product Strength*	Dose*	Frequency*
-- Select Product --		Dose	Frequency

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Medical Information

Type of Pain:*

○ Cancer Pain ○ Non-Cancer Pain

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Verify Opioid Tolerance

Opioid Moiety*

--Moiety--

Moiety/Strength/Route/Formulation*

Quantity*	Units*	Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Patient Status and Opioid Tolerance Form

Patient Status and Opioid Tolerance Form

You must complete and submit this form to the TIRF REMS prior to each subsequent prescription for outpatient use.
Prescriptions will not be authorized for dispensing until this continuation form s on file at the TIRF REMS.

PatientTerry Smith — Enrolled as of 6/26/2019

Date of Birth: 9/22/1989
Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:

Product Name* -- Select Product --
Product Strength*
Dose* Dose
Frequency* Frequency

Concomitant Medications (check all that apply):*

- [x] Benzodiazepines
- [ ] Barbiturates
- [ ] Prescription Insomnia Medications
- [ ] Gabapentinoids
- [x] Antipsychotics
- [ ] Other CNS depressant
- [ ] Sedative Hypnotics
- [ ] Sodium Oxybate
- [ ] None
- [ ] Tranquilizers
- [ ] Alcohol
- [ ] Muscle Relaxants
- [ ] Prescription Cannabinoids

Medical Information

Type of Pain:*

( ) Cancer Pain ( ) Non-Cancer Pain

Adverse Events of Special Interest (AESI)

Adverse events that MUST be reported to the TIRF medicines REMS:

- Accidental exposure
- Addiction
- Misuse
- Overdose
- Abuse
- Other serious adverse event

To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*

(•) Yes ( ) No

Check all that apply

- [ ] Experienced an overdose of their TIRF medicines medicine (**Overdose** - ingestion of an excessive amount of drug that is considered lethal or toxic, either intentionally or accidentally)
- [ ] Shown signs or symptoms of addiction to their TIRF medicines medicine (**Addiction** – a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance. Signs and symptoms include: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal)
- [ ] Misused or been suspected of misusing their TIRF medicines medicine (**Misuse** - the use of a medicinal product without a prescription or in a manner other than as directed by a physician, including use without a prescription of one's own; use in greater amounts to feel euphoria (i.e. to get high), more often, or for a period longer than prescribed; or use in any other way not directed by the prescribing physician)
- [ ] Abused or been suspected of abusing their TIRF medicines medicine (**Abuse** - intentional non-therapeutic use of a medicinal product, even once, for its rewarding psychological or physiological or euphoric effect, and often associated with physical dependence)
- [ ] Someone else has been accidentally exposed to the patient's TIRF medicines medicine (**Accidental exposure** - unintended exposure of a medicinal product to someone other than to whom it was prescribed)
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Verify Opioid Tolerance

Opioid Moiety* --Moiety--

Moiety/Strength/Route/Formulation*

Quantity* **Units*** **Frequency***

Moiety	Formulation	Strength	Route	Dose	Frequency

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Mobile Phone: 920-727-3214
Home Phone:

Product Name* -- Select Product --
Product Strength*
Dose* Dose
Frequency* Frequency

Concomitant Medication (check all that apply):*

- [x] Benzodiazepines
- [ ] Gabapentinoids
- [ ] Sedative Hypnotics
- [ ] Tranquilizers
- [ ] Muscle Relaxants
- [ ] Barbiturates
- [x] Antipsychotics
- [ ] Sodium Oxybate
- [ ] Alcohol
- [ ] Prescription Cannabinoids
- [ ] Prescription Insomnia Medications
- [ ] Other CNS depressant
- [ ] None

Medical Information

Type of Pain:*

○ Cancer Pain ○ Non-Cancer Pain

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--Moiety--

Moiety/Strength/Route/formulation*

Quantity* **Units*** **Frequency***

Moiety	Formulation	Strength	Route	Dose	Frequency

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- [ ] ≥ 25 mg oral oxymorphone/day
- [ ] An equianalgesic dose of another opioid
- [ ] ≥ 25 micrograms transdermal fentanyl/hour
- [ ] ≥ 8 mg oral hydromorphone/day
- [ ] ≥ 60 mg oral hydrocodone/day

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Address:	273 New Saddle Lane Hickory, NC 28601	Home Phone:	

Product Name*	Product Strength*	Dose*	Frequency*
-- Select Product --		Dose	Frequency

Concomitant Medications (check all that apply):*

- [x] Benzodiazepines
- [ ] Barbiturates
- [ ] Prescription Insomnia Medications
- [ ] Gabapentinoids
- [x] Antipsychotics
- [ ] Other CNS depressant
- [ ] Sedative Hypnotics
- [ ] Sodium Oxybate
- [ ] None
- [ ] Tranquilizers
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Medical Information

Type of Pain:*

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(•) Yes ( ) No

Check all that apply

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Verify Opioid Tolerance

Opioid Moiety*

Codeine

Moiety/Strength/Route/Formulation*

--Select--

Quantity*	Units*	Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

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Product Name* -- Select Product --
Product Strength*
Dose* Dose
Frequency* Frequency

Concomitant Medications (check all that apply):*

- [x] Benzodiazepines
- [ ] Barbiturates
- [ ] Prescription Insomnia Medications
- [ ] Gabapentinoids
- [x] Antipsychotics
- [ ] Other CNS depressant
- [ ] Sedative Hypnotics
- [ ] Sodium Oxybate
- [ ] None
- [ ] Tranquilizers
- [ ] Alcohol
- [ ] Muscle Relaxants
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Medical Information

Type of Pain:*

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Adverse Events of Special Interest (AESI)

Adverse events that MUST be reported to the TIRF medicines REMS

- Accidental exposure
- Addiction
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- Abuse
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To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*

(•) Yes ( ) No

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Verify Opioid Tolerance

Opioid Moiety*
Codeine

Moiety/Strength/Route/Formulation*
ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/60 mg) ORAL TABLET

Quantity* 2
Units* --Select--
Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for ore week or longer (check all that apply):*

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Date of Birth:	9/22/1989	Mobile Phone:	920-727-3214
Address:	273 New Saddle Lane Hickory, NC 28601	Home Phone:	

Product Name*	Product Strength*	Dose*	Frequency*
-- Select Product --		Dose	Frequency

Concomitant Medications (check all that apply):*

- [x] Benzodiazepines
- [ ] Barbiturates
- [ ] Prescription Insomnia Medications
- [ ] Gabapentinoids
- [x] Antipsychotics
- [ ] Other CNS depressant
- [ ] Sedative Hypnotics
- [ ] Sodium Oxybate
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Medical Information

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(•) Yes ( ) No

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Verify Opioid Tolerance

Opioid Moiety*

Codeine

Moiety/Strength/Route/Formulation*

ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/60 mg) ORAL TABLET

Quantity*	Units*	Frequency*
2	tablet(s)	--Select--

Moiety	Formulation	Strength	Route	Dose	Frequency

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Product Name* | Product Strength* | Dose* | Frequency*

-- Select Product -- | | Dose | Frequency

Concomitant Medications (check all that apply):*

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Verify Opioid Tolerance

Opioid Moiety*

--Moiety--

Moiety/Strength/Route/Formulation*

Quantity* | **Units*** | **Frequency***

	--Select--	--Select--

Moiety	Formulation	Strength	Route	Dose	Frequency	
ACETAMINOPHEN/CODEINE ANHYDROUS	TABLET	300 mg/60 mg	ORAL	2 tablet(s)	Three Times a Day	✖

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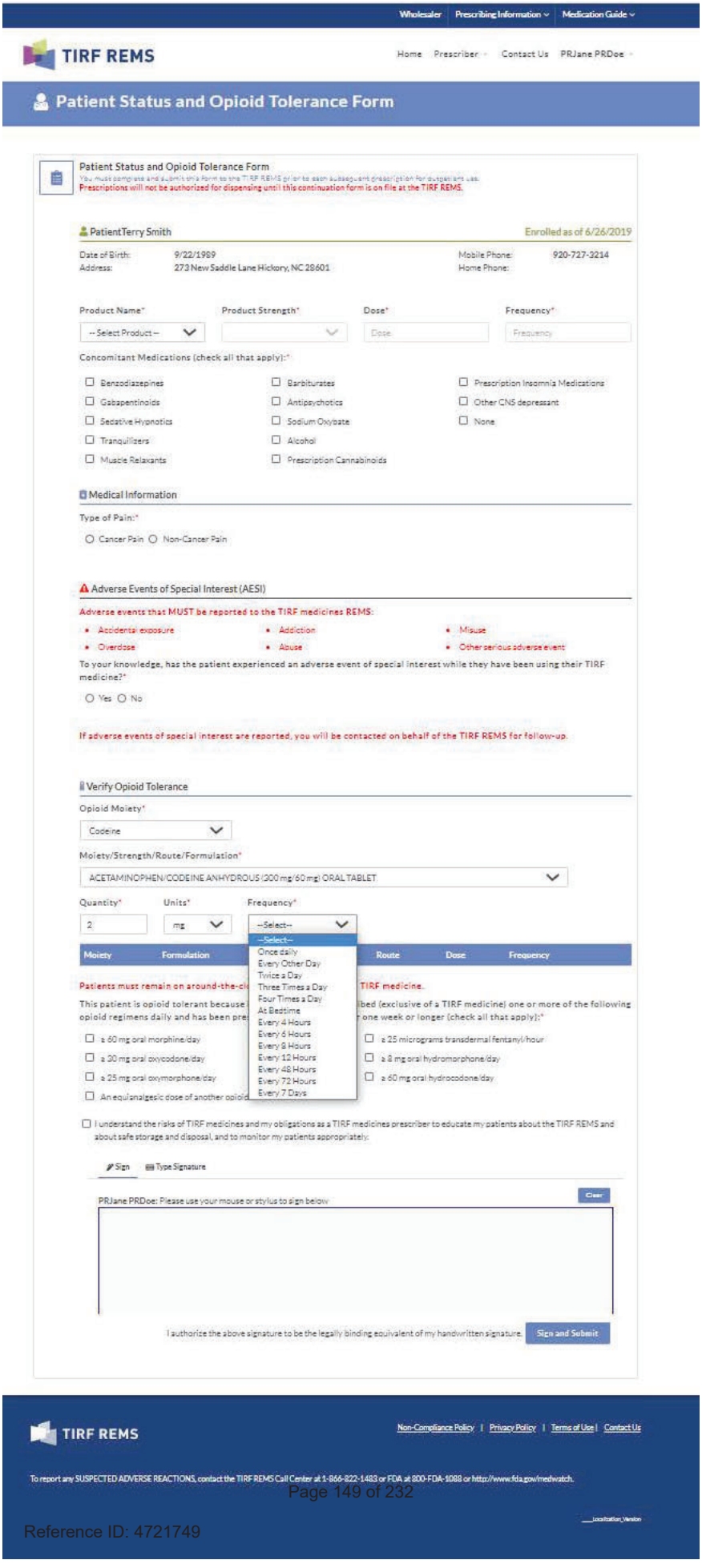

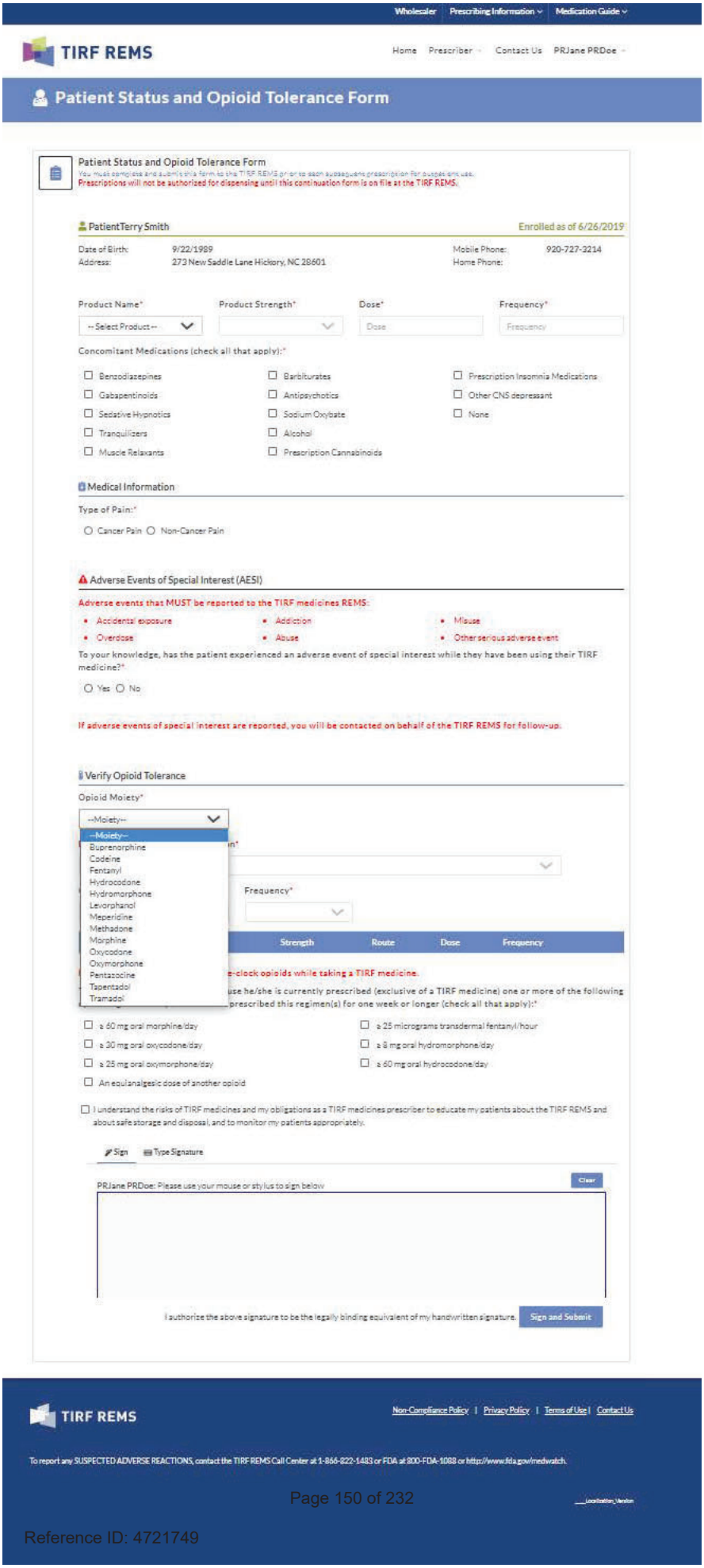
Wholesaler
Prescribing Information
Medication Guide
TIRF REMS
Home
Prescriber
Contact Us
PRJane PRDoe
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Mobile Phone: 920-727-3214
Home Phone:
Product Name*
--Select Product--
Product Strength*
Dose*
Dose
Frequency*
Frequency
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
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Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
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Medical Information
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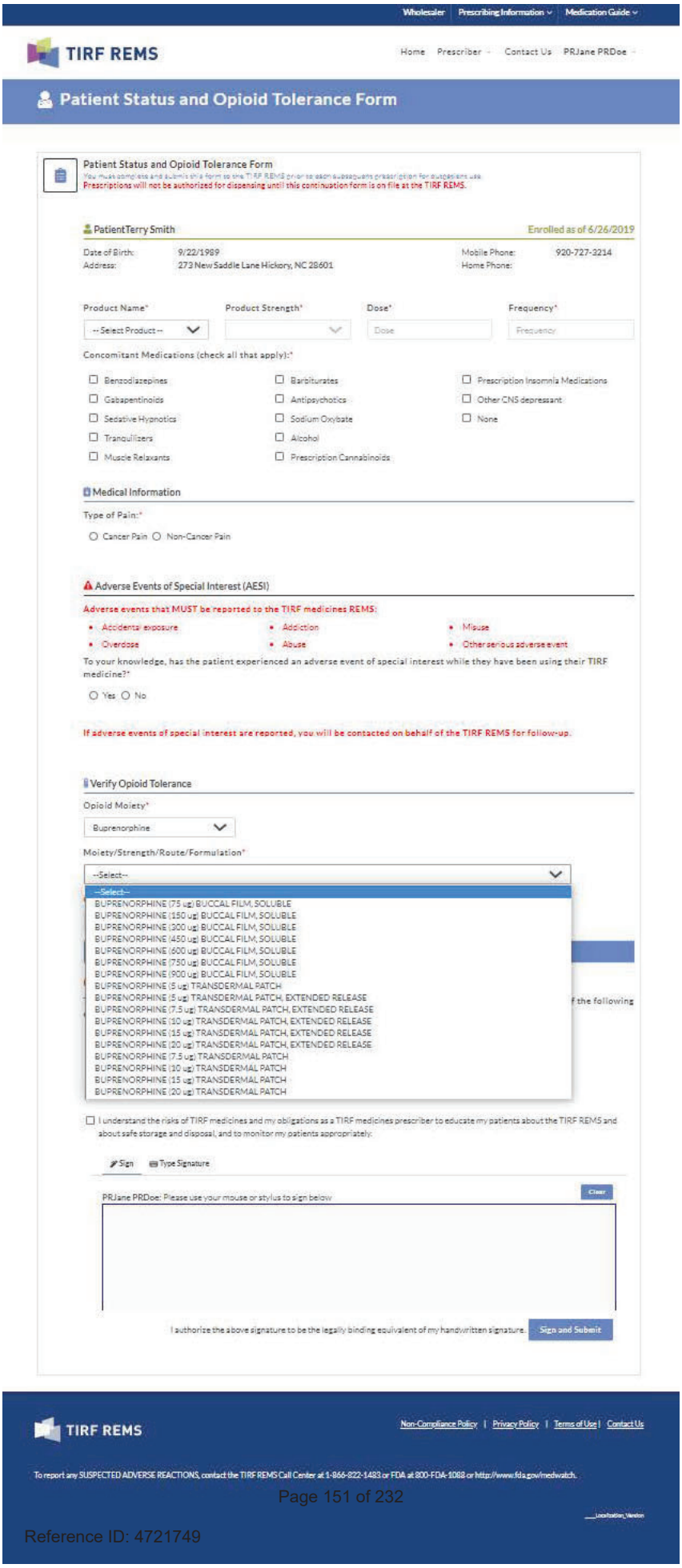
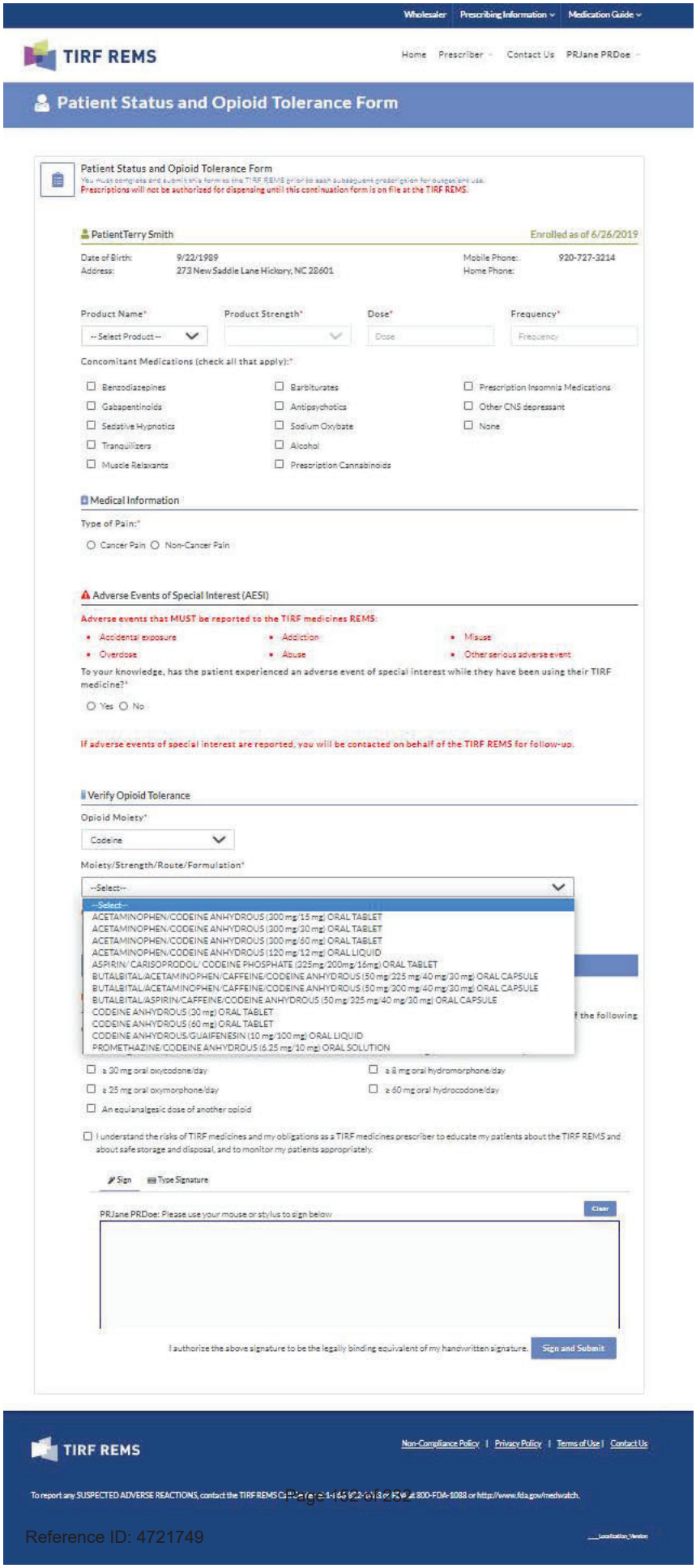
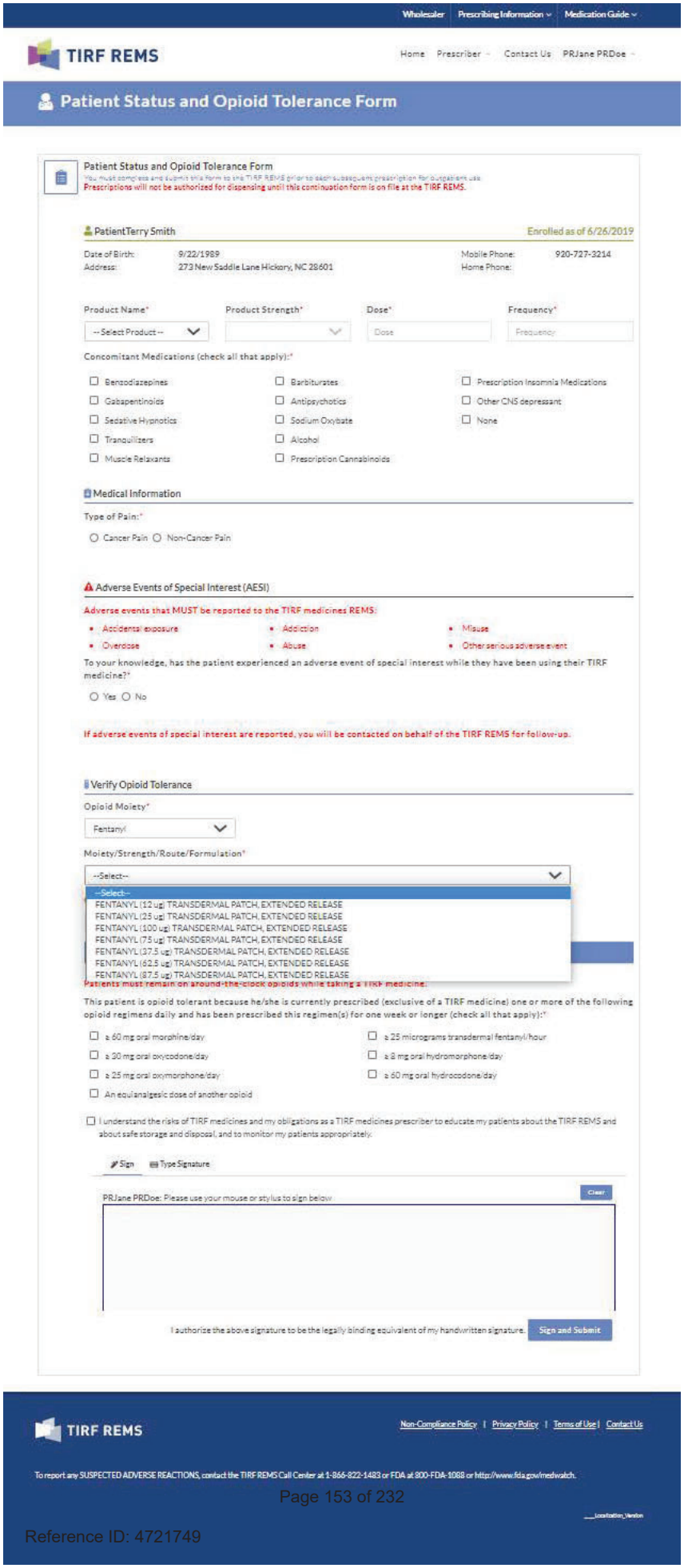
Cancer Pain
Non-Cancer Pain
Adverse Events of Special Interest (AESI)
Adverse events that MUST be reported to the TIRF medicines REMS:
Accidental exposure
Addiction
Misuse
Overdose
Abuse
Other serious adverse event
To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*
Yes
No
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.
Verify Opioid Tolerance
Opioid Moiety*
--Moiety--
--Moiety--
Buprenorphine
Codeine
Fentanyl
Hydrocodone
Hydromorphone
Levorphanol
Meperidine
Methadone
Morphine
Oxycodone
Oxymorphone
Pentazocine
Tapentadol
Tramadol
Frequency*
Strength
Route
Dose
Frequency
-clock opioids while taking a TIRF medicine.
use he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following
prescribed this regimen(s) for one week or longer (check all that apply):*
≥ 60 mg oral morphine/day
≥ 25 micrograms transdermal fentanyl/hour
≥ 30 mg oral oxycodone/day
≥ 8 mg oral hydromorphone/day
≥ 25 mg oral oxymorphone/day
≥ 60 mg oral hydrocodone/day
An equianalgesic dose of another opioid
I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
Sign and Submit
TIRF REMS
Non-Compliance Policy | Privacy Policy | Terms of Use | Contact Us
To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.



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PRJane PRDoe
Patient Status and Opioid Tolerance Form
Patient Status and Opioid Tolerance Form
You must complete and submit this form to the TIRF REMS prior to each subsequent prescription for outpatient use.
Prescriptions will not be authorized for dispensing until this continuation form is on file at the TIRF REMS.
Patient Terry Smith
Enrolled as of 6/26/2019
Date of Birth: 9/22/1989
Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:
Product Name*
-- Select Product --
Product Strength*
Dose*
Dose
Frequency*
Frequency
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
Antipsychotics
Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
Tranquilizers
Alcohol
Muscle Relaxants
Prescription Cannabinoids
Medical Information
Type of Pain:*
Cancer Pain
Non-Cancer Pain
Adverse Events of Special Interest (AESI)
Adverse events that MUST be reported to the TIRF medicines REMS:
Accidental exposure
Addiction
Misuse
Overdose
Abuse
Other serious adverse event
To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*
Yes
No
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.
Verify Opioid Tolerance
Opioid Moiety*
Fentanyl
Moiety/Strength/Route/Formulation*
--Select--
--Select--
FENTANYL (12 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (25 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (100 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (75 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (37.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (62.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (87.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
Patients must remain on around-the-clock opioids while taking a TIRF medicine.
This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*
≥ 60 mg oral morphine/day
≥ 25 micrograms transdermal fentanyl/hour
≥ 30 mg oral oxycodone/day
≥ 8 mg oral hydromorphone/day
≥ 25 mg oral oxymorphone/day
≥ 60 mg oral hydrocodone/day
An equianalgesic dose of another opioid
I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
Sign and Submit
TIRF REMS
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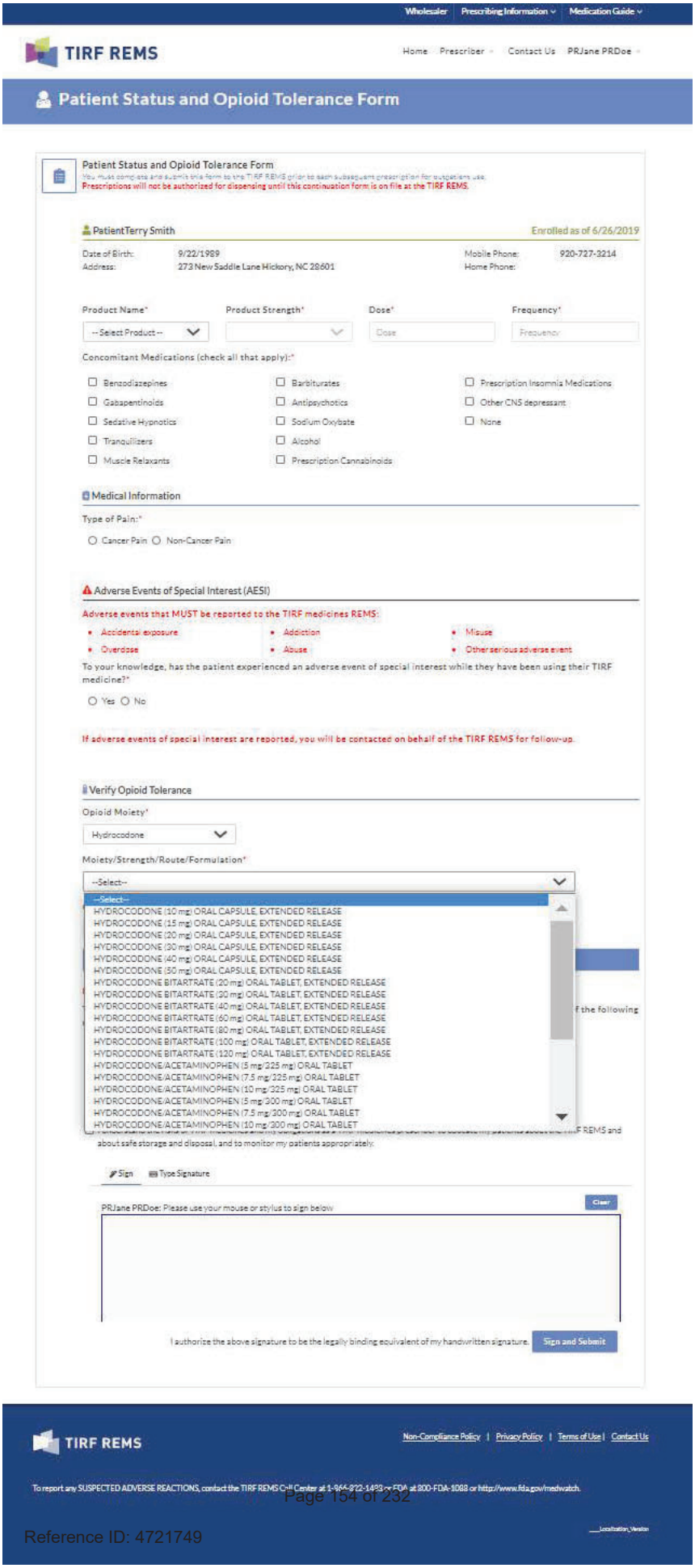

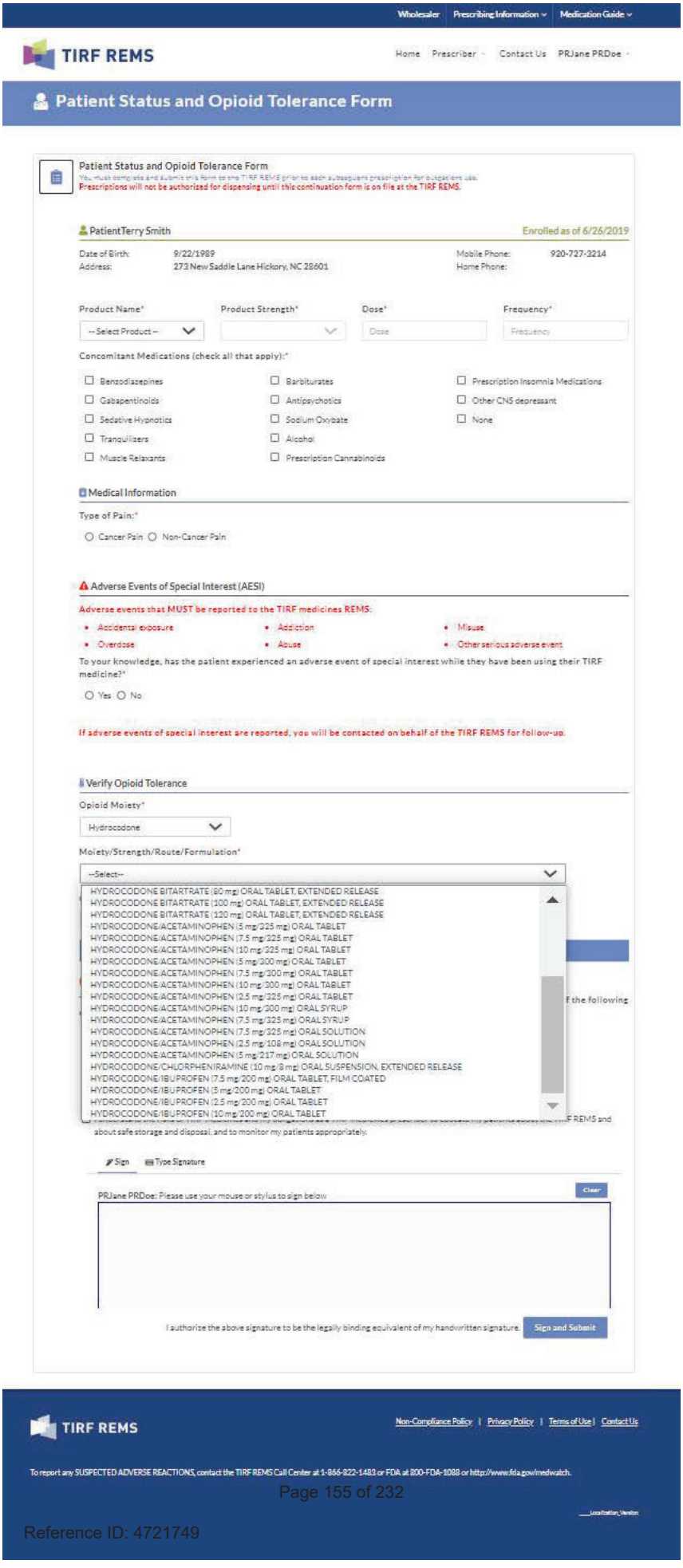

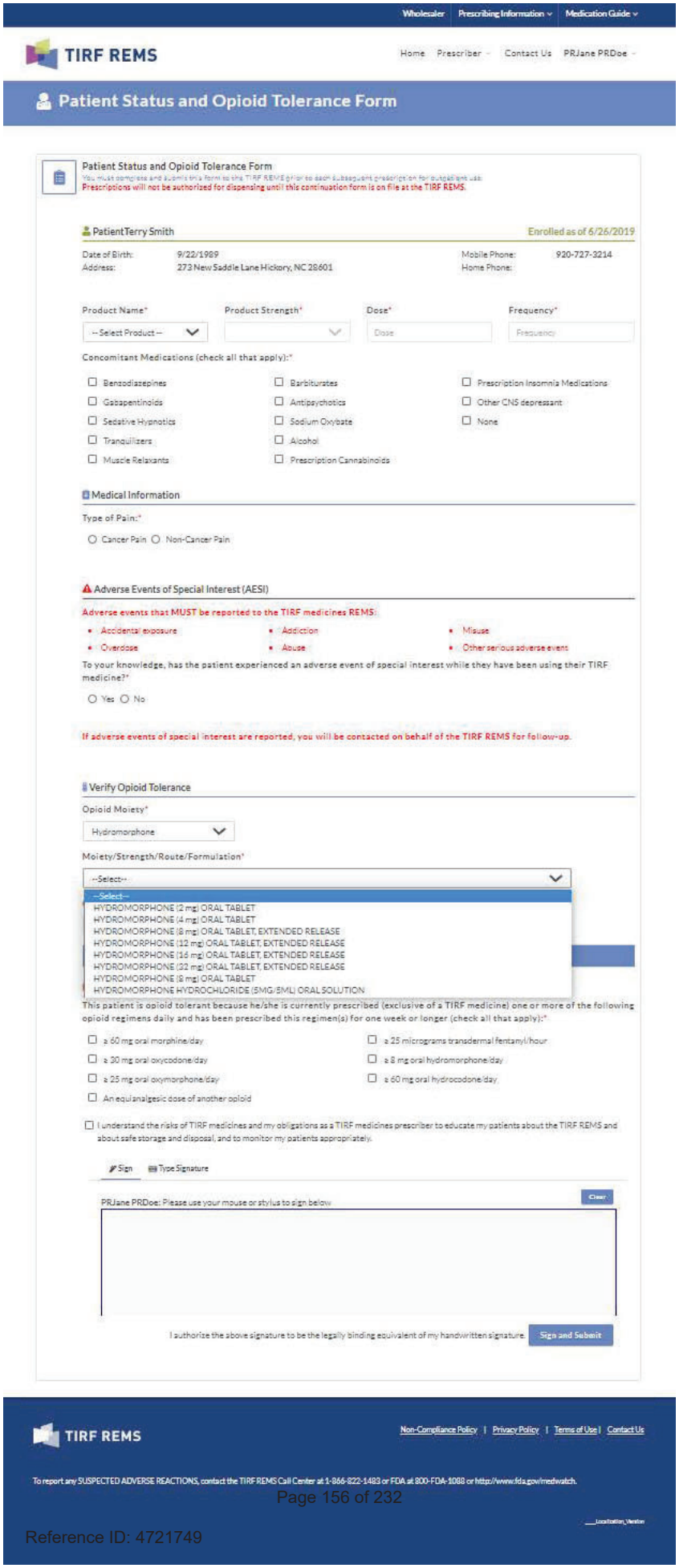

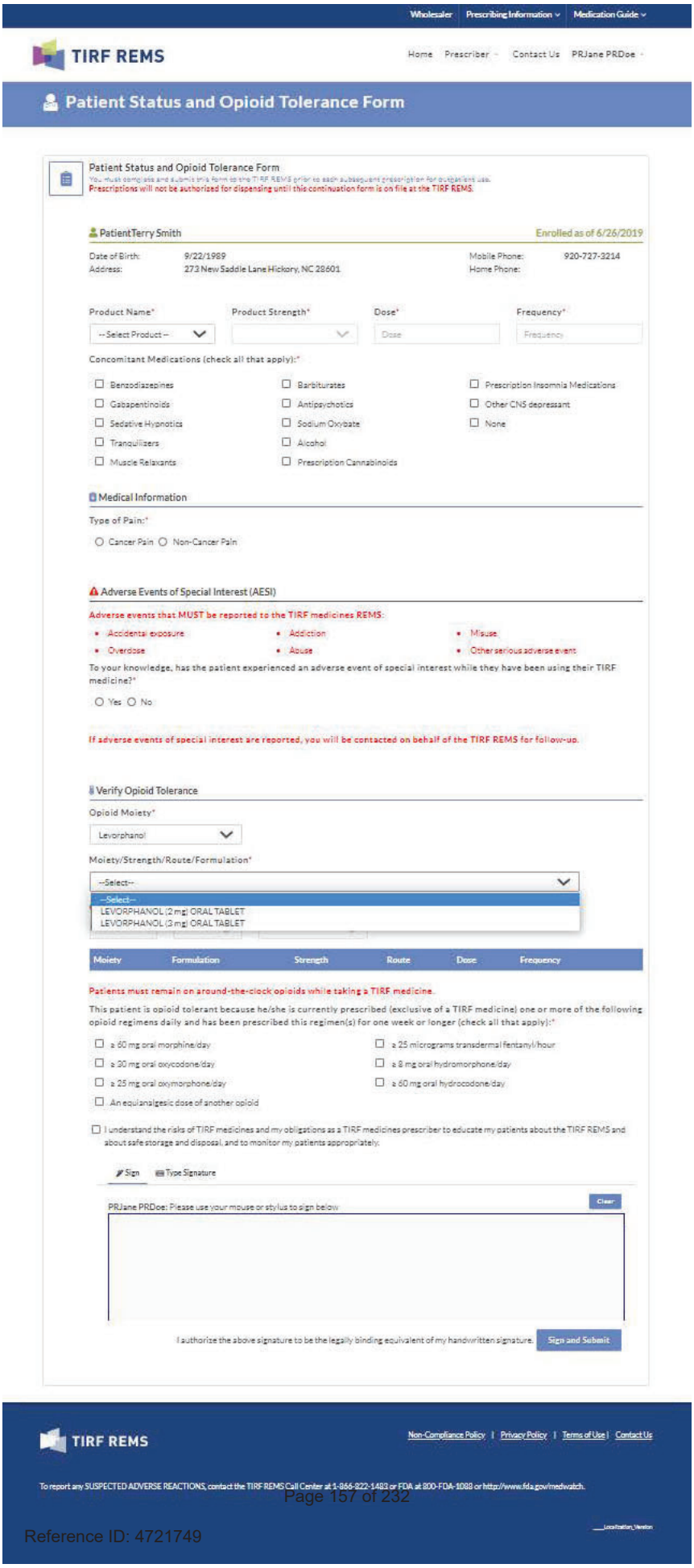

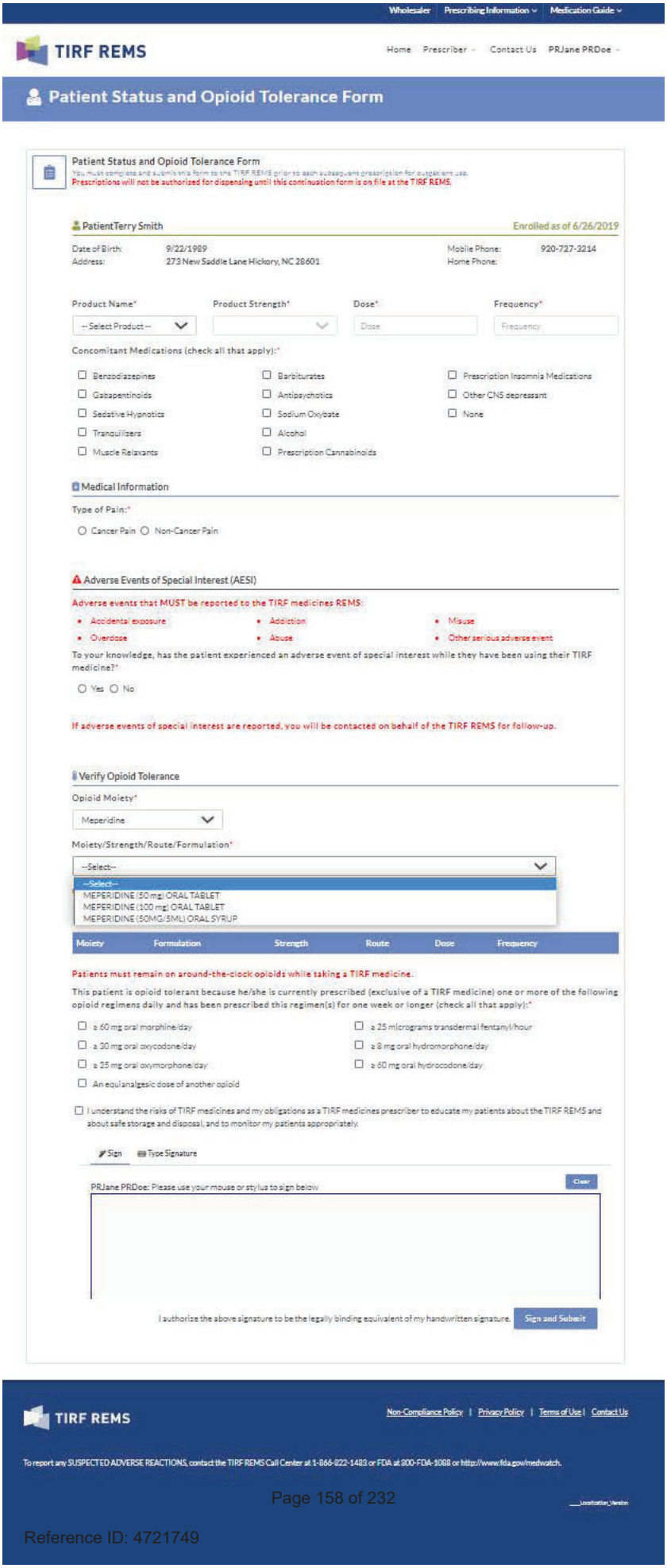

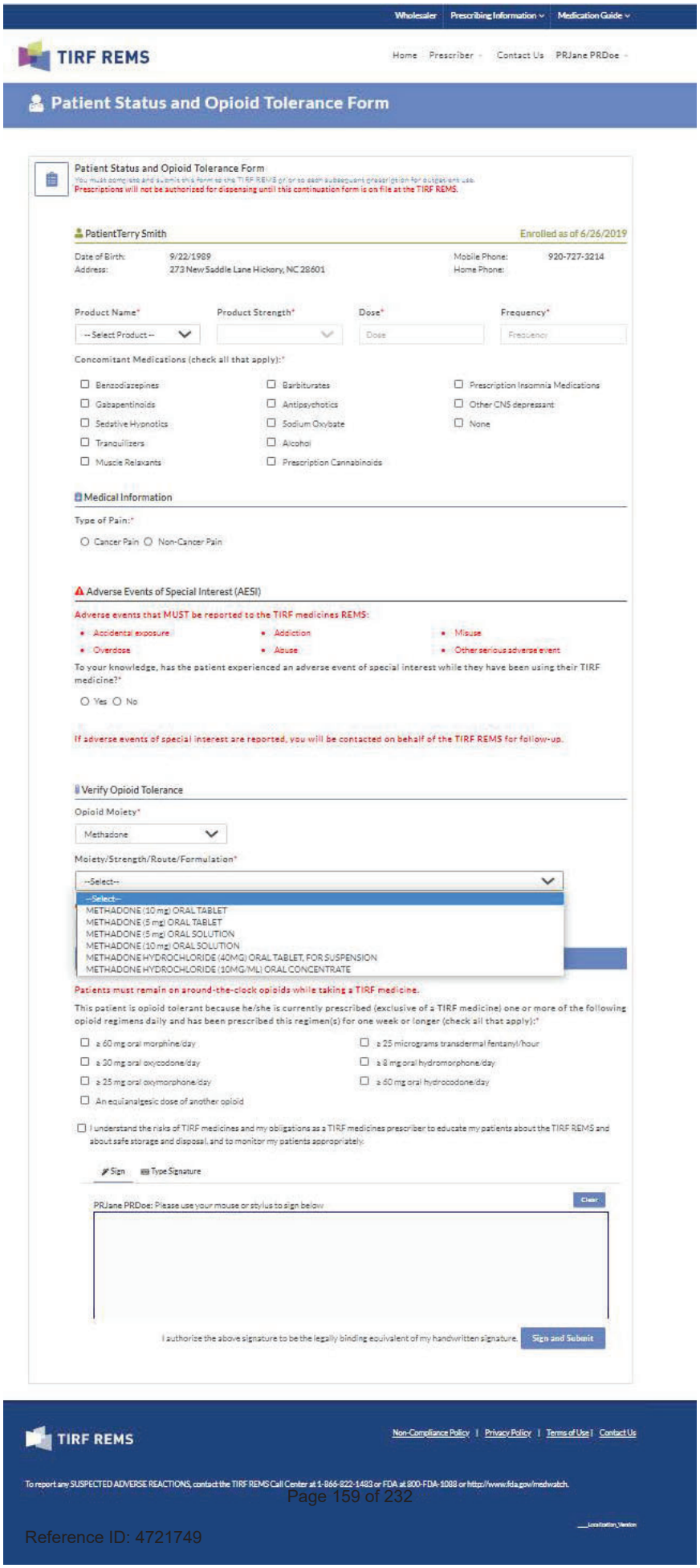
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Enrolled as of 6/26/2019
Date of Birth: 9/22/1989
Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:
Product Name*
-- Select Product --
Product Strength*
Dose*
Dose
Frequency*
Frequency
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
Antipsychotics
Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
Tranquilizers
Alcohol
Muscle Relaxants
Prescription Cannabinoids
Medical Information
Type of Pain:*
Cancer Pain
Non-Cancer Pain
Adverse Events of Special Interest (AESI)
Adverse events that MUST be reported to the TIRF medicines REMS:
Accidental exposure
Addiction
Misuse
Overdose
Abuse
Other serious adverse event
To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*
Yes
No
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.
Verify Opioid Tolerance
Opioid Moiety*
Methadone
Moiety/Strength/Route/Formulation*
--Select--
--Select--
METHADONE (10 mg) ORAL TABLET
METHADONE (5 mg) ORAL TABLET
METHADONE (5 mg) ORAL SOLUTION
METHADONE (10 mg) ORAL SOLUTION
METHADONE HYDROCHLORIDE (40MG) ORAL TABLET, FOR SUSPENSION
METHADONE HYDROCHLORIDE (10MG/ML) ORAL CONCENTRATE
Patients must remain on around-the-clock opioids while taking a TIRF medicine.
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≥ 25 micrograms transdermal fentanyl/hour
≥ 30 mg oral oxycodone/day
≥ 8 mg oral hydromorphone/day
≥ 25 mg oral oxymorphone/day
≥ 60 mg oral hydrocodone/day
An equianalgesic dose of another opioid
I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
Sign and Submit
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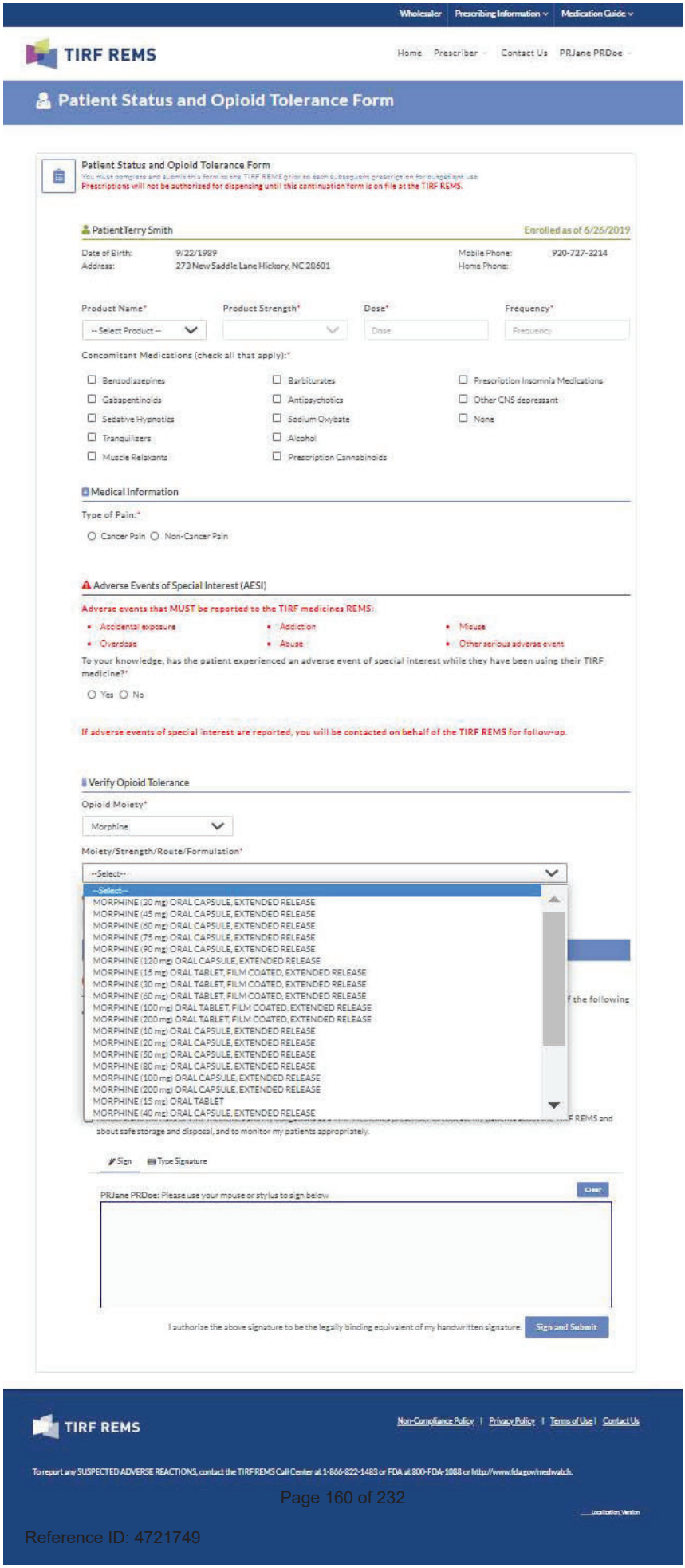

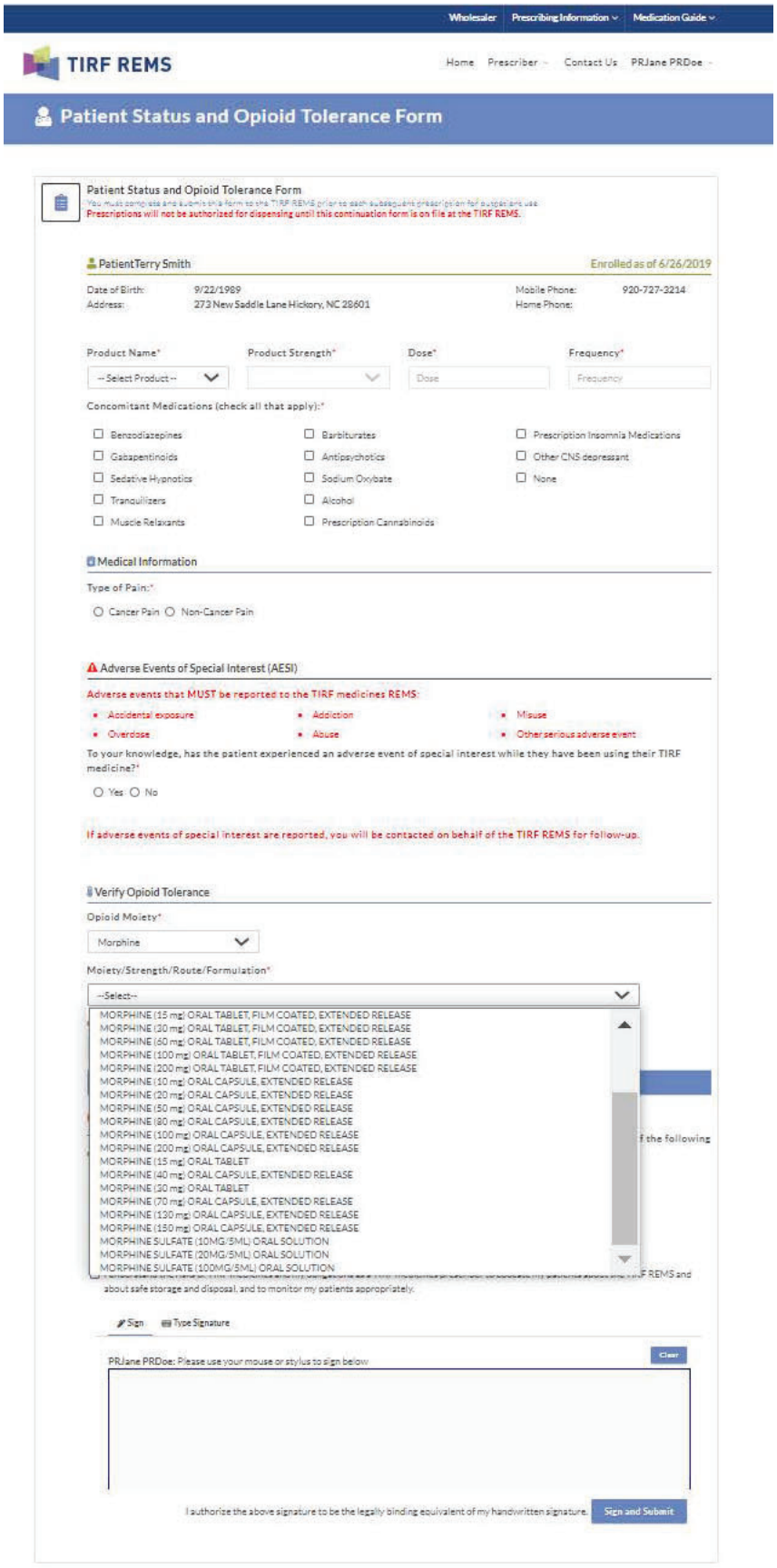
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Patient Status and Opioid Tolerance Form
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PatientTerry Smith
Enrolled as of 6/26/2019
Date of Birth: 9/22/1989
Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:
Product Name*
-- Select Product --
Product Strength*
Dose*
Dose
Frequency*
Frequency
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
Antipsychotics
Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
Tranquilizers
Alcohol
Muscle Relaxants
Prescription Cannabinoids
Medical Information
Type of Pain:*
Cancer Pain
Non-Cancer Pain
Adverse Events of Special Interest (AESI)
Adverse events that MUST be reported to the TIRF medicines REMS:
Accidental exposure
Addiction
Misuse
Overdose
Abuse
Other serious adverse event
To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*
Yes
No
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.
Verify Opioid Tolerance
Opioid Moiety*
Morphine
Moiety/Strength/Route/Formulation*
--Select--
MORPHINE (15 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (30 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (60 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (100 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (200 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (10 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (20 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (50 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (80 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (100 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (200 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (15 mg) ORAL TABLET
MORPHINE (40 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (30 mg) ORAL TABLET
MORPHINE (70 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (130 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (150 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE SULFATE (10MG/5ML) ORAL SOLUTION
MORPHINE SULFATE (20MG/5ML) ORAL SOLUTION
MORPHINE SULFATE (100MG/5ML) ORAL SOLUTION
f the following
F REMS and
about safe storage and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
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TIRF REMS
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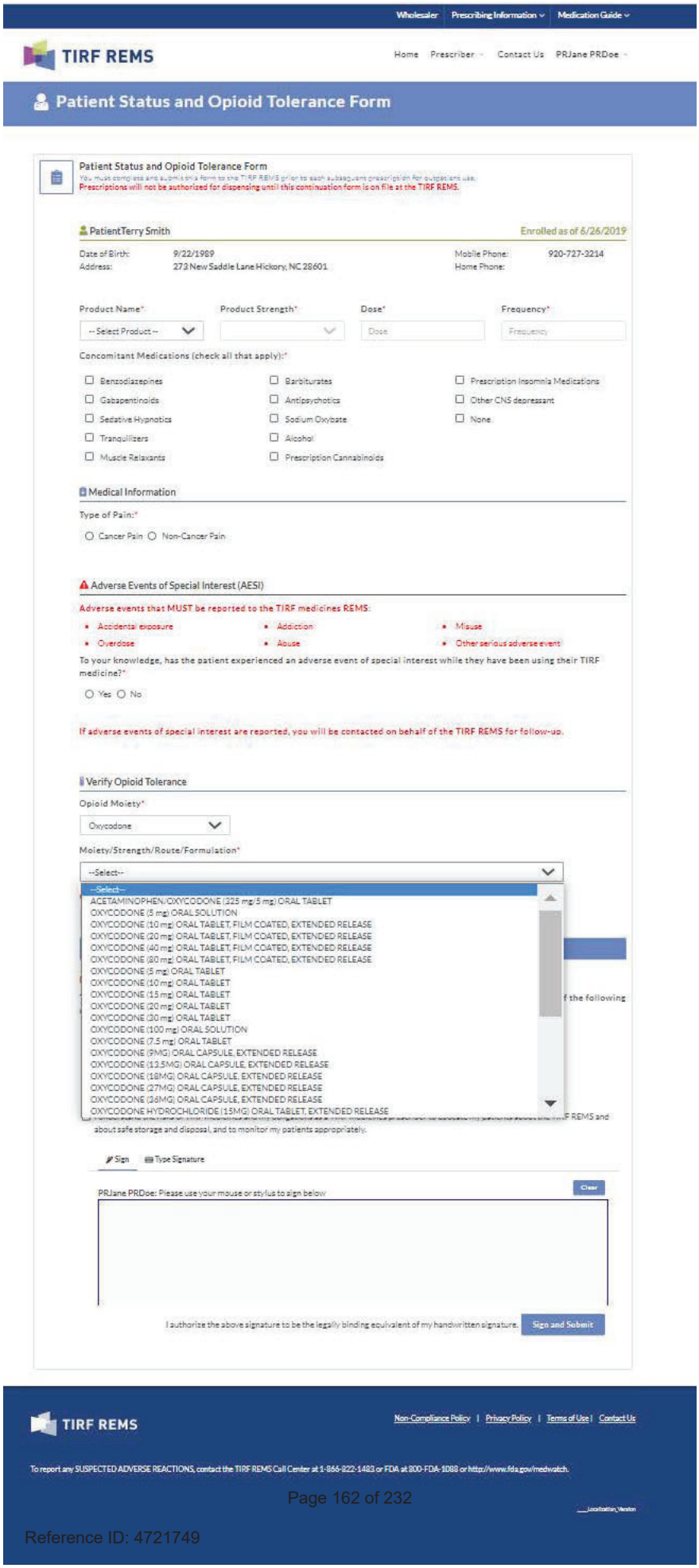
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PatientTerry Smith
Enrolled as of 6/26/2019
Date of Birth: 9/22/1989
Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:
Product Name*
-- Select Product --
Product Strength*
Dose*
Dose
Frequency*
Frequency
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
Antipsychotics
Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
Tranquilizers
Alcohol
Muscle Relaxants
Prescription Cannabinoids
Medical Information
Type of Pain:*
Cancer Pain
Non-Cancer Pain
Adverse Events of Special Interest (AESI)
Adverse events that MUST be reported to the TIRF medicines REMS:
Accidental exposure
Addiction
Misuse
Overdose
Abuse
Other serious adverse event
To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*
Yes
No
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.
Verify Opioid Tolerance
Opioid Moiety*
Oxycodone
Moiety/Strength/Route/Formulation*
--Select--
--Select--
ACETAMINOPHEN/OXYCODONE (325 mg/5 mg) ORAL TABLET
OXYCODONE (5 mg) ORAL SOLUTION
OXYCODONE (10 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (20 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (40 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (80 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (5 mg) ORAL TABLET
OXYCODONE (10 mg) ORAL TABLET
OXYCODONE (15 mg) ORAL TABLET
OXYCODONE (20 mg) ORAL TABLET
OXYCODONE (30 mg) ORAL TABLET
OXYCODONE (100 mg) ORAL SOLUTION
OXYCODONE (7.5 mg) ORAL TABLET
OXYCODONE (9MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (13.5MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (18MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (27MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (36MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE HYDROCHLORIDE (1.5MG) ORAL TABLET, EXTENDED RELEASE
f the following
about safe storage and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
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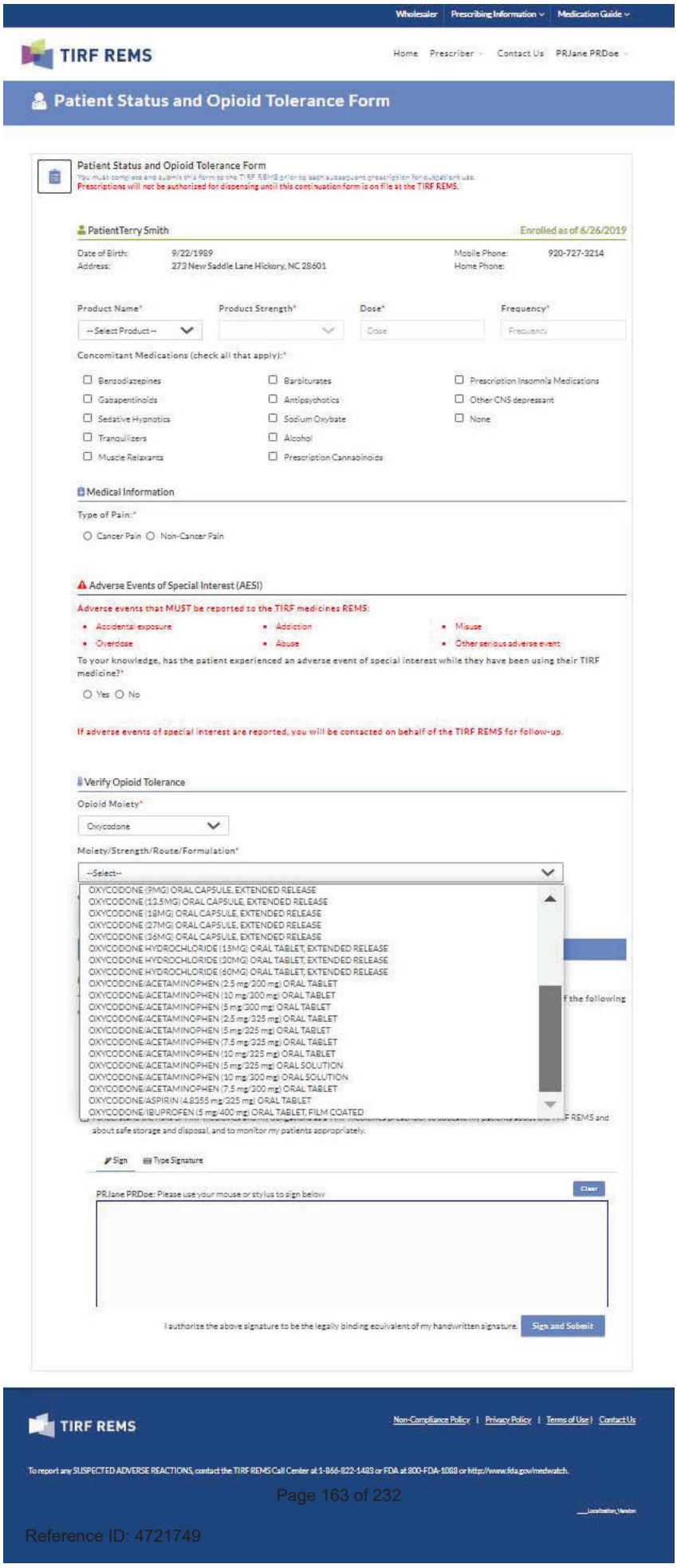

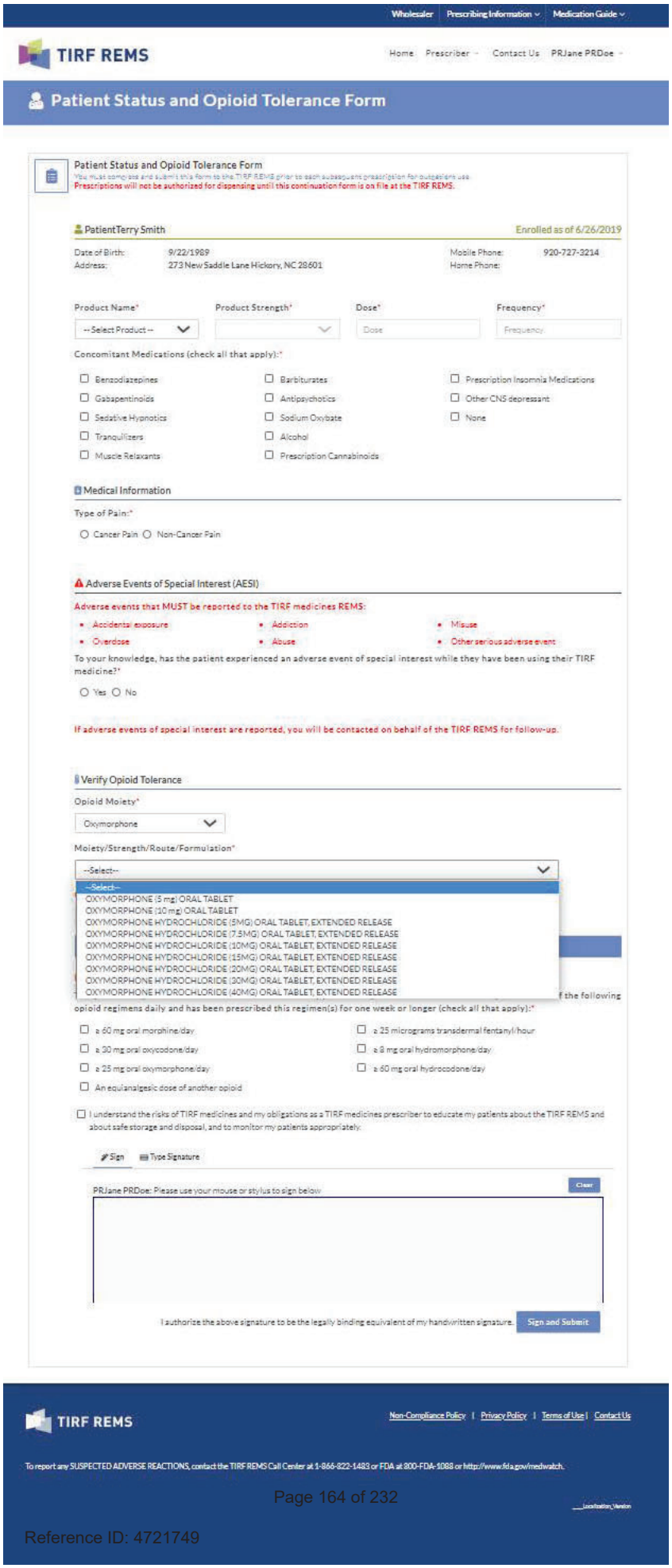

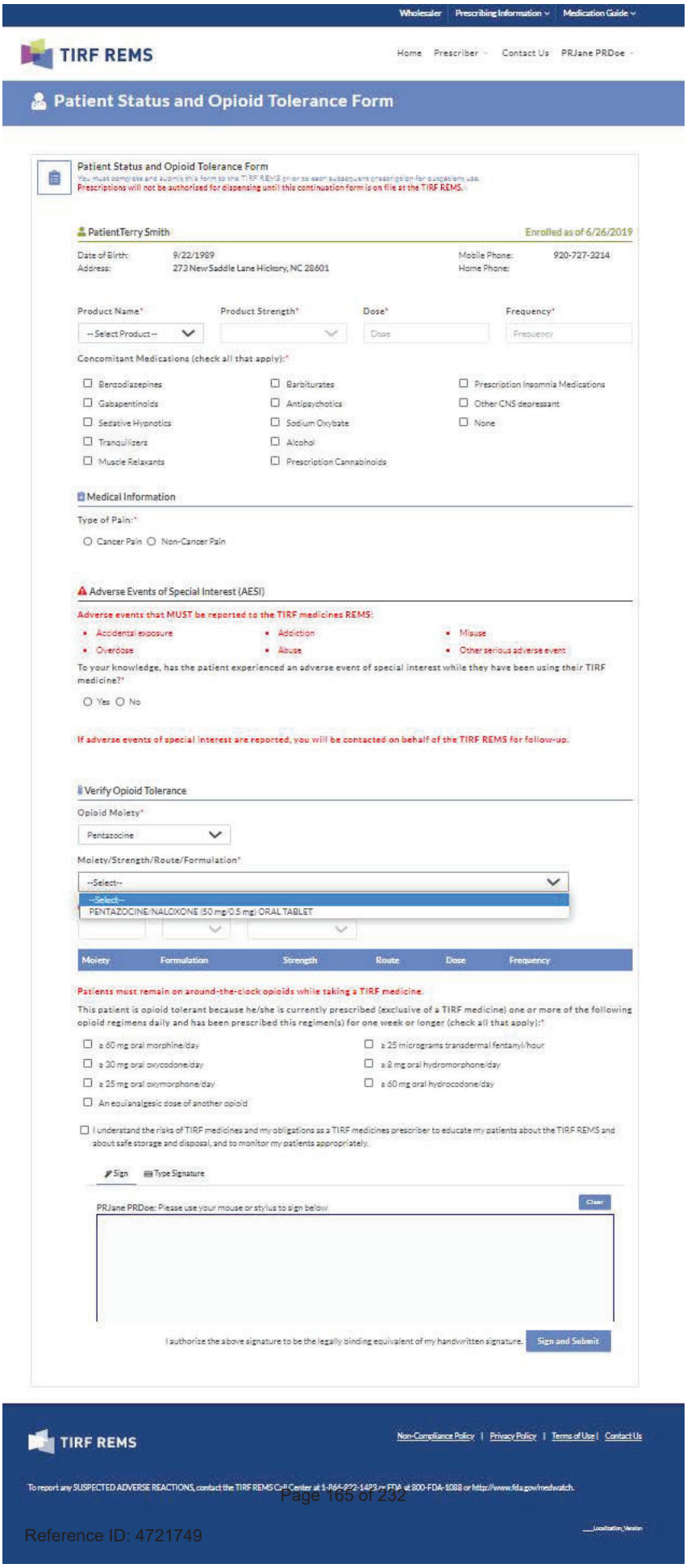

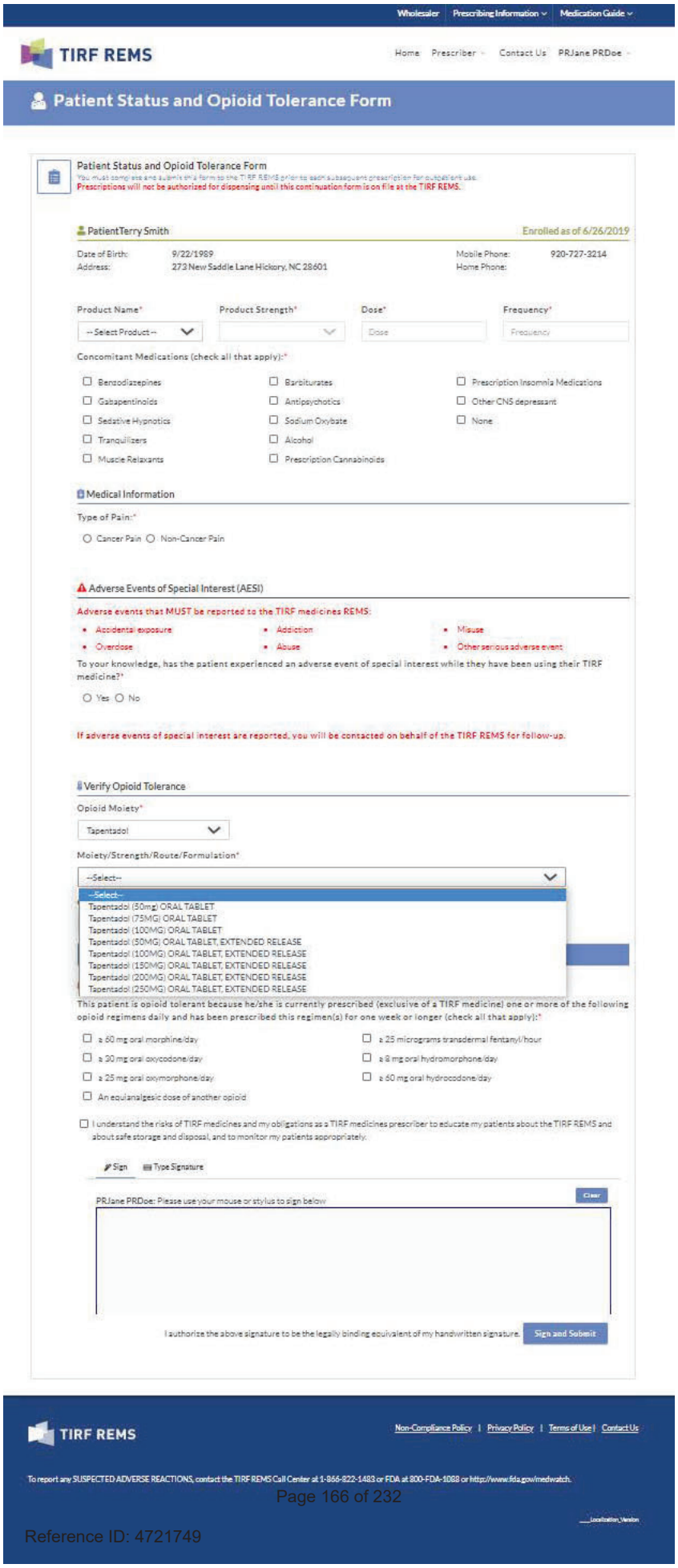

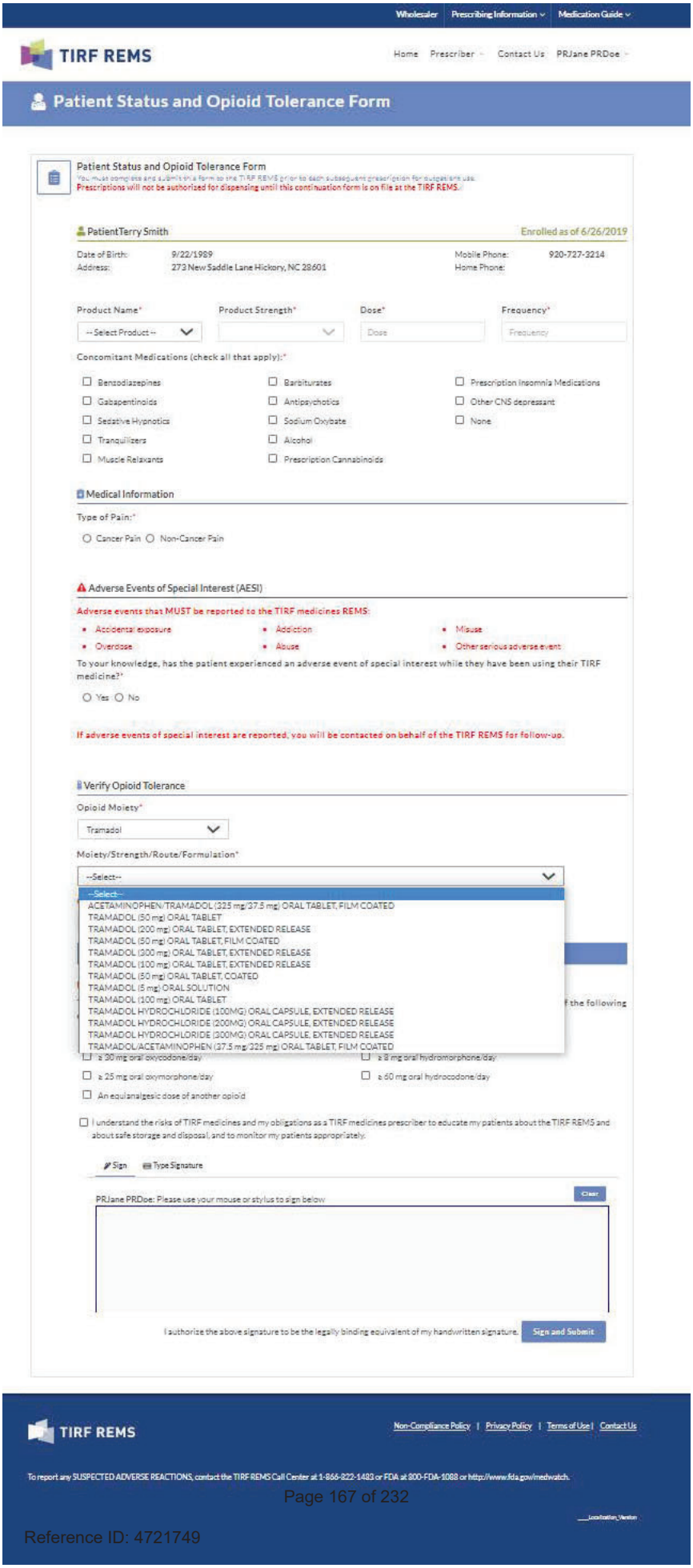
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Address: 273 New Saddle Lane Hickory, NC 28601
Mobile Phone: 920-727-3214
Home Phone:
Product Name*
-- Select Product --
Product Strength*
Dose*
Dose
Frequency*
Frequency
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
Antipsychotics
Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
Tranquilizers
Alcohol
Muscle Relaxants
Prescription Cannabinoids
Medical Information
Type of Pain:*
Cancer Pain
Non-Cancer Pain
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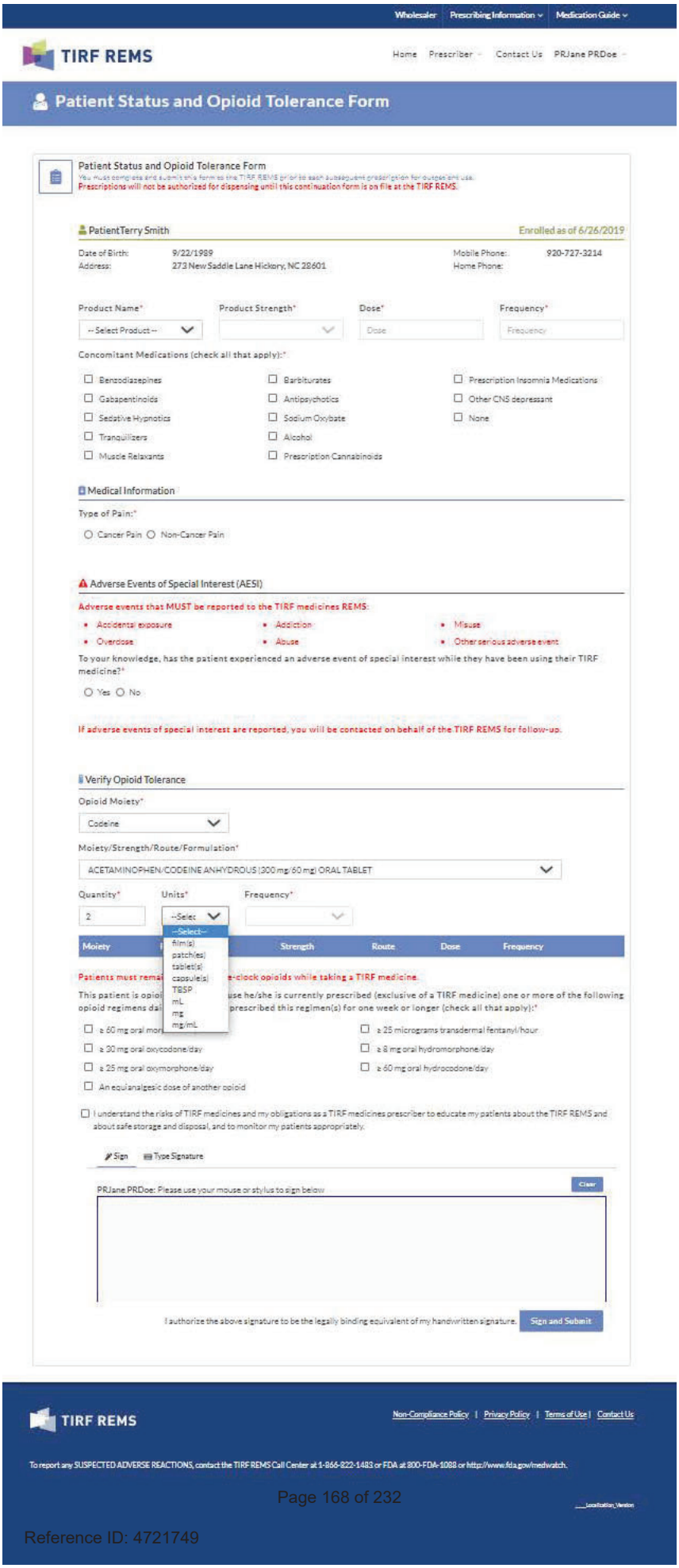
Addiction
Misuse
Overdose
Abuse
Other serious adverse event
To your knowledge, has the patient experienced an adverse event of special interest while they have been using their TIRF medicine?*
Yes
No
If adverse events of special interest are reported, you will be contacted on behalf of the TIRF REMS for follow-up.
Verify Opioid Tolerance
Opioid Moiety*
Tramadol
Moiety/Strength/Route/Formulation*
--Select--
--Select--
ACETAMINOPHEN/TRAMADOL (325 mg/37.5 mg) ORAL TABLET, FILM COATED
TRAMADOL (50 mg) ORAL TABLET
TRAMADOL (200 mg) ORAL TABLET, EXTENDED RELEASE
TRAMADOL (50 mg) ORAL TABLET, FILM COATED
TRAMADOL (300 mg) ORAL TABLET, EXTENDED RELEASE
TRAMADOL (100 mg) ORAL TABLET, EXTENDED RELEASE
TRAMADOL (50 mg) ORAL TABLET, COATED
TRAMADOL (5 mg) ORAL SOLUTION
TRAMADOL (100 mg) ORAL TABLET
TRAMADOL HYDROCHLORIDE (100MG) ORAL CAPSULE, EXTENDED RELEASE
TRAMADOL HYDROCHLORIDE (200MG) ORAL CAPSULE, EXTENDED RELEASE
TRAMADOL HYDROCHLORIDE (300MG) ORAL CAPSULE, EXTENDED RELEASE
TRAMADOL/ACETAMINOPHEN (37.5 mg/325 mg) ORAL TABLET, FILM COATED
f the following
≥ 30 mg oral oxycodone/day
≥ 8 mg oral hydromorphone/day
≥ 25 mg oral oxymorphone/day
≥ 60 mg oral hydrocodone/day
An equianalgesic dose of another opioid
I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
Sign and Submit
TIRF REMS
Non-Compliance Policy | Privacy Policy | Terms of Use | Contact Us
To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.



Patient Enrollment

Patient Information

First Name* | **M.I.** | **Last Name*** | **Date of Birth***

First Name | Midd | Last Name | mm/dd/yyyy

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* | **Address Line 2**

Address Line 1 | Address Line 2

City* | **State*** | **Zip Code***

City | State | Zip Code

Email Address* | **Number***

Email Address | nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile® ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name | **Last Name** | **Relationship**

First Name | Last Name | Mother, Father...

Number | **Email Address**

nnn-nnn-nnnn | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name* | **Product Strength*** | **Dose*** | **Frequency***

--Select Product-- | | Dose | Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety*

--Moiety--

Moiety/Strength/Route/Formulation*

Quantity* | **Units*** | **Frequency***

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25-microgram transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PR Jane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Wholesaler | Prescribing Information | Medication Guide

TIRF REMS

Home | Prescriber | Contact Us | PRJane PRDoe

Patient Enrollment

Patient Information

First Name* | M.I. | Last Name* | Date of Birth*

Megan | Middl | Brown | 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1* | Address Line 2

Address Line 1 | Address Line 2

City* | State* | Zip Code*

City | State | Zip Code

Email Address* | Number*

Megan.Brown@examoto.net | nnn-nnn-nnnn

○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship

First Name | Last Name | Mother, Father...

Number | Email Address

nnn-nnn-nnnn | Email Address

Patient / Guardian Agreement

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The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name* | Product Strength* | Dose* | Frequency*

-- Select Product -- | | Dose | Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Barbiturates
☐ Prescription Insomnia Medications
☐ Gabapentinoids
☐ Antipsychotics
☐ Other CNS depressant
☐ Sedative Hypnotics
☐ Sodium Oxybate
☐ None
☐ Tranquilizers
☐ Alcohol
☐ Muscle Relaxants
☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety*

--Moiety--

Moiety/Strength/Route/Formulation*

Quantity* | Units* | Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

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☐ ≥ 25 micrograms transdermal fentanyl/hour
☐ ≥ 30 mg oral oxycodone/day
☐ ≥ 8 mg oral hydromorphone/day
☐ ≥ 25 mg oral oxymorphone/day
☐ ≥ 60 mg oral hydrocodone/day
☐ An equianalgesic dose of another opioid

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Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below

Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* | M.I. | Last Name* | Date of Birth*

Megan | Middl | Brown | 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* | Address Line 2

Address Line 1 | Address Line 2

City* | State* | Zip Code*

City | State | Zip Code

Email Address* | Number*

Megan.Brown@examoto.net | nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship

First Name | Last Name | Mother, Father...

Number | Email Address

nnn-nnn-nnnn | Email Address

Patient / Guardian Agreement

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Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can open the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* | Product Strength* | Dose* | Frequency*

--Select Product-- | | Dose | Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☑ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety*

--Moiety--

Moiety/Strength/Route/Formulation*

Quantity* | Units* | Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

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- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | **M.I.** Midd | **Last Name*** Brown | **Date of Birth*** 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net

Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name First Name | **Last Name** Last Name | **Relationship** Mother, Father...

Number nnn-nnn-nnnn | **Email Address** Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

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Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name* -- Select Product -- | **Product Strength*** | **Dose*** Dose | **Frequency*** Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☑ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* --Moiety--

Moiety/Strength/Route/Formulation*

Quantity* | **Units*** | **Frequency***

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

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- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | **M.I.** Middl | **Last Name*** Brown | **Date of Birth*** 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net

Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name First Name | **Last Name** Last Name | **Relationship** Mother, Father...

Number nnn-nnn-nnnn | **Email Address** Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

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Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name*	Product Strength*	Dose*	Frequency*
--Select Product--		Dose	Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☑ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Codeine

Moiety/Strength/Route/Formulation* --Select--

Quantity*	Units*	Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

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- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name*	M.I.	Last Name*	Date of Birth*
Megan	Middl	Brown	07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1
Address Line 2 Address Line 2

City* City
State* State
Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net
Number* nnn-nnn-nnnn
○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

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Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name	Last Name	Relationship
First Name	Last Name	Mother, Father...

Number	Email Address
nnn-nnn-nnnn	Email Address

Patient / Guardian Agreement

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Share My Device — Sign on My Device

Provide QR Code — Sign on Patient's Phone

Send Email — Use this option to send your patient an email to sign the agreement at a later time. — Send Email

Print PDF — Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name*	Product Strength*	Dose*	Frequency*
-- Select Product --		Dose	Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☑ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Codeine

Moiety/Strength/Route/Formulation* ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/60 mg) ORAL TABLET

Quantity*	Units*	Frequency*
2	--Select--	

Moiety	Formulation	Strength	Route	Dose	Frequency

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- ☐ ≥ 60 mg oral hydrocodone/day

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Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below [Clear]

I authorize the above signature to be the legally binding equivalent of my handwritten signature. [Sign and Submit]

[Cancel]

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Patient Enrollment

Patient Information

First Name* | M.I. | Last Name* | Date of Birth*

Megan | Middl | Brown | 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* | Address Line 2

Address Line 1 | Address Line 2

City* | State* | Zip Code*

City | State | Zip Code

Email Address* | Number*

Megan.Brown@examoto.net | nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship

First Name | Last Name | Mother, Father,...

Number | Email Address

nnn-nnn-nnnn | Email Address

Patient / Guardian Agreement

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Use this option to have your tablet or PC sent your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the consent agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* | Product Strength* | Dose* | Frequency*

--Select Product-- | | Dose | Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☑ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety*: Codeine

Moiety/Strength/Route/Formulation*: ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/60 mg) ORAL TABLET

Quantity* | Units* | Frequency*

2 | tablet(s) | --Select--

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | **M.I.** Midd | **Last Name*** Brown | **Date of Birth*** 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net

Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name First Name | **Last Name** Last Name | **Relationship** Mother, Father...

Number nnn-nnn-nnnn | **Email Address** Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name* -- Select Product -- | **Product Strength*** | **Dose*** Dose | **Frequency*** Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☑ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Codeine

Moiety/Strength/Route/Formulation* ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/60 mg) ORAL TABLET

Quantity* 2 | **Units*** tablet(s) | **Frequency*** Three Times a Day | Add

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact* ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact* ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to provide a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the digital agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* -- Select Product -- | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☑ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* --Moiety--

Moiety/Strength/Route/Formulation*

Quantity* | Units* --Select-- | Frequency* --Select--

Moiety	Formulation	Strength	Route	Dose	Frequency	
ACETAMINOPHEN/CODEINE ANHYDROUS	TABLET	300 mg/60 mg	ORAL	2 tablet(s)	Three Times a Day	✖

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan

M.I. Middl

Last Name* Brown

Date of Birth* 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net

Number* nnn-nnn-nnnn

○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name First Name

Last Name Last Name

Relationship Mother, Father...

Number nnn-nnn-nnnn

Email Address Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

Cancel


Patient / Guardian Agreement
TIRF Medicines can cause your breathing to stop – which can lead to death.
Safety Rules for TIRF Medicines
You have agreed to take a TIRF Medicine and follow all the safety rules to make it less likely you or others will experience serious harm.
My healthcare provider has talked to me about the safe use of TIRF medicines using the Medication Guide and Patient Counseling Guide.
I will only use this medicine if I am regularly using another opioid, around-the-clock, for constant pain.
If I stop taking my around-the-clock opioid pain medicine, I MUST stop taking my TIRF medicine.
I will never share or give my TIRF medicine to anyone else, even if they have the same symptoms.
My TIRF medicine could cause harm to others or even death. A dose that is okay for me could cause an overdose and death for someone else.
I will store my TIRF medicine in a safe and secure place away from children. I understand that accidental use by a child or anyone for whom the medicine was not prescribed, can cause death.
I have been told how to properly dispose of my partially used or unneeded TIRF medicine remaining from my prescription. I will dispose of my TIRF medicine properly as soon as I no longer need it.
I will contact my healthcare provider if my TIRF medicine does not relieve my pain. I will not change the dose of my TIRF medicine myself or take it more often than my healthcare provider has directed.
I must enroll in the TIRF REMS and Patient Registry by completing the Patient Enrollment Form with my healthcare provider.
I understand that the TIRF REMS and its agents may use and share my personal information to manage the program, and information all about patients who get TIRF medicines will be stored in a private and secure database. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TIRF REMS. However, my name will not be shared.
I give permission for the TIRF REMS and its agents or vendors to contact me by phone, mail, or email to support the administration of the TIRF REMS Program.
I will tell my healthcare provider if I, or anyone else, experience any adverse event of accidental exposure, abuse, misuse, addiction, and overdose.
I will re-enroll in the TIRF REMS by completing the Patient Enrollment Form with my healthcare provider every two years during treatment.
Sign
Type Signature
Clear
Megan Brown: Please use your mouse or stylus to sign below
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
Sign and Submit
Share My Device
Provide QR Code
Send Email
Print PDF
Sign on My Device
Sign on Patient's Phone
Send Email
Print PDF
TIRF REMS

Wholesaler | Prescribing Information | Medication Guide

TIRF REMS

Contact Us | PRJane PRDoe

Patient Enro

Patient Information

First Name*

Megan

Sex

Male | Female

Race (check all that apply)

White
Asian
Black or African American

Address Line 1*

Address Line 1

City*

City

Email Address*

Megan.Brown@examoto.net

Preferred Time of Contact*

Morning | Afternoon

Is there a child in the home o

Yes | No

Patient Representative (if requi

First Name

Number

Email

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device

Use this option to share your tablet or PC with your patient to sign the agreement.

Sign on My Device

Provide QR Code

Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.

Sign on Patient's Phone

Send Email

Use this option to send your patient an email to sign the agreement at a later time.

Send Email

Print PDF

Use this option to print a paper copy of the agreement for signature.

Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*

Yes | No

Product Name* | Product Strength* | Dose* | Frequency*

- Select Product -

Type of Pain:*

Cancer Pain | Non-Cancer Pain

Concomitant Medications (check all that apply):*

Verify Opioid Tolerance

Opioid Moiety*

-Moiety-

Moiety/Strength/Route/Formulation*

Quantity* | Units* | Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

Sign | Type Signature

Clear

Sign and Submit

Cancel

TIRF REMS

Non-Compliance Policy | Privacy Policy | Terms of Use | Contact Us

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch

Provide QR Code

Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.

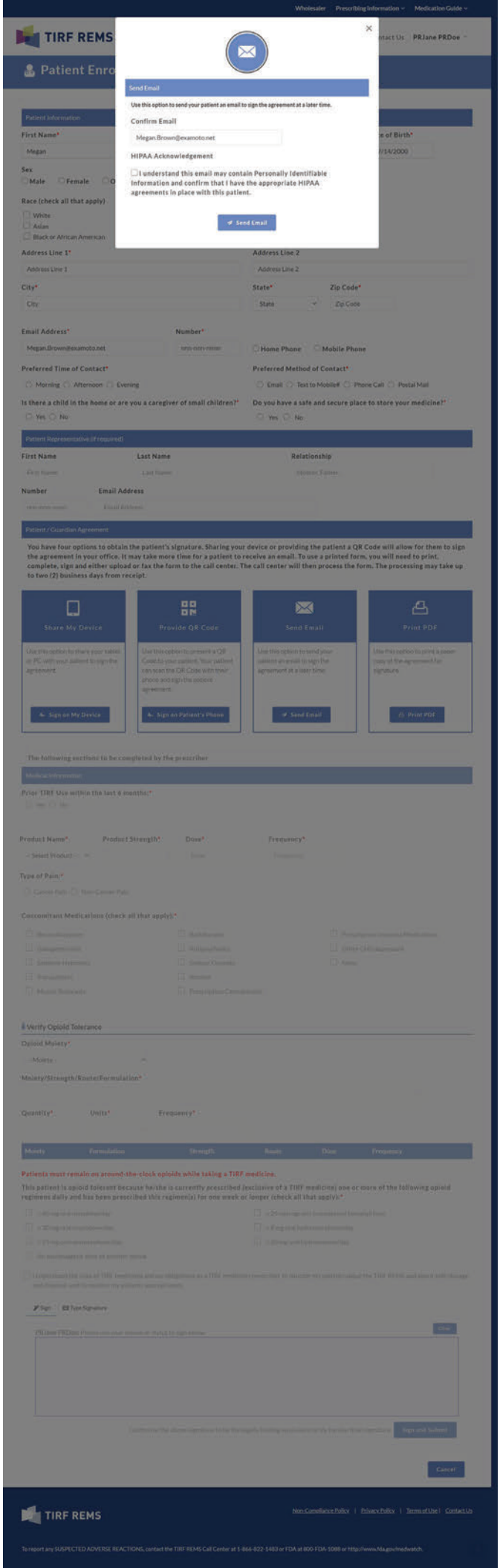
Directions

1 Have your patient point their modern phone camera at the personalized QR Code. Older phones may require an App.

2 Have your patient click on the provided link and sign.

Click the button below to generate a QR code for this patient. This will create a custom invite link that the patient can scan to complete the enrollment.

Send Email


Wholesaler
Prescribing Information
Medication Guide
TIRF REMS
PRJane PRDoe
Patient Enro
Send Email
Use this option to send your patient an email to sign the agreement at a later time.
Confirm Email
Megan.Brown@examoto.net
HIPAA Acknowledgement
I understand this email may contain Personally Identifiable Information and confirm that I have the appropriate HIPAA agreements in place with this patient.
Send Email
Patient Information
First Name*
Megan
Sex
Male
Female
Race (check all that apply)
White
Asian
Black or African American
Address Line 1*
Address Line 1
Address Line 2
Address Line 2
City*
City
State*
State
Zip Code*
Zip Code
Email Address*
Megan.Brown@examoto.net
Number*
Home Phone
Mobile Phone
Preferred Time of Contact*
Morning
Afternoon
Evening
Preferred Method of Contact*
Email
Text to Mobile#
Phone Call
Postal Mail
Is there a child in the home or are you a caregiver of small children?*
Yes
No
Do you have a safe and secure place to store your medicine?*
Yes
No
Patient Representative (if required)
First Name
Last Name
Relationship
Number
Email Address
Patient / Guardian Agreement
You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.
Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
Sign on My Device
Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the consent agreement.
Sign on Patient's Phone
Send Email
Use this option to send your patient an email to sign the agreement at a later time.
Send Email
Print PDF
Use this option to print a paper copy of the agreement for signature.
Print PDF
The following sections to be completed by the prescriber
Medical Information
Prior TIRF Use within the last 6 months:*
Product Name*
Product Strength*
Dose*
Frequency*
Select Product
Type of Pain:*
Cancer Pain
Non-Cancer Pain
Concomitant Medications (check all that apply):*
Verify Opioid Tolerance
Opioid Moiety*
Moiety
Moiety/Strength/Route/Formulation*
Quantity*
Units*
Frequency*
Moiety
Formulation
Strength
Route
Dose
Frequency
Patients must remain on around-the-clock opioids while taking a TIRF medicine.
This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*
Sign
Type Signature
Clear
Sign and Submit
Cancel
TIRF REMS
Non-Compliance Policy
Privacy Policy
Terms of Use
Contact Us
To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Wholesaler | Prescribing Information | Medication Guide

TIRF REMS | Contact Us | PRJane PRDoe

Patient Enro

Print PDF

Use this option to print a paper copy of the agreement for signature.

Print

Patient Information

First Name* Megan

Date of Birth* 7/14/2000

Sex
Male Female

Race (check all that apply)
White
Asian
Black or African American

Address Line 1*

City*

State Zip Code

Email Address* Megan.Brown@examoto.net

Number* Home Phone Mobile Phone

Preferred Time of Contact*
Morning Afternoon Evening

Preferred Method of Contact*
Email Text to Mobile# Phone Call Postal Mail

Is there a child in the home or are you a caregiver of small children?*
Yes No

Do you have a safe and secure place to store your medicine?*
Yes No

Patient Representative (if required)

First Name Last Name Relationship

Number Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
Sign on My Device

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the consent agreement.
Sign on Patient's Phone

Send Email
Use this option to send your patient an email to sign the agreement at a later time.
Send Email

Print PDF
Use this option to print a paper copy of the agreement for signature.
Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
Yes No

Product Name* Product Strength* Dose* Frequency*
- Select Product -

Type of Pain:*
Cancer Pain Non-Cancer Pain

Concomitant Medications (check all that apply):*

Verify Opioid Tolerance

Opioid Moiety*
-Moiety-

Moiety/Strength/Route/Formulation

Quantity* Units* Frequency*

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

Sign Type Signature

Clear

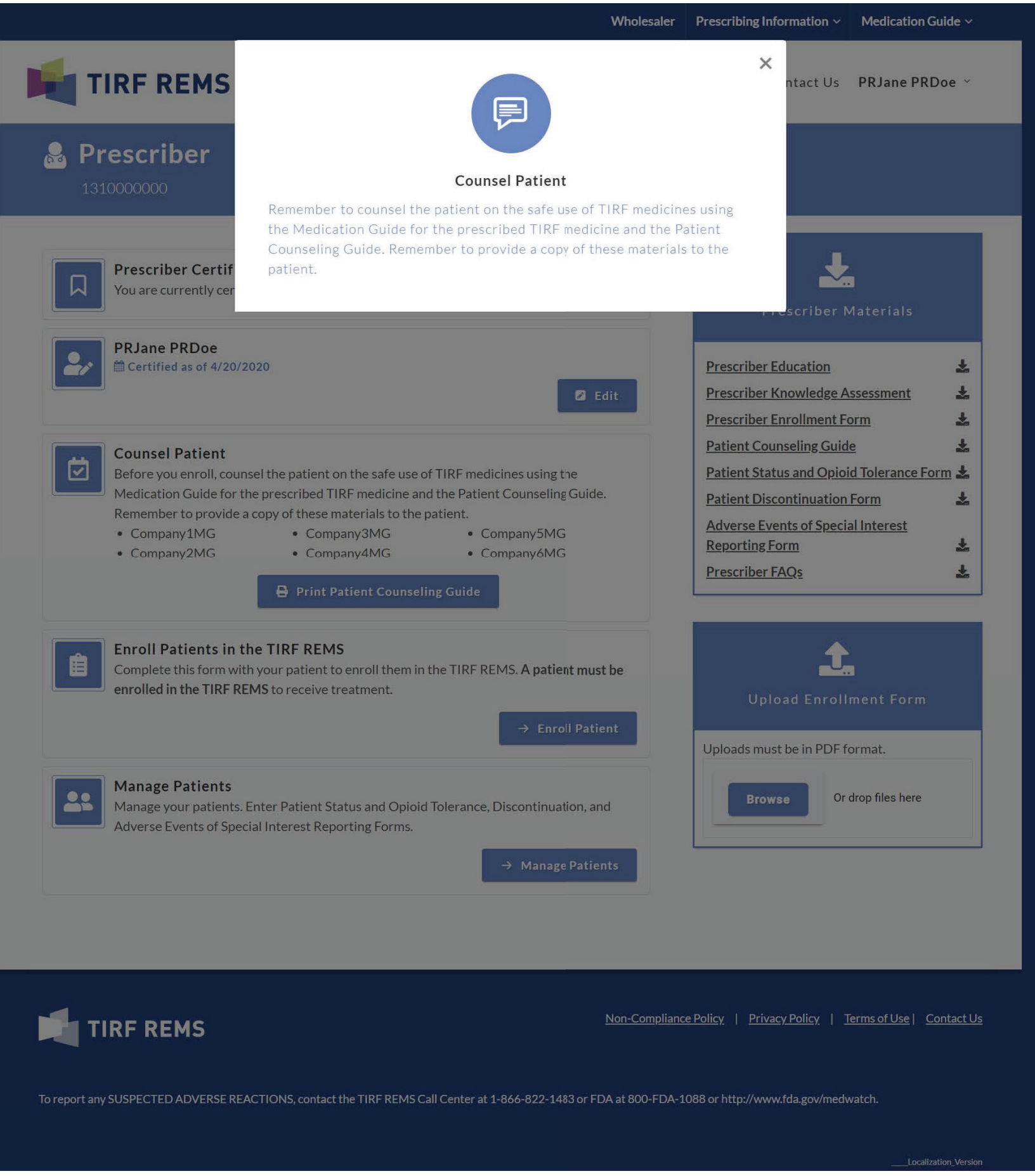
Sign and Submit

Cancel

TIRF REMS

Non-Compliance Policy | Privacy Policy | Terms of Use | Contact Us

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.


Wholesaler
Prescribing Information
Medication Guide
TIRF REMS
ntact Us
PRJane PRDoe
Prescriber
1310000000
Counsel Patient
Remember to counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Remember to provide a copy of these materials to the patient.
Prescriber Certif
You are currently cer
PRJane PRDoe
Certified as of 4/20/2020
Edit
Counsel Patient
Before you enroll, counsel the patient on the safe use of TIRF medicines using the Medication Guide for the prescribed TIRF medicine and the Patient Counseling Guide. Remember to provide a copy of these materials to the patient.
Company1MG
Company2MG
Company3MG
Company4MG
Company5MG
Company6MG
Print Patient Counseling Guide
Enroll Patients in the TIRF REMS
Complete this form with your patient to enroll them in the TIRF REMS. A patient must be enrolled in the TIRF REMS to receive treatment.
Enroll Patient
Manage Patients
Manage your patients. Enter Patient Status and Opioid Tolerance, Discontinuation, and Adverse Events of Special Interest Reporting Forms.
Manage Patients
Prescriber Materials
Prescriber Education
Prescriber Knowledge Assessment
Prescriber Enrollment Form
Patient Counseling Guide
Patient Status and Opioid Tolerance Form
Patient Discontinuation Form
Adverse Events of Special Interest Reporting Form
Prescriber FAQs
Upload Enrollment Form
Uploads must be in PDF format.
Browse
Or drop files here
TIRF REMS
Non-Compliance Policy | Privacy Policy | Terms of Use | Contact Us
To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.
___Localization_Version

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* -- Select Product -- | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Codeine

Moiety/Strength/Route/Formulation* ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/30 mg) ORAL TABLET

Quantity* 2 | Units* mg | Frequency* --Select--

--Select--
Once daily
Every Other Day
Twice a Day
Three Times a Day
Four Times a Day
At Bedtime
Every 4 Hours
Every 6 Hours
Every 8 Hours
Every 12 Hours
Every 48 Hours
Every 72 Hours
Every 7 Days

Moiety	Formulation	Route	Dose	Frequency

Patients must remain on around-the-clock [illegible] medicine.

This patient is opioid tolerant because he/she [illegible] exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this [illegible] longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

✍ Sign | ⌨ Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name*: Megan | M.I.: Middl | Last Name*: Brown | Date of Birth*: 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1*: Address Line 1

Address Line 2: Address Line 2

City*: City | State*: State | Zip Code*: Zip Code

Email Address*: Megan.Brown@examoto.net | Number*: nnn-nnn-nnnn | ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name: First Name | Last Name: Last Name | Relationship: Mother, Father...

Number: nnn-nnn-nnnn | Email Address: Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device — Sign on My Device

Provide QR Code — Sign on Patient's Phone

Send Email — Use this option to send your patient an email to sign the agreement at a later time. — Send Email

Print PDF — Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name*: -- Select Produc | Product Strength* | Dose*: Dose | Frequency*: Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety*: --Moiety--

- --Moiety--
- Buprenorphine
- Codeine
- Fentanyl
- Hydrocodone
- Hydromorphone
- Levorphanol
- Meperidine
- Methadone
- Morphine
- Oxycodone
- Oxymorphone
- Pentazocine
- Tapentadol
- Tramadol

Frequency*

Strength	Route	Dose	Frequency

...ck opioids while taking a TIRF medicine.

...e/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid ... this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. — Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact* ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact* ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name First Name | Last Name Last Name | Relationship Mother, Father...

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code on their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Buprenorphine

Moiety/Strength/Route/Formulation* --Select--

--Select--
BUPRENORPHINE (75 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (150 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (300 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (450 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (600 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (750 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (900 ug) BUCCAL FILM, SOLUBLE
BUPRENORPHINE (5 ug) TRANSDERMAL PATCH
BUPRENORPHINE (5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
BUPRENORPHINE (7.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
BUPRENORPHINE (10 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
BUPRENORPHINE (15 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
BUPRENORPHINE (20 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
BUPRENORPHINE (7.5 ug) TRANSDERMAL PATCH
BUPRENORPHINE (10 ug) TRANSDERMAL PATCH
BUPRENORPHINE (15 ug) TRANSDERMAL PATCH
BUPRENORPHINE (20 ug) TRANSDERMAL PATCH

ng opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino?: ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*: ○ Yes ○ No

Do you have a safe and secure place to store your medicine?*: ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* --Select Product-- | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Codeine

Moiety/Strength/Route/Formulation* --Select--

--Select--
ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/15 mg) ORAL TABLET
ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/30 mg) ORAL TABLET
ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/60 mg) ORAL TABLET
ACETAMINOPHEN/CODEINE ANHYDROUS (120 mg/12 mg) ORAL LIQUID
ASPIRIN/ CARISOPRODOL/ CODEINE PHOSPHATE (325mg/200mg/16mg) ORAL TABLET
BUTALBITAL/ACETAMINOPHEN/CAFFEINE/CODEINE ANHYDROUS (50 mg/325 mg/40 mg/30 mg) ORAL CAPSULE
BUTALBITAL/ACETAMINOPHEN/CAFFEINE/CODEINE ANHYDROUS (50 mg/300 mg/40 mg/30 mg) ORAL CAPSULE
BUTALBITAL/ASPIRIN/CAFFEINE/CODEINE ANHYDROUS (50 mg/325 mg/40 mg/30 mg) ORAL CAPSULE
CODEINE ANHYDROUS (30 mg) ORAL TABLET
CODEINE ANHYDROUS (60 mg) ORAL TABLET
CODEINE ANHYDROUS/GUAIFENESIN (10 mg/100 mg) ORAL LIQUID
PROMETHAZINE/CODEINE ANHYDROUS (6.25 mg/10 mg) ORAL SOLUTION

ng opioid

- ☐ a 30 mg oral oxycodone/day
- ☐ a 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ a 8 mg oral hydromorphone/day
- ☐ a 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examotu.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement as a start link.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* -- Select Product -- | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Gabapentinoids
☐ Sedative Hypnotics
☐ Tranquilizers
☐ Muscle Relaxants
☐ Barbiturates
☐ Antipsychotics
☐ Sodium Oxybate
☐ Alcohol
☐ Prescription Cannabinoids
☐ Prescription Insomnia Medications
☐ Other CNS depressant
☐ None

Verify Opioid Tolerance

Opioid Moiety* Fentanyl

Moiety/Strength/Route/Formulation* --Select--

--Select--
FENTANYL (12 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (25 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (100 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (75 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (37.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (62.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE
FENTANYL (87.5 ug) TRANSDERMAL PATCH, EXTENDED RELEASE

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

☐ ≥ 60 mg oral morphine/day
☐ ≥ 30 mg oral oxycodone/day
☐ ≥ 25 mg oral oxymorphone/day
☐ An equianalgesic dose of another opioid
☐ ≥ 25 micrograms transdermal fentanyl/hour
☐ ≥ 8 mg oral hydromorphone/day
☐ ≥ 60 mg oral hydrocodone/day

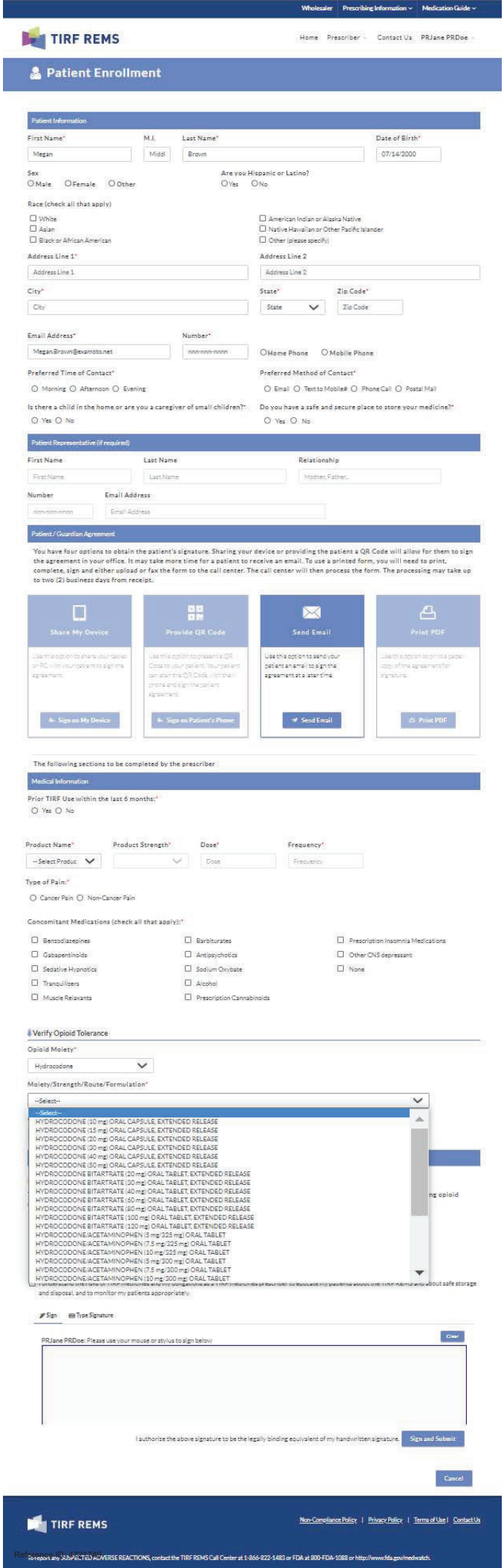
☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel


Wholesaler
Prescribing Information
Medication Guide
TIRF REMS
Home
Prescriber
Contact Us
PRJane PRDoe
Patient Enrollment
Patient Information
First Name*
Megan
M.I.
Middl
Last Name*
Brown
Date of Birth*
07/14/2000
Sex
Male
Female
Other
Are you Hispanic or Latino?
Yes
No
Race (check all that apply)
White
Asian
Black or African American
American Indian or Alaska Native
Native Hawaiian or Other Pacific Islander
Other (please specify)
Address Line 1*
Address Line 1
Address Line 2
Address Line 2
City*
City
State*
State
Zip Code*
Zip Code
Email Address*
Megan.Brown@examoto.net
Number*
nnn-nnn-nnnn
Home Phone
Mobile Phone
Preferred Time of Contact*
Morning
Afternoon
Evening
Preferred Method of Contact*
Email
Text to Mobile#
Phone Call
Postal Mail
Is there a child in the home or are you a caregiver of small children?*
Yes
No
Do you have a safe and secure place to store your medicine?*
Yes
No
Patient Representative (if required)
First Name
First Name
Last Name
Last Name
Relationship
Mother, Father...
Number
nnn-nnn-nnnn
Email Address
Email Address
Patient / Guardian Agreement
You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.
Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
Sign on My Device
Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
Sign on Patient's Phone
Send Email
Use this option to send your patient an email to sign the agreement at a later time.
Send Email
Print PDF
Use this option to print a paper copy of the agreement for signature.
Print PDF
The following sections to be completed by the prescriber
Medical Information
Prior TIRF Use within the last 6 months:*
Yes
No
Product Name*
--Select Produc
Product Strength*
Dose*
Dose
Frequency*
Frequency
Type of Pain:*
Cancer Pain
Non-Cancer Pain
Concomitant Medications (check all that apply):*
Benzodiazepines
Barbiturates
Prescription Insomnia Medications
Gabapentinoids
Antipsychotics
Other CNS depressant
Sedative Hypnotics
Sodium Oxybate
None
Tranquilizers
Alcohol
Muscle Relaxants
Prescription Cannabinoids
Verify Opioid Tolerance
Opioid Moiety*
Hydrocodone
Moiety/Strength/Route/Formulation*
--Select--
--Select--
HYDROCODONE (10 mg) ORAL CAPSULE, EXTENDED RELEASE
HYDROCODONE (15 mg) ORAL CAPSULE, EXTENDED RELEASE
HYDROCODONE (20 mg) ORAL CAPSULE, EXTENDED RELEASE
HYDROCODONE (30 mg) ORAL CAPSULE, EXTENDED RELEASE
HYDROCODONE (40 mg) ORAL CAPSULE, EXTENDED RELEASE
HYDROCODONE (50 mg) ORAL CAPSULE, EXTENDED RELEASE
HYDROCODONE BITARTRATE (20 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE BITARTRATE (30 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE BITARTRATE (40 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE BITARTRATE (60 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE BITARTRATE (80 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE BITARTRATE (100 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE BITARTRATE (120 mg) ORAL TABLET, EXTENDED RELEASE
HYDROCODONE/ACETAMINOPHEN (5 mg/325 mg) ORAL TABLET
HYDROCODONE/ACETAMINOPHEN (7.5 mg/325 mg) ORAL TABLET
HYDROCODONE/ACETAMINOPHEN (10 mg/325 mg) ORAL TABLET
HYDROCODONE/ACETAMINOPHEN (5 mg/300 mg) ORAL TABLET
HYDROCODONE/ACETAMINOPHEN (7.5 mg/300 mg) ORAL TABLET
HYDROCODONE/ACETAMINOPHEN (10 mg/300 mg) ORAL TABLET
ng opioid
and disposal, and to monitor my patients appropriately.
Sign
Type Signature
PRJane PRDoe: Please use your mouse or stylus to sign below
Clear
I authorize the above signature to be the legally binding equivalent of my handwritten signature.
Sign and Submit
Cancel
TIRF REMS
Non-Compliance Policy
Privacy Policy
Terms of Use
Contact Us
To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Patient Enrollment

Patient Information

First Name*: Megan | M.I.: Middl | Last Name*: Brown | Date of Birth*: 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1*: Address Line 1 | Address Line 2: Address Line 2

City*: City | State*: State | Zip Code*: Zip Code

Email Address*: Megan.Brown@examoto.net | Number*: nnn-nnn-nnnn | ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name: First Name | Last Name: Last Name | Relationship: Mother, Father...

Number: nnn-nnn-nnnn | Email Address: Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
[Sign on My Device]

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
[Sign on Patient's Phone]

Send Email
Use this option to send your patient an email to sign the agreement at a later time.
[Send Email]

Print PDF
Use this option to print a paper copy of the agreement for signature.
[Print PDF]

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name*: -- Select Produc | Product Strength*: | Dose*: Dose | Frequency*: Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Gabapentinoids
☐ Sedative Hypnotics
☐ Tranquilizers
☐ Muscle Relaxants
☐ Barbiturates
☐ Antipsychotics
☐ Sodium Oxybate
☐ Alcohol
☐ Prescription Cannabinoids
☐ Prescription Insomnia Medications
☐ Other CNS depressant
☐ None

Verify Opioid Tolerance

Opioid Moiety*: Hydrocodone

Moiety/Strength/Route/Formulation*: --Select--

- HYDROCODONE BITARTRATE (80 mg) ORAL TABLET, EXTENDED RELEASE
- HYDROCODONE BITARTRATE (100 mg) ORAL TABLET, EXTENDED RELEASE
- HYDROCODONE BITARTRATE (120 mg) ORAL TABLET, EXTENDED RELEASE
- HYDROCODONE/ACETAMINOPHEN (5 mg/325 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (7.5 mg/325 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (10 mg/325 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (5 mg/300 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (7.5 mg/300 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (10 mg/300 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (2.5 mg/325 mg) ORAL TABLET
- HYDROCODONE/ACETAMINOPHEN (10 mg/300 mg) ORAL SYRUP
- HYDROCODONE/ACETAMINOPHEN (7.5 mg/325 mg) ORAL SYRUP
- HYDROCODONE/ACETAMINOPHEN (7.5 mg/325 mg) ORAL SOLUTION
- HYDROCODONE/ACETAMINOPHEN (2.5 mg/108 mg) ORAL SOLUTION
- HYDROCODONE/ACETAMINOPHEN (5 mg/217 mg) ORAL SOLUTION
- HYDROCODONE/CHLORPHENIRAMINE (10 mg/8 mg) ORAL SUSPENSION, EXTENDED RELEASE
- HYDROCODONE/IBUPROFEN (7.5 mg/200 mg) ORAL TABLET, FILM COATED
- HYDROCODONE/IBUPROFEN (5 mg/200 mg) ORAL TABLET
- HYDROCODONE/IBUPROFEN (2.5 mg/200 mg) ORAL TABLET
- HYDROCODONE/IBUPROFEN (10 mg/200 mg) ORAL TABLET

...ng opioid

☐ ... about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below [Clear]

I authorize the above signature to be the legally binding equivalent of my handwritten signature. [Sign and Submit]

[Cancel]

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino?: ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*: ○ Yes ○ No

Do you have a safe and secure place to store your medicine?*: ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Hydromorphone

Moiety/Strength/Route/Formulation* --Select--

--Select--
HYDROMORPHONE (2 mg) ORAL TABLET
HYDROMORPHONE (4 mg) ORAL TABLET
HYDROMORPHONE (8 mg) ORAL TABLET, EXTENDED RELEASE
HYDROMORPHONE (12 mg) ORAL TABLET, EXTENDED RELEASE
HYDROMORPHONE (16 mg) ORAL TABLET, EXTENDED RELEASE
HYDROMORPHONE (32 mg) ORAL TABLET, EXTENDED RELEASE
HYDROMORPHONE (8 mg) ORAL TABLET
HYDROMORPHONE HYDROCHLORIDE (5MG/5ML) ORAL SOLUTION

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examotu.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient/Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

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Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code on their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Levorphanol

Moiety/Strength/Route/Formulation* --Select--

--Select--
LEVORPHANOL (2 mg) ORAL TABLET
LEVORPHANOL (3 mg) ORAL TABLET

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address (Email Address)

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* (--Select Product--) | Product Strength* | Dose* (Dose) | Frequency* (Frequency)

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Meperidine

Moiety/Strength/Route/Formulation* --Select--

--Select--
MEPERIDINE (50 mg) ORAL TABLET
MEPERIDINE (100 mg) ORAL TABLET
MEPERIDINE (50MG/5ML) ORAL SYRUP

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply):

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* -- Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Barbiturates
☐ Prescription Insomnia Medications
☐ Gabapentinoids
☐ Antipsychotics
☐ Other CNS depressant
☐ Sedative Hypnotics
☐ Sodium Oxybate
☐ None
☐ Tranquilizers
☐ Alcohol
☐ Muscle Relaxants
☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Methadone

Moiety/Strength/Route/Formulation* --Select--

--Select--
METHADONE (10 mg) ORAL TABLET
METHADONE (5 mg) ORAL TABLET
METHADONE (5 mg) ORAL SOLUTION
METHADONE (10 mg) ORAL SOLUTION
METHADONE HYDROCHLORIDE (40MG) ORAL TABLET, FOR SUSPENSION
METHADONE HYDROCHLORIDE (10MG/ML) ORAL CONCENTRATE

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

☐ ≥ 60 mg oral morphine/day
☐ ≥ 25 micrograms transdermal fentanyl/hour
☐ ≥ 30 mg oral oxycodone/day
☐ ≥ 8 mg oral hydromorphone/day
☐ ≥ 25 mg oral oxymorphone/day
☐ ≥ 60 mg oral hydrocodone/day
☐ An equianalgesic dose of another opioid

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name*: Megan
M.I.: Middl
Last Name*: Brown
Date of Birth*: 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1*: Address Line 1
Address Line 2: Address Line 2

City*: City
State*: State
Zip Code*: Zip Code

Email Address*: Megan.Brown@examoto.net
Number*: nnn-nnn-nnnn
○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name: First Name
Last Name: Last Name
Relationship: Mother, Father...

Number: nnn-nnn-nnnn
Email Address: Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
[Sign on My Device]

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
[Sign on Patient's Phone]

Send Email
Use this option to send your patient an email to sign the agreement at a later time.
[Send Email]

Print PDF
Use this option to print a paper copy of the agreement for signature.
[Print PDF]

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name*: -- Select Produc
Product Strength*:
Dose*: Dose
Frequency*: Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety*: Morphine

Moiety/Strength/Route/Formulation*: --Select--

--Select--
MORPHINE (30 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (45 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (60 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (75 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (90 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (120 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (15 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (30 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (60 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (100 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (200 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (10 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (20 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (50 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (80 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (100 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (200 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (15 mg) ORAL TABLET
MORPHINE (40 mg) ORAL CAPSULE, EXTENDED RELEASE

...ng opioid

☐ ...about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below [Clear]

I authorize the above signature to be the legally binding equivalent of my handwritten signature. [Sign and Submit]

[Cancel]

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship Mother, Father...

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* -- Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Morphine

Molety/Strength/Route/Formulation* --Select--

MORPHINE (15 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (30 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (60 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (100 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (200 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
MORPHINE (10 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (20 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (50 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (60 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (100 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (200 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (15 mg) ORAL TABLET
MORPHINE (40 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (30 mg) ORAL TABLET
MORPHINE (70 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (130 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE (150 mg) ORAL CAPSULE, EXTENDED RELEASE
MORPHINE SULFATE (10MG/5ML) ORAL SOLUTION
MORPHINE SULFATE (20MG/5ML) ORAL SOLUTION
MORPHINE SULFATE (100MG/5ML) ORAL SOLUTION

...ng opioid

...and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Wholesaler | Prescribing Information | Medication Guide

TIRF REMS

Home | Prescriber | Contact Us | PRJane PRDoe

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship Mother, Father...

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Oxycodone

Moiety/Strength/Route/Formulation* --Select--

--Select--
ACETAMINOPHEN/OXYCODONE (325 mg/5 mg) ORAL TABLET
OXYCODONE (5 mg) ORAL SOLUTION
OXYCODONE (10 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (20 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (40 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (80 mg) ORAL TABLET, FILM COATED, EXTENDED RELEASE
OXYCODONE (5 mg) ORAL TABLET
OXYCODONE (10 mg) ORAL TABLET
OXYCODONE (15 mg) ORAL TABLET
OXYCODONE (20 mg) ORAL TABLET
OXYCODONE (30 mg) ORAL TABLET
OXYCODONE (100 mg) ORAL SOLUTION
OXYCODONE (7.5 mg) ORAL TABLET
OXYCODONE (9MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (13.5MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (18MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (27MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (36MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE HYDROCHLORIDE (15MG) ORAL TABLET, EXTENDED RELEASE

ng opioid

and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact* ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact* ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship Mother, Father...

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

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Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
Sign on My Device

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
Sign on Patient's Phone

Send Email
Use this option to send your patient an email to sign the agreement, plus a short me...
Send Email

Print PDF
Use this option to print a paper copy of the agreement for a signature.
Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety* Oxycodone

Moiety/Strength/Route/Formulation* --Select--

OXYCODONE (9MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (13.5MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (18MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (27MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE (36MG) ORAL CAPSULE, EXTENDED RELEASE
OXYCODONE HYDROCHLORIDE (15MG) ORAL TABLET, EXTENDED RELEASE
OXYCODONE HYDROCHLORIDE (30MG) ORAL TABLET, EXTENDED RELEASE
OXYCODONE HYDROCHLORIDE (60MG) ORAL TABLET, EXTENDED RELEASE
OXYCODONE/ACETAMINOPHEN (2.5 mg/300 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (10 mg/300 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (5 mg/300 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (2.5 mg/325 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (5 mg/325 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (7.5 mg/325 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (10 mg/325 mg) ORAL TABLET
OXYCODONE/ACETAMINOPHEN (5 mg/325 mg) ORAL SOLUTION
OXYCODONE/ACETAMINOPHEN (10 mg/300 mg) ORAL SOLUTION
OXYCODONE/ACETAMINOPHEN (7.5 mg/300 mg) ORAL TABLET
OXYCODONE/ASPIRIN (4.8355 mg/325 mg) ORAL TABLET
OXYCODONE/IBUPROFEN (5 mg/400 mg) ORAL TABLET, FILM COATED

...ng opioid

...and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Middl | Last Name* Brown | Date of Birth* 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Email Address* Megan.Brown@examotis.net

Number* nnn-nnn-nnnn
○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name First Name | Last Name Last Name | Relationship Mother, Father...

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
Sign on My Device

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
Sign on Patient's Phone

Send Email
Use this option to send your patient an email to sign the agreement at a later time.
Send Email

Print PDF
Use this option to print a paper copy of the agreement for signature.
Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Gabapentinoids
☐ Sedative Hypnotics
☐ Tranquilizers
☐ Muscle Relaxants
☐ Barbiturates
☐ Antipsychotics
☐ Sodium Oxybate
☐ Alcohol
☐ Prescription Cannabinoids
☐ Prescription Insomnia Medications
☐ Other CNS depressant
☐ None

Verify Opioid Tolerance

Opioid Moiety* Oxymorphone

Moiety/Strength/Route/Formulation* --Select--

--Select--
OXYMORPHONE (5 mg) ORAL TABLET
OXYMORPHONE (10 mg) ORAL TABLET
OXYMORPHONE HYDROCHLORIDE (5MG) ORAL TABLET, EXTENDED RELEASE
OXYMORPHONE HYDROCHLORIDE (7.5MG) ORAL TABLET, EXTENDED RELEASE
OXYMORPHONE HYDROCHLORIDE (10MG) ORAL TABLET, EXTENDED RELEASE
OXYMORPHONE HYDROCHLORIDE (15MG) ORAL TABLET, EXTENDED RELEASE
OXYMORPHONE HYDROCHLORIDE (20MG) ORAL TABLET, EXTENDED RELEASE
OXYMORPHONE HYDROCHLORIDE (30MG) ORAL TABLET, EXTENDED RELEASE
OXYMORPHONE HYDROCHLORIDE (40MG) ORAL TABLET, EXTENDED RELEASE

…ng opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

☐ ≥ 60 mg oral morphine/day
☐ ≥ 30 mg oral oxycodone/day
☐ ≥ 25 mg oral oxymorphone/day
☐ An equianalgesic dose of another opioid
☐ ≥ 25 micrograms transdermal fentanyl/hour
☐ ≥ 8 mg oral hydromorphone/day
☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name*: Megan   M.I.: Middl   Last Name*: Brown   Date of Birth*: 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1*: Address Line 1   Address Line 2: Address Line 2

City*: City   State*: State   Zip Code*: Zip Code

Email Address*: Megan.Brown@examoto.net   Number*: nnn-nnn-nnnn   ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*: ○ Yes ○ No

Do you have a safe and secure place to store your medicine?*: ○ Yes ○ No

Patient Representative (if required)

First Name: First Name   Last Name: Last Name   Relationship: Mother, Father...

Number: nnn-nnn-nnnn   Email Address: Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
[Sign on My Device]

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
[Sign on Patient's Phone]

Send Email
Use this option to send your patient an email to sign the agreement at a later time.
[Send Email]

Print PDF
Use this option to print a paper copy of the agreement for signature.
[Print PDF]

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*: ○ Yes ○ No

Product Name*: -- Select Produc   Product Strength*:   Dose*: Dose   Frequency*: Frequency

Type of Pain:*: ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Gabapentinoids
- ☐ Sedative Hypnotics
- ☐ Tranquilizers
- ☐ Muscle Relaxants
- ☐ Barbiturates
- ☐ Antipsychotics
- ☐ Sodium Oxybate
- ☐ Alcohol
- ☐ Prescription Cannabinoids
- ☐ Prescription Insomnia Medications
- ☐ Other CNS depressant
- ☐ None

Verify Opioid Tolerance

Opioid Moiety*: Pentazocine

Moiety/Strength/Route/Formulation*: --Select--

- --Select--
- PENTAZOCINE/NALOXONE (50 mg/0.5 mg) ORAL TABLET

Moiety	Formulation	Strength	Route	Dose	Frequency

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ An equianalgesic dose of another opioid
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below   [Clear]

I authorize the above signature to be the legally binding equivalent of my handwritten signature. [Sign and Submit]

[Cancel]

Reference ID: 4721749

Patient Enrollment

Patient Information

First Name* Megan | M.I. Middl | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino?: ○ Yes ○ No

Race (check all that apply)

- ☐ White
- ☐ Asian
- ☐ Black or African American
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*: ○ Yes ○ No

Do you have a safe and secure place to store your medicine?*: ○ Yes ○ No

Patient Representative (If required)

First Name | Last Name | Relationship Mother, Father...

Number nnn-nnn-nnnn | Email Address Email Address

Patient / Guardian Agreement

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Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code, enter their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*: ○ Yes ○ No

Product Name* --Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:*: ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

- ☐ Benzodiazepines
- ☐ Barbiturates
- ☐ Prescription Insomnia Medications
- ☐ Gabapentinoids
- ☐ Antipsychotics
- ☐ Other CNS depressant
- ☐ Sedative Hypnotics
- ☐ Sodium Oxybate
- ☐ None
- ☐ Tranquilizers
- ☐ Alcohol
- ☐ Muscle Relaxants
- ☐ Prescription Cannabinoids

Verify Opioid Tolerance

Opioid Moiety* Tapentadol

Moiety/Strength/Route/Formulation* --Select--

--Select--
Tapentadol (50mg) ORAL TABLET
Tapentadol (75MG) ORAL TABLET
Tapentadol (100MG) ORAL TABLET
Tapentadol (50MG) ORAL TABLET, EXTENDED RELEASE
Tapentadol (100MG) ORAL TABLET, EXTENDED RELEASE
Tapentadol (150MG) ORAL TABLET, EXTENDED RELEASE
Tapentadol (200MG) ORAL TABLET, EXTENDED RELEASE
Tapentadol (250MG) ORAL TABLET, EXTENDED RELEASE

This patient is opioid tolerant because he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and has been prescribed this regimen(s) for one week or longer (check all that apply):*

- ☐ ≥ 60 mg oral morphine/day
- ☐ ≥ 25 micrograms transdermal fentanyl/hour
- ☐ ≥ 30 mg oral oxycodone/day
- ☐ ≥ 8 mg oral hydromorphone/day
- ☐ ≥ 25 mg oral oxymorphone/day
- ☐ ≥ 60 mg oral hydrocodone/day
- ☐ An equianalgesic dose of another opioid

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Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below. Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* | M.I. | Last Name* | Date of Birth*

Megan | Midd | Brown | 07/14/2000

Sex
○ Male ○ Female ○ Other

Are you Hispanic or Latino?
○ Yes ○ No

Race (check all that apply)

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1* | Address Line 2

Address Line 1 | Address Line 2

City* | State* | Zip Code*

City | State | Zip Code

Email Address* | Number*

Megan.Brown@examotv.net | nnn-nnn-nnnn

○ Home Phone ○ Mobile Phone

Preferred Time of Contact*
○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*
○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?*
○ Yes ○ No

Do you have a safe and secure place to store your medicine?*
○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship

First Name | Last Name | Mother, Father...

Number | Email Address

nnn-nnn-nnnn | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device
Use this option to share your tablet or PC with your patient to sign the agreement.
Sign on My Device

Provide QR Code
Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.
Sign on Patient's Phone

Send Email
Use this option to send your patient an email to sign the agreement at a store & fax.
Send Email

Print PDF
Use this option to print a paper copy of the agreement for signature.
Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:*
○ Yes ○ No

Product Name* | Product Strength* | Dose* | Frequency*

-- Select Produc | | Dose | Frequency

Type of Pain:*
○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Gabapentinoids
☐ Sedative Hypnotics
☐ Tranquilizers
☐ Muscle Relaxants
☐ Barbiturates
☐ Antipsychotics
☐ Sodium Oxybate
☐ Alcohol
☐ Prescription Cannabinoids
☐ Prescription Insomnia Medications
☐ Other CNS depressant
☐ None

Verify Opioid Tolerance

Opioid Moiety*

Tramadol

Moiety/Strength/Route/Formulation*

--Select--

--Select--
ACETAMINOPHEN/TRAMADOL (325 mg/37.5 mg) ORAL TABLET, FILM COATED
TRAMADOL (50 mg) ORAL TABLET
TRAMADOL (200 mg) ORAL TABLET, EXTENDED RELEASE
TRAMADOL (50 mg) ORAL TABLET, FILM COATED
TRAMADOL (300 mg) ORAL TABLET, EXTENDED RELEASE
TRAMADOL (100 mg) ORAL TABLET, EXTENDED RELEASE
TRAMADOL (50 mg) ORAL TABLET, COATED
TRAMADOL (5 mg) ORAL SOLUTION
TRAMADOL (100 mg) ORAL TABLET
TRAMADOL HYDROCHLORIDE (100MG) ORAL CAPSULE, EXTENDED RELEASE
TRAMADOL HYDROCHLORIDE (200MG) ORAL CAPSULE, EXTENDED RELEASE
TRAMADOL HYDROCHLORIDE (300MG) ORAL CAPSULE, EXTENDED RELEASE
TRAMADOL/ACETAMINOPHEN (37.5 mg/325 mg) ORAL TABLET, FILM COATED

ng opioid

☐ ≥ 30 mg oral oxycodone/day
☐ ≥ 25 mg oral oxymorphone/day
☐ An equianalgesic dose of another opioid
☐ ≥ 8 mg oral hydromorphone/day
☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below

Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature.

Sign and Submit

Cancel

Patient Enrollment

Patient Information

First Name* Megan | M.I. Midd | Last Name* Brown | Date of Birth* 07/14/2000

Sex: ○ Male ○ Female ○ Other

Are you Hispanic or Latino? ○ Yes ○ No

Race (check all that apply)

☐ White
☐ Asian
☐ Black or African American
☐ American Indian or Alaska Native
☐ Native Hawaiian or Other Pacific Islander
☐ Other (please specify)

Address Line 1* Address Line 1 | Address Line 2 Address Line 2

City* City | State* State | Zip Code* Zip Code

Email Address* Megan.Brown@examoto.net | Number* nnn-nnn-nnnn ○ Home Phone ○ Mobile Phone

Preferred Time of Contact*: ○ Morning ○ Afternoon ○ Evening

Preferred Method of Contact*: ○ Email ○ Text to Mobile# ○ Phone Call ○ Postal Mail

Is there a child in the home or are you a caregiver of small children?* ○ Yes ○ No

Do you have a safe and secure place to store your medicine?* ○ Yes ○ No

Patient Representative (if required)

First Name | Last Name | Relationship (Mother, Father...)

Number (nnn-nnn-nnnn) | Email Address

Patient / Guardian Agreement

You have four options to obtain the patient's signature. Sharing your device or providing the patient a QR Code will allow for them to sign the agreement in your office. It may take more time for a patient to receive an email. To use a printed form, you will need to print, complete, sign and either upload or fax the form to the call center. The call center will then process the form. The processing may take up to two (2) business days from receipt.

Share My Device	Provide QR Code	Send Email	Print PDF
Use this option to share your tablet or PC with your patient to sign the agreement.	Use this option to present a QR Code to your patient. Your patient can scan the QR Code with their phone and sign the patient agreement.	Use this option to send your patient an email to sign the agreement at a later time.	Use this option to print a paper copy of the agreement for signature.
Sign on My Device	Sign on Patient's Phone	Send Email	Print PDF

The following sections to be completed by the prescriber

Medical Information

Prior TIRF Use within the last 6 months:* ○ Yes ○ No

Product Name* -- Select Produc | Product Strength* | Dose* Dose | Frequency* Frequency

Type of Pain:* ○ Cancer Pain ○ Non-Cancer Pain

Concomitant Medications (check all that apply):*

☐ Benzodiazepines
☐ Gabapentinoids
☐ Sedative Hypnotics
☐ Tranquilizers
☐ Muscle Relaxants
☐ Barbiturates
☐ Antipsychotics
☐ Sodium Oxybate
☐ Alcohol
☐ Prescription Cannabinoids
☐ Prescription Insomnia Medications
☐ Other CNS depressant
☐ None

Verify Opioid Tolerance

Opioid Moiety* Codeine

Moiety/Strength/Route/Formulation* ACETAMINOPHEN/CODEINE ANHYDROUS (300 mg/30 mg) ORAL TABLET

Quantity* 2 | Units* --Select-- | Frequency*

--Select--
film(s)
patch(es)
tablet(s)
capsule(s)
TBSP
mL
mg
mg/mL

Moiety	Strength	Route	Dose	Frequency

Patients must remain [illegible] ock opioids while taking a TIRF medicine.

This patient is opioid [illegible] he/she is currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and ha[illegible] this regimen(s) for one week or longer (check all that apply):*

☐ ≥ 60 mg oral morph[illegible]
☐ ≥ 30 mg oral oxycodone/day
☐ ≥ 25 mg oral oxymorphone/day
☐ An equianalgesic dose of another opioid
☐ ≥ 25 micrograms transdermal fentanyl/hour
☐ ≥ 8 mg oral hydromorphone/day
☐ ≥ 60 mg oral hydrocodone/day

☐ I understand the risks of TIRF medicines and my obligations as a TIRF medicines prescriber to educate my patients about the TIRF REMS and about safe storage and disposal, and to monitor my patients appropriately.

Sign | Type Signature

PRJane PRDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. Sign and Submit

Cancel

Pharmacy

Inpatient Pharmacy Group

To certify your pharmacy:
Your pharmacy is currently certified.

Pharmacy Personnel
A pharmacy can have multiple personnel with online accounts. You may invite personnel, reset their passwords, or remove them.

→ Manage Personnel

Pharmacies
A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative.

→ Manage Pharmacies

Pharmacy Materials

- Pharmacy Education
- Pharmacy Knowledge Assessment
- Inpatient Pharmacy Enrollment Form
- Outpatient Pharmacy Enrollment Form
- Pharmacy FAQ

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

___Localization_Version

Pharmacy

Outpatient Pharmacy Group

To certify your pharmacy:

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Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

→ Obtain Patient RDA

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Pharmacy

Outpatient Pharmacy Group

Site Biennial Confirmation Notice

Your pharmacy's TIRF REMS biennial confirmation is expiring soon. To dispense Transmucosal Immediate-Release Fentanyl medicines you must:

1 **Authorized Representative Biennial Confirmation**

For your Pharmacy or Pharmacies to remain certified, you must confirm that you are the Authorized Representative every two years.

☐ **I, RxOutPatJane AuthRepDoe, am the REMS Authorized Representative for Outpatient Pharmacy Group**

Complete

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Pharmacy

Examoto Pharmacy Group

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Complete

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Pharmacy - Knowledge Assessment

TIRF Pharmacy KA

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0 of 11 questions in progress

1. The patients described are all experiencing breakthrough cancer pain, but ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine? Select one option

- 12-year-old sarcoma patient, using 25 mcg/hour transdermal fentanyl patches for her underlying persistent cancer pain.
- Adult female with advanced breast cancer; on 60 mg of oral morphine daily for the past 4 weeks.
- Adult male with advanced lung cancer, his underlying persistent pain is managed with transdermal fentanyl patches for the past 3 months.
- Adult male with multiple myeloma who has bone pain currently managed with 50 mg oral oxymorphone daily for the last 2 weeks.
- Adult female with advanced sarcoma who has been taking a daily dose of 12 mg oral hydromorphone for the last 3 weeks.

2. Pharmacists can assist in prevention of diversion or accidental exposure of TIRF medicines by people for whom they are not prescribed. Which of the following statements is TRUE?

- Pharmacists should counsel TIRF medicine users to keep their TIRF medicine out of reach of children and pets.
- Pharmacists should counsel TIRF medicine users to refer to safe disposal guidelines in the TIRF product-specific Medication Guide.
- Pharmacists should counsel patients not to share their TIRF medicine with anyone else even if their symptoms are the same as it could result in serious life threatening and/or fatal respiratory depression.
- Remind patients to call their prescriber if they have questions about usage of their TIRF medicine.
- All of the above.

3. A patient's prescriber has ordered a new TIRF medicine for the patient. What dose must they start with?

- An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
- The dose the prescriber believes is appropriate based on the previous clinical history of TIRF medicine use.
- The lowest available dose, unless individual product Prescribing Information provides product-specific guidance.
- The median available dose.
- The dose the prescriber believes is appropriate based on their clinical experience.

4. Select the following statement which is FALSE.

- Before dispensing, the pharmacy must check the patient's medication use for a change in opioid tolerance. This could include reviewing data from various sources (e.g. -available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.)
- When a patient's breakthrough cancer pain is not relieved by their TIRFmedicine, he/she may repeat their dose of TIRF medicine every 20 minutes until they achieve pain relief.
- TIRF medicines are not interchangeable on a microgram-per-microgram basis.
- The prescriber must not convert from the first TIRF medicine dose to another TIRF medicine at the equivalent dose. The different TIRF medicines have different absorption and bioavailability profiles, and conversion to an equivalent dose of a second TIRF product could result in a fentanyl overdose.

5. Which of the following is not a pharmacy requirement in the TIRF REMS?

- The authorized representative must train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the TIRF REMS using the Pharmacy Education.
- The authorized representative must re-enroll in the TIRF REMS by completing the Outpatient Pharmacy Enrollment Form.
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- The pharmacy may dispense the first prescription to the patient before the patient is enrolled in the TIRF REMS as long as the patient is enrolled before the next dispensing.

6. A patient is taking a TIRF medicine and the doctor would like to prescribe erythromycin, a CYP3A4 inhibitor. Which of the following statements is TRUE?

- The patient cannot be prescribed erythromycin, because using it at the same time as a TIRF medicine could be fatal.
- Use of a TIRF medicine with a CYP3A4 inhibitor may require dosage adjustment of the TIRF medicine; carefully monitor the patient for opioid toxicity, otherwise such use may cause potentially fatal respiratory depression.
- There is no possible drug interaction between CYP3A4 inhibitors and TIRF medicines.
- The dose of the TIRF medicine must be reduced by one half if a CYP3A4 inhibitor is prescribed in the same patient.

7. Before dispensing a TIRF medicine, pharmacists must provide a patient with the Medication Guide. Which of the following counseling statements is FALSE?

- TIRF medicines contain fentanyl in an amount that could be fatal to children of all ages, in individuals for whom they were not prescribed, and in those who are not opioid tolerant.
- Inform patients that TIRF medicines must not be used to treat acute or postoperative pain, including headache/migraine, dental pain or acute pain in the emergency department.
- Instruct patients that, if they stop taking their around-the-clock opioid medicine, they can continue to take their TIRF medicine.
- Instruct patients to never share their TIRF medicine with anyone else, even if that person has the same symptoms.

8. There is a risk of fatal overdose with inappropriate use of TIRF medicines. Which one of the following answers is most accurate?

- TIRF medicines can be fatal if taken by children.
- TIRF medicines can be fatal if taken by anyone for whom it is not prescribed.
- TIRF medicines can be fatal if taken by anyone who is not opioid-tolerant.
- All of the above.

9. Which of the following statements is FALSE?

- A REMS Dispense Authorization is required before dispensing TIRF medicines at all outpatient pharmacies.
- A REMS Dispense Authorization is not required when the patient is paying by cash rather than submitting a traditional pharmacy benefit claim.
- A REMS Dispense Authorization is not required prior to dispensing TIRFmedicines to hospital inpatients.
- A REMS Dispense Authorization at an outpatient pharmacy confirms that the required opioid tolerance verification is on file with the TIRF REMS prior to dispensing.

10. Which one of the following statements is most accurate regarding the safe storage and disposal of TIRF medicines?

- TIRF medicines should be stored in a safe and secure place, out of sight and out of reach of all others, especially children.
- TIRF medicines should be protected from theft.
- Dispose of partially used or unneeded TIRF medicine by following the TIRF medicine-specific procedure specified in the Medication Guide.
- All of the above.

11. As an authorized representative for my pharmacy, which of the following is not my responsibility?

- Make sure that my staff and I confirm pharmacy, patient and prescriber enrollment in the TIRF REMS and patient opioid tolerance by obtaining a REMS Dispense Authorization prior to every outpatient dispensing of a TIRF medicine.
- Enroll and train all sub-stores if my pharmacy acts as a chain headquarters pharmacy in the TIRF REMS.
- Provide a Patient Status and Opioid Tolerance Form to the TIRF REMS for every prescription prior to dispensing.
- My pharmacy must not sell, loan or transfer TIRF medicine inventory to any other pharmacy, institution, distributor, or prescriber.

Submit KA

Pharmacy - Knowledge Assessment

TIRF Pharmacy KA

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Knowledge Assessment Incomplete

9 correct answers ou of 11 (Failed)

1. The patients described are all experiencing breakthrough cancer pain, bu ONE is not an appropriate patient for a TIRF medicine. Which patient should not receive a TIRF medicine? Select one option ✓

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- ( ) An appropriate dose based on the dose of the opioid medicine used for underlying persistent cancer pain.
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- ( ) Before dispensing, the pharmacy must check the patient's medication use for a change in opioid tolerance. This could include reviewing data from various sources (e.g., available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TRF REMS.)
- (●) When a patient's breakthrough cancer pain is not relieved by their TIRFmedicine, he/she may repeat their dose of TIRF medicine every 20 minutes until they achieve pain relief.
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- ( ) There is no possible drug interaction between CYP3A4 inhibitors and TRF medicines.
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Try Again | Home

Pharmacy - Knowledge Assessment

There are errors, please correct the items below:

- You have exceeded the maximum number of allowed attempts to pass the knowledge assessment
- To reattempt the knowledge assessment you must first review the Pharmacy Education and then call the TIRF REMS Call Center at 1-866-822-1483 to reset your account
- You will be denied enrollment into the TIRF REMS after six failed attempts to complete the knowledge assessment

Home

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___Localization_Version

Pharmacy - Knowledge Assessment

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____Localization_Version

Pharmacy - Knowledge Assessment

TIRF Pharmacy KA

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Knowledge Assessment Complete

11 correct answers out of 11 (Passed)

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Home

Pharmacy

Outpatient Pharmacy Group

Additional Pharmacy

Organizational NPI Number*

Use organizational NPI to populate form: Organizational NPI Number

(Select address type to populate form)

○ Office Address ○ Mailing Address

Pharmacy Name*

Pharmacy Name

Address Line 1*

Address Line 1

Address Line 2

Address Line 2

City*

City

State*

State

Zip Code*

Zip Code

Phone*

nnn-nnn-nnnn

Extension

nnn...

Fax*

nnn-nnn-nnnn

Chain ID

Chain ID

You may assign this pharmacy to one or more staff members below:

Show 10 entries Search:

	Name
☑	RxOutPatJane AuthRepDoe
☐	RxOutPatJohn StaffSmith
☐	RxOutPatMike StaffGreen
☐	RxOutPatSally StaffJones

Authorized Representative Staff

Cancel Save

Pharmacy

Outpatient Pharmacy Group

Pharmacies

A pharmacy can have multiple pharmacies grouped together under the responsibility of a Pharmacy Authorized Representative.
You may add, remove, or edit the pharmacies in this pharmacy group.

Add Pharmacy

Show 10 entries

Search:

Action	NPI	Name	Pharmacy Type	Consumer Type	Status
Delete Edit	2110000000	OutPat Test Pharmacy	Outpatient Pharmacy	Mail Order	Certified as of 4/20/2020
Delete Edit	2110000002	OutPat Test Sub02 Pharmacy	Inpatient Pharmacy	Walk-in	Certified as of 4/20/2020
Delete Edit	2110000001	OutPat Test Sub01 Pharmacy	Inpatient Pharmacy	Mail Order	Certified as of 4/20/2020

Showing 1 to 3 of 3 entries

Previous 1 Next

Return

Pharmacy

Outpatient Pharmacy Group

RxOutPatJane AuthRepDoe
Authorized Representative
Certified as of 4/20/2020

Edit | View Enrollment PDF

Pharmacy Personnel

A pharmacy can have multiple personnel with online accounts. You may invite personnel, reset their passwords, or remove them. You may add an authorized representative or staff to your pharmacy.

Add Authorized Representative or Staff

Show 10 entries | Search:

Action	Role	Name	Email Address	Status	Added	Days Inactive
Delete Edit	Authorized Representative	RxOutPatJane AuthRepDoe	RxAuthRepOutPat@examoto.net	Certified as of 4/20/2020	4/20/2020	0
Delete Edit	Staff	RxOutPatJohn StaffSmith	RxStaffOutPat@examoto.net	Authorized	4/20/2020	191
Delete Edit	Staff	RxOutPatMike StaffGreen	RxStaffOutPat02@examoto.net	Authorized	4/20/2020	191
Delete Edit	Staff	RxOutPatSally StaffJones	RxStaffOutPat01@examoto.net	Authorized	4/20/2020	191

Delete | Edit | Authorized Representative | Staff

Showing 1 to 4 of 4 entries

Previous 1 Next

Return

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Pharmacy

Outpatient Pharmacy Group

Additional Staff

Personnel Type:

- (•) Authorized Representative
- ( ) Pharmacy Staff

Authorized Representative Information

First Name: First Name

Last Name: Last Name

Title: Title

Credentials: ( ) RPh ( ) PharmD ( ) BCPS ( ) Other

Phone: Phone

Fax: Fax

Email Address: Email Address

Preferred Method of Contact: ( ) Email ( ) Text to Mobile# ( ) Phone Call

You are the Authorized Representative for the following:

Show 10 entries Search:

	Name	Zip Code
☑	OutPat Test Pharmacy: 2110000000	10726-7773
☑	OutPat Test Sub02 Pharmacy: 2110000002	19002
☑	OutPat Test Sub01 Pharmacy: 2110000001	40254-1274

Showing 1 to 3 of 3 entries Previous 1 Next

Cancel Send Invite

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Pharmacy

Outpatient Pharmacy Group

Additional Staff

Personnel Type:

- ○ Authorized Representative
- ◉ Pharmacy Staff

Pharmacy Staff Information

First Name: First Name

Last Name: Last Name

Title: Title

Credentials: ○ RPh ○ PharmD ○ BCPS ○ Other

Phone: Phone

Fax: Fax

Email Address: Email Address

Preferred Method of Contact: ○ Email ○ Text to Mobile# ○ Phone Call

You may assign this staff member to one or more pharmacies below:

Show 10 entries Search:

	Name	Zip Code
☐	OutPat Test Pharmacy: 2110000000	10726-7773
☐	OutPat Test Sub02 Pharmacy: 2110000002	19002
☐	OutPat Test Sub01 Pharmacy: 2110000001	40254-1274

Showing 1 to 3 of 3 entries Previous 1 Next

Cancel Send Invite

Pharmacy Enrollment

To become certified in the TIRF REMS and dispense TIRF medicines, a pharmacy must designate an Authorized Representative to:

1. Review the **Pharmacy Education**
2. Complete and submit the **Pharmacy Knowledge Assessment** to the TIRF REMS
3. Complete and submit this **Pharmacy Enrollment Form** to the TIRF REMS

Pharmacy Type (Please pick a Pharmacy Type. Different pharmacies have different REMS requirements.)

◯ Inpatient Pharmacy ◯ Outpatient Pharmacy

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

____Localization_Version

Pharmacy Enrollment

To become certified in the TIRF REMS and dispense TIRF medicines, a pharmacy must designate an Authorized Representative to:

1. Review the **Pharmacy Education**
2. Complete and submit the **Pharmacy Knowledge Assessment** to the TIRF REMS
3. Complete and submit this **Pharmacy Enrollment Form** to the TIRF REMS

Pharmacy Type (Please pick a Pharmacy Type. Different pharmacies have different REMS requirements.)

○ Inpatient Pharmacy ◉ Outpatient Pharmacy

Pharmacy Information

Organizational NPI Number*

Use organizational NPI to populate form: Organizational NPI Number

(Select address type to populate form)

○ Office Address ○ Mailing Address

Pharmacy Name*

Pharmacy Name

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Phone* nnn-nnn-nnnn

Extension nnn...

Fax* nnn-nnn-nnnn

Chain ID Chain ID

The name, location, and phone number of your pharmacy will be publicly available on TIRFREMSaccess.com. If you do not want your information available, please call the TIRF REMS Call Center at 1-866-822-1483.

Authorized Representative Information

First Name* RxOutPatJane

Last Name* AuthRepDoe

Credentials*

○ RPh ○ PharmD ○ BCPS ○ Other

Title or Position* Title or Position

Phone* nnn-nnn-nnnn

Fax* nnn-nnn-nnnn

EmailAddress RxAuthRepOutPat@examoto.net

Preferred Method of Contact*

○ Email ○ Text to Mobile# ○ Phone Call

Pharmacy Authorized Representative Responsibilities

As the Authorized Representative, I must:

- Review the **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Establish processes and procedures to check the patient's medication use for a change in opioid tolerance.
- Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS using the **Pharmacy Education**.

Before dispensing, all pharmacy staff must:

- Provide the patient with the product-specific **Medication Guide**.
- Assess the patient's medication use for a change in opioid tolerant status. Document and submit the results to the REMS.
- Obtain authorization to dispense each prescription by contacting the REMS to verify that the prescriber and the patient are enrolled, and the patient is opioid tolerant.

All pharmacy staff must:

- Not distribute, transfer, loan, or sell TIRF medicines.
- Maintain records of staff training.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed.
- Report serious adverse events of accidental exposure, misuse, abuse, addiction, and overdose associated with the TIRF medicine to the REMS using the **Adverse Events of Special Interest Reporting Form**.

To maintain certification to dispense, any new authorized representative must:

- Review the **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Enroll in the REMS by completing the **Outpatient Pharmacy Enrollment Form**.

Sign | Type Signature

RxOutPatJane AuthRepDoe: Please use your mouse or stylus to sign below

Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature.

Sign and Submit

Pharmacy Enrollment

To become certified in the TIRF REMS and dispense TIRF medicines, a pharmacy must designate an Authorized Representative to:

1. Review the **Pharmacy Education**
2. Complete and submit the **Pharmacy Knowledge Assessment** to the TIRF REMS
3. Complete and submit this **Pharmacy Enrollment Form** to the TIRF REMS

Pharmacy Type (Please pick a Pharmacy Type. Different pharmacies have different REMS requirements.)

◉ Inpatient Pharmacy ○ Outpatient Pharmacy

Pharmacy Information

Organizational NPI Number*

Use organizational NPI to populate form: Organizational NPI Number

(Select address type to populate form)

○ Office Address ○ Mailing Address

Pharmacy Name*

Pharmacy Name

Address Line 1* Address Line 1

Address Line 2 Address Line 2

City* City

State* State

Zip Code* Zip Code

Phone* nnn-nnn-nnnn

Extension nnn...

Fax* nnn-nnn-nnnn

The name, location, and phone number of your pharmacy will be publicly available on TIRFREMSaccess.com. If you do not want your information available, please call the TIRF REMS Call Center at 1-866-822-1483.

Authorized Representative Information

First Name* RxInPatJane

Last Name* AuthRepDoe

Credentials*

○ RPh ○ PharmD ○ BCPS ○ Other

Title or Position* Title or Position

Phone* nnn-nnn-nnnn

Fax* nnn-nnn-nnnn

Email Address RxAuthRepInPat@examoto.net

Preferred Method of Contact*

○ Email ○ Text to Mobile# ○ Phone Call

Pharmacy Authorized Representative Responsibilities

As the Authorized Representative, I must:

- Review the **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS using the **Pharmacy Education**.
- Establish processes and procedures to verify that the patient is opioid tolerant.

All pharmacy staff must:

- Verify the patient is opioid tolerant through the processes and procedures established as a requirement of the REMS.

All pharmacy staff must:

- Not distribute, transfer, loan, or sell TIRF medicines.
- Maintain records of staff training.
- Comply with audits carried out by the manufacturers or a third party acting on behalf of the manufacturers to ensure that all processes and procedures are in place and are being followed.
- Not dispense TIRF medicines for outpatient use.

To maintain certification to dispense, any new authorized representative must:

- Review the **Pharmacy Education**.
- Successfully complete the **Pharmacy Knowledge Assessment** and submit it to the REMS.
- Enroll in the REMS by completing the **Inpatient Pharmacy Enrollment Form**.

Sign | Type Signature

RxInPatJane AuthRepDoe: Please use your mouse or stylus to sign below — Clear

I authorize the above signature to be the legally binding equivalent of my handwritten signature. **Sign and Submit**

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.
Find an enrolled patient below:

1 Find a patient by entering the patient's information below:

First Name: First Name

Last Name: wil

Date of Birth: mm/dd/yyyy

Phone Or Email: Phone Or Email

Match Found

(•) PatientJulie Williams (DOB:6/13/1970)

Cancel | Continue

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

____Localization_Version

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- ○ Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ○ Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

☐ Reviewed the following REMS data:

Prescriber Reported:
≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

☐ Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? ℹ Opioid Tolerance Criteria

- ○ Yes, the medication is appropriate for the patient
- ○ No

Verify

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

Obtain RDA

C Cancel

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- (●) Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ( ) Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

- [x] Reviewed the following REMS data:

Prescriber Reported:
≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

- [x] Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? Opioid Tolerance Criteria

- (●) Yes, the medication is appropriate for the patient
- ( ) No

Verify

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

Obtain RDA

Cancel

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- ○ Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ◉ Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

☑ Reviewed the following REMS data:

Prescriber Reported:
≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

☑ Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? [ℹ Opioid Tolerance Criteria]

- ◉ Yes, the medication is appropriate for the patient
- ○ No

[Verify]

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

[Obtain RDA]

[C Cancel]

Patients must remain on around-the-clock opioids while taking a TIRF medicine.

To be opioid tolerant, a patient must be currently prescribed (exclusive of a TIRF medicine) one or more of the following opioid regimens daily and have been prescribed this regimen(s) for one week or longer:

- ≥ 60 mg oral morphine/day
- ≥ 30 mg oral oxycodone/day
- ≥ 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid
- ≥ 25 micrograms transdermal fentanyl/hour
- ≥ 8 mg oral hydromorphone/day
- ≥ 60 mg oral hydrocodone/day

Obtain a Patient'

An RDA is a receipt f

tly met.

Patient Enrolled as of 4/20/2020

Name: PatientJulie V
Date of Birth: 6/13/1970

-4439
Email Address: Patient@examoto.net

Prescriber Certified as of 4/20/2020

Prescriber: PRJane PRDoe
Address: 12 Parker Avenue
Chambersburg, PA 17201

NPI: 1310000000

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- (●) Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ( ) Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

☑ Reviewed the following REMS data:

Prescriber Reported:
≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

☑ Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? ℹ Opioid Tolerance Criteria

- (●) Yes, the medication is appropriate for the patient
- ( ) No

Verify

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

Obtain RDA

Cancel

SUCCESS
Rx Verification Recorded

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- (●) Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ( ) Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

☑ Reviewed the following REMS data:

Prescriber Reported:	
≥ 8 mg oral hydromorphone/day	

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

☑ Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? [i Opioid Tolerance Criteria]

- (●) Yes, the medication is appropriate for the patient
- ( ) No

[Verify]

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

RDA: d5fbbe14 [Copy] [Print] [Reverse]

Obtained by RxOutPatJane AuthRepDoe on 10/28/2020 at 6:12 PM Coordinated Universal Time

⊖ Detail

Safe Use Conditions:

- ✓ Patient is Enrolled: PatientJulie Williams
- ✓ To PRJane PRDoe's knowledge, Patient, PatientJulie Williams, is Opioid Tolerant
- ✓ Pharmacy Personnel is Certified: RxOutPatJane AuthRepDoe
- ✓ Pharmacy is Certified
- ✓ Pharmacy Personnel, RxOutPatJane AuthRepDoe, verified Opioid Tolerance for Patient, PatientJulie Williams
- ✓ Prescriber is Certified: PRJane PRDoe

Dispensation Information

Date	Manufacturer	NDC Code	Days Supply	Quantity
mm/dd/yyyy	Manufacturers			

[Save]

SUCCESS

Rx Verification Recorded

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

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Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- (●) Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ( ) Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

- [x] Reviewed the following REMS data:

Prescriber Reported:	
≥ 8 mg oral hydromorphone/day	

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

- [x] Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? Opioid Tolerance Criteria

- (●) Yes, the medication is appropriate for the patient
- ( ) No

Verify

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

RDA: d5fbbe14 Copy Print

Reverse

Obtained by RxOutPatJane AuthRepDoe on 10/28/2020 at 6:12 PM Coordinated Universal Time

Detail

Safe Use Conditions:

- ✓ Patient is Enrolled: PatientJulie Williams
- ✓ To PRJane PRDoe's knowledge, Patient, PatientJulie Williams, is Opioid Tolerant
- ✓ Pharmacy Personnel is Certified: RxOutPatJane AuthRepDoe
- ✓ Pharmacy is Certified
- ✓ Pharmacy Personnel, RxOutPatJane AuthRepDoe, verified Opioid Tolerance for Patient, PatientJulie Williams
- ✓ Prescriber is Certified: PRJane PRDoe

Dispensation Information

Date	Manufacturer	NDC Code	Days Supply	Quantity
10/28/2020	Company4	05640-0407-45	30	30

Save

SUCCESS
RDA Dispensation Information saved.

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

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— Or —

- ( ) Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

[x] Reviewed the following REMS data:

Prescriber Reported:
≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

[x] Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? Opioid Tolerance Criteria

- (●) Yes, the medication is appropriate for the patient
- ( ) No

Verify

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

RDA: d5fbbe14 Copy Print

Obtained by RxOutPatJane AuthRepDoe on 10/28/2020 at 6:12 PM Coordinated Universal Time

Detail

Safe Use Conditions:

- ✓ Patient is Enrolled: PatientJulie Williams
- ✓ To PRJane PRDoe's knowledge, Patient, PatientJulie Williams, is Opioid Tolerant
- ✓ Pharmacy Personnel is Certified: RxOutPatJane AuthRepDoe
- ✓ Pharmacy is Certified
- ✓ Pharmacy Personnel, RxOutPatJane AuthRepDoe, verified Opioid Tolerance for Patient, PatientJulie Williams
- ✓ Prescriber is Certified: PRJane PRDoe

Prescription dispense recorded for this RDA.

Return

To report any SUSPECTED ADVERSE REACTIONS, contact the TIRF REMS Call Center at 1-866-822-1483 or FDA at 800-FDA-1088 or http://www.fda.gov/medwatch.

Localization Version

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

- ○ Checked the patient's opioid tolerance by reviewing data from available state Prescription Drug Monitoring Programs (PDMPs), the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

— Or —

- ◉ Do not have access to Prescription Drug Monitoring Program data for this patient. I have reviewed the opioid tolerance data provided by the prescriber for this patient, the patient's records in the pharmacy's management system, and information provided by the TIRF REMS.

☑ Reviewed the following REMS data:

Prescriber Reported:
≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

☑ Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? [i Opioid Tolerance Criteria]

- ○ Yes, the medication is appropriate for the patient
- ◉ No

Please describe the reason for discrepancy below

reason for discrepancy gets added here

[Verify]

REMS Dispense Authorization (RDA)

A REMS Dispense Authorization is a receipt from the TIRF REMS indicating that the safe use conditions managed by the REMS are currently in place. Store this receipt with your records. This verifies that all requirements have been satisfied and that a REMS Dispense Authorization (RDA) has been issued.

[Obtain RDA]

[Cancel]

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

I provided the patient with the product-specific Medication Guide and I:

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≥ 8 mg oral hydromorphone/day

Adverse Events of Special Interest Reported	
Abused or been suspected of abusing their TIRF medicine	9/11/2020

[x] Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? Opioid Tolerance Criteria

- ( ) Yes, the medication is appropriate for the patient
- (●) No

Please describe the reason for discrepancy below

reason for discrepancy gets added here

Verify

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Obtain RDA

Cancel

SUCCESS
Rx Verification Recorded

Pharmacy

Outpatient Pharmacy Group

Obtain a Patient's REMS Dispense Authorization (RDA)

An RDA is a receipt from the TIRF REMS signifying that the REMS requirements to dispense for this patient are currently met.

Patient

Enrolled as of 4/20/2020

Name:	PatientJulie Williams	Zip Code:	30180
Date of Birth:	6/13/1970	Phone:	204-896-4439
		Email Address:	Patient@examoto.net

Prescriber

Certified as of 4/20/2020

Prescriber:	PRJane PRDoe	NPI:	1310000000
Address:	12 Parker Avenue Chambersburg, PA 17201		

Pharmacy Verification

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Abused or been suspected of abusing their TIRF medicine	9/11/2020

[x] Followed my pharmacy's procedures for TIRF medicines.

Based on the information provided, is the medication appropriate for the patient? Opioid Tolerance Criteria

- ( ) Yes, the medication is appropriate for the patient
- (●) No

Please describe the reason for discrepancy below

reason for discrepancy gets added here

Verify

STOP! Do Not Dispense

Please contact the patient's prescriber to discuss the discrepancy in the opioid tolerance information. After the discussion with the prescriber, if you agree that the medication is appropriate for the patient, please attempt to obtain the RDA again. Based on this discussion, the prescriber may need to submit a new Patient Status and Opioid Tolerance Form to update the opioid tolerance information for this patient.

REMS Dispense Authorization (RDA)

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Obtain RDA

Cancel

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARK A LIBERATORE
12/23/2020 04:05:28 PM