TIRF REMS

Transmucosal Immediate-Release Fentanyl (TIRF) REMS

Frequently Asked Questions

I. ALL STAKEHOLDERS FAQs

What is a TIRF medicine?

TIRF medicines are transmucosal immediate-release fentanyl prescription medicines used to manage breakthrough pain in adults with cancer who are already taking, and who are tolerant to other opioid (narcotic) pain medicines around-the-clock for their underlying, persistent cancer pain. Click here to see a full list of TIRF medicines.

What is a REMS?

REMS stands for "Risk Evaluation and Mitigation Strategy." A Risk Evaluation and Mitigation Strategy (REMS) is a risk management program required by the FDA to help ensure that the benefits of a drug outweigh the risks. The FDA has determined that a REMS is necessary for all marketed TIRF medicines.

What are the goals of the TIRF REMS?

Because of the risk for accidental exposure, misuse, abuse, addiction, and overdose, TIRF medicines are available only through a restricted program called the TIRF REMS.

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.

What are the components of the TIRF REMS?

An overview of the requirements for prescribers, patients, pharmacies, and distributors is included below:

- **Healthcare providers** who prescribe TIRF medicines for outpatient use must review the prescriber educational materials, successfully complete the Knowledge Assessment, enroll in the REMS, and commit to comply with the REMS requirements.

- **Patients** who are prescribed a TIRF medicine in an outpatient setting must sign a Patient Enrollment Form, which explains the risks and benefits of the drug, to be able to receive their TIRF medicine. This Form will also enroll the patient into a

registry to assess safe use and trends in accidental exposure, misuse, abuse, addiction, and overdose associated with TIRF medicines.

- **Outpatient pharmacies** that dispense TIRF medicines for outpatient use must be certified, train their pharmacy staff on the REMS requirements, and agree to comply with the REMS requirements. The pharmacy must designate an authorized representative to complete the certification process on behalf of the pharmacy. The authorized representative must review the Education Program, successfully complete the Knowledge Assessment, and complete the Outpatient Pharmacy Enrollment Form. Pharmacy staff must register online to access the Education Program and complete the Knowledge Assessment for training purposes.
- **Inpatient pharmacies** that dispense TIRF medicines for inpatient use must be certified, train their pharmacy staff on the REMS requirements, and agree to comply with the REMS requirements. The pharmacy must designate an authorized representative to complete the certification process on behalf of the pharmacy. The authorized representative must review the Education Program, successfully complete the Knowledge Assessment, and complete the Inpatient Pharmacy Enrollment Form. Pharmacy staff must register online to access the Education Program and complete the Knowledge Assessment for training purposes.
- **Wholesalers and distributors** that distribute TIRF medicines must enroll in the program and commit to distributing only to certified pharmacies.

The educational materials referenced above are available to prescribers and pharmacies through the TIRF REMS. In the outpatient setting, FDA-approved Medication Guides will be provided to patients by prescribers and pharmacists during counseling about the proper use of TIRF medicines.

Inpatient Use Only - Prescribers who prescribe TIRF medicines that will only be used in an inpatient setting (e.g., hospitals, hospices, or long-term care facilities) are not required to enroll in the TIRF REMS. Similarly, patients who receive TIRF medicines in an inpatient setting are not required to enroll in the TIRF REMS. Long-term care and hospice patients who obtain their medications from outpatient pharmacies must be enrolled.

Why does the TIRF REMS require prescriber certification for outpatient prescribing?

Prescriber certification is required to help ensure that prescribers receive education on the safe use of TIRF medicines, specifically that the safe use of TIRF medicines requires the patient to be opioid-tolerant.

To become enrolled, prescribers must review the Prescriber Education Program including the Full Prescribing Information, successfully complete the Knowledge Assessment, and complete and submit a Prescriber Enrollment Form to the TIRF REMS.

Does the TIRF REMS require certification for prescribers who prescribe TIRF medicines for inpatient use only?

No. Healthcare providers who prescribe TIRF medicines for inpatient use only are not

required to enroll in the TIRF REMS.

Why does the TIRF REMS require pharmacy certification?

Pharmacy certification is required to help ensure that all relevant staff involved in dispensing TIRF medicines receive education on the safe use of TIRF medicines, specifically that the safe use of TIRF medicines requires the patient to be opioid-tolerant.

Only enrolled pharmacies are eligible to receive shipments of TIRF medicines and/or to dispense prescriptions written by enrolled prescribers for outpatients. A designated authorized representative must review the Education Program and successfully complete the Knowledge Assessment. Only then can the authorized representative complete and submit an enrollment form on behalf of the pharmacy. The authorized representative will train other staff within the pharmacy in the appropriate dispensing of TIRF medicines according to the TIRF REMS.

Prescriptions for outpatient use written by prescribers who are not enrolled in the REMS will not be authorized by the TIRF REMS and TIRF medicines will not be dispensed to an outpatient who is not enrolled.

Why does the TIRF REMS require a Patient Enrollment Form?

The TIRF REMS requires all prescribers to complete and sign a Patient Enrollment Form with each new patient in the outpatient setting, before writing the patient's first prescription for their TIRF medicine. The Patient Enrollment Form helps to ensure that each patient for whom the TIRF medicine has been prescribed is appropriately counseled on the safe use and storage of their TIRF medicine. The prescriber must also verify on the Patient Enrollment Form that the patient is opioid-tolerant. The prescriber must submit a copy to the TIRF REMS before writing the patient's first prescription for TIRF medicine.

A Patient Enrollment Form is not required for inpatient use of TIRF medicines.

Where do I find a list of pharmacies that participate in the TIRF REMS?

The TIRF REMS website homepage contains a feature called "Find" that allows patients and prescribers to find enrolled pharmacies. This information can also be obtained by calling the TIRF REMS Call Center at 1-**866-822-1483**.

How can I obtain TIRF REMS materials?

All TIRF REMS education materials and forms are available and can be downloaded from www.TIRFREMSaccess.com using Adobe Acrobat Reader. Materials are also available by calling the TIRF REMS call center at 1-**866-822-1483** for assistance.

How do I contact the TIRF REMS?

You can contact the TIRF REMS by calling the TIRF REMS Call Center at 1-**866-822-1483**.

How can I report adverse events?

Promptly report serious adverse events, including reports of accidental exposure, misuse, abuse, addiction, and overdose to the TIRF REMS using the Adverse Events of Special Interest Reporting Form. The form may be completed online or by faxing a completed form to the TIRF REMS at **1-866-822-1483**.

In addition, you may report adverse event information to the FDA MedWatch Reporting System by telephone at **(800) FDA-1088** or by mail using Form 3500, available at **www.fda.gov/medwatch**.

II. Patient FAQs

As a patient, how do I participate in the TIRF REMS?

If you and your prescriber decide that a TIRF medicine is right for you, you will receive counseling from the prescriber on the safe use of TIRF medicines using the Medication Guide and the Patient Counseling Guide. You must sign a Patient Enrollment Form with your prescriber. You must be taking around-the-clock opioid pain medicine for one week or longer before starting your TIRF medicine and for the entire duration of therapy with your TIRF medicine. Your prescriber will help you find and will send your prescription to a pharmacy participating in the TIRF REMS.

Patients in an inpatient setting are not required to participate in the TIRF REMS in order to be prescribed and dispensed TIRF medicines for inpatient use only. However, if your prescriber gives you a prescription for a TIRF medicine to take at home once you leave the inpatient facility, you must sign a Patient Enrollment Form with your prescriber to participate in the TIRF REMS.

Do I have to re-enroll in the TIRF REMS?

You must re-enroll in the TIRF REMS every two years. You will receive counseling from the prescriber on the safe use of TIRF medicines using the Medication Guide and the Patient Counseling Guide. You must sign a Patient Enrollment Form with your prescriber to complete the re-enrollment.

Will I need to re-enroll in the TIRF REMS again if I transfer to a different prescriber?

No. However, your new prescriber will need to submit a *Patient Status and Opioid Tolerance Form* before your next prescription can be filled.

How would I know if I need to transfer to a different prescriber?

You would need to transfer to a different prescriber if your current prescriber is no longer participating in the TIRF REMS. If this happens, your current prescriber would not be allowed to write a prescription for a TIRF medicine. Your prescriber may tell you he or she is no longer participating in the TIRF REMS or you may be contacted by the TIRF REMS Call Center to tell you.

Where do I find a list of pharmacies that participate in the TIRF REMS?

The TIRF REMS website homepage contains a feature called “Find” that allows patients and prescribers to find enrolled pharmacies. This information can also be obtained by calling the TIRF REMS Call Center at 1-**866-822-1483**.

III. Outpatient Pharmacy FAQs

How does an outpatient pharmacy certify in the TIRF REMS?

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 certify the pharmacy, the authorized representative must review the Education Program, successfully complete the Knowledge Assessment, and complete the Outpatient Pharmacy Enrollment Form through the website, or complete and fax the signed Knowledge Assessment and enrollment form to the TIRF REMS at **1-866-822-1487**. The authorized representative must use the Pharmacy Education, located on the TIRF REMS website, to train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS.

How long is a pharmacy's certification effective in the TIRF REMS?

A pharmacy's certification is valid as long as the pharmacy meets the REMS requirements. However, 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.

What does an outpatient pharmacy have to do before dispensing a TIRF medicine?

The outpatient pharmacy must establish processes and procedures to check the patient's medication use for a change in opioid tolerance. Before dispensing, the outpatient pharmacy must check the patient's 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 as part of obtaining authorization to dispense each prescription. This can be completed online or by calling the TIRF REMS Call Center at **1-866-822-1483**.

Outpatient pharmacies must confirm the patient's opioid tolerance by ensuring that a REMS Dispense Authorization (RDA) is obtained from the TIRF REMS program for <u>every</u> TIRF medicine prescription transaction. An RDA can be obtained online or by calling the TIRF REMS Call Center. A pharmacy <u>must not dispense</u> a TIRF medicine without receiving an RDA. Failure to comply with this requirement may be grounds for un-enrollment from the program.

If the patient's prescription is denied, will the TIRF REMS system explain the reason?

Before dispensing a TIRF prescription for an outpatient, the pharmacy must obtain a REMS Dispense Authorization. When a dispense authorization is denied, the TIRF REMS system will provide a specific explanation for the denial. For assistance, please call the TIRF REMS Call Center at **1-866-822-1483** to obtain information related to a denial.

How does a pharmacy obtain TIRF medicines from a wholesaler-distributor?

Only enrolled wholesaler-distributors are allowed to distribute TIRF medicines to certified pharmacies. The TIRF REMS provides access to a list of certified pharmacies. Wholesaler-distributors must verify that a pharmacy is certified before distributing

TIRF medicines to the pharmacy.

IV. Inpatient Pharmacy FAQs

How do I enroll as an inpatient pharmacy?

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 certify the pharmacy, the authorized representative must review the Education Program, successfully complete the Knowledge Assessment, and complete the Inpatient Pharmacy Enrollment Form through the website, or complete and fax the signed Knowledge Assessment and enrollment form to the TIRF REMS at **1-866-822-1487**. The authorized representative must use the Pharmacy Education, located on the TIRF REMS website, to train all relevant staff involved in dispensing of TIRF medicines on the risks associated with TIRF medicines and the requirements of the REMS.

Additional information about the TIRF REMS Education Program and enrollment can be obtained through the TIRF REMS (www.TIRFREMSaccess.com) or by calling 1-**866-822-1483**.

How long is a pharmacy's certification effective in TIRF REMS?

A pharmacy's certification is valid as long as the pharmacy meets the REMS requirements. However, 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.

Do inpatient pharmacies have to obtain a REMS Dispense Authorization before dispensing?

No, inpatient pharmacies are not required to obtain a REMS Dispense Authorization before dispensing. However, the pharmacy is required to verify the patient is opioid tolerant through the processes and procedures established as a requirement of the TIRF REMS.

Can inpatient pharmacies obtain TIRF medicines in a healthcare facility?

Yes. However, the inpatient pharmacy within or associated with the healthcare facility must be certified in the TIRF REMS before inpatient pharmacies can purchase TIRF medicines.

Additional information can be obtained from www.TIRFREMSaccess.com or by calling the TIRF REMS call center at 1-**866-822-1483**.

V. Prescriber FAQs

What is the certification process?

The prescriber must review the Education Program, successfully complete the Knowledge Assessment, and complete an enrollment form through the website at www.TIRFREMSaccess.com, or complete and fax the signed Knowledge Assessment and enrollment form to the TIRF REMS at 1-**866-822-1487**.

A prescriber may obtain an enrollment form online from the TIRF REMS website (www.TIRFREMSaccess.com) or by calling 1-**866-822-1483**.

The program requires that a signed enrollment form and Knowledge Assessment be received by the TIRF REMS for each prescriber who requests certification. Only healthcare providers who will prescribe TIRF medicines for outpatient use are required to be certified in the TIRF REMS.

How long is my certification effective in the TIRF REMS?

Your certification is effective for two (2) years. You will be required to re-certify in the TIRF REMS every two (2) years if you wish to continue dispensing these products. You will be notified by the TIRF REMS in advance of the need to re-certify.

What other requirements do I have in the TIRF REMS?

You must assess the patient for opioid tolerance, appropriateness of dose, misuse, abuse, addiction, and overdose before each prescription. You must document the patient's opioid tolerance on the Patient Enrollment Form before the first prescription. You must document the patient's opioid tolerance and report all serious adverse events, including adverse events of special interest on the Patient Status and Opioid Tolerance Form for each subsequent prescription.

What is an opioid-tolerant patient?

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

Where do I find a list of pharmacies that participate in the TIRF REMS?

The TIRF REMS website homepage contains a feature called "Find" that allows patients and prescribers to find enrolled pharmacies. This information can also be obtained by calling the TIRF REMS Call Center at 1-**866-822-1483**.

Can I write an order for TIRF medicines for inpatient use?

Yes, prescribers can write orders for TIRF medicines for inpatient use without the prescriber or the patient being enrolled in the TIRF REMS. However, the inpatient pharmacy needs to be enrolled in the TIRF REMS to receive and dispense TIRF medicines to inpatients in the healthcare facility.

If a prescriber is discharging a patient with a TIRF medicine prescription intended to be filled by an outpatient pharmacy, then the prescriber must be enrolled in the TIRF REMS and complete a Patient Enrollment Form. The prescription for outpatient use can only be filled through an enrolled outpatient pharmacy.

Additional information on the TIRF REMS Education Program and enrollment can be obtained through the TIRF REMS (www.TIRFREMSaccess.com) or by calling 1-**866-822-1483**.

VI. Wholesaler-Distributor FAQs

Does a wholesaler-distributor have to enroll in the TIRF REMS?

Yes, wholesaler-distributors must enroll in the TIRF REMS to be able to purchase and distribute TIRF medicines.

How long is my enrollment effective in TIRF REMS?

Your enrollment in the TIRF REMS does not expire.

What are the TIRF REMS requirements for a wholesaler-distributor?

To enroll in the TIRF REMS, a wholesaler-distributor must complete and sign the Wholesaler-Distributor Enrollment Form. In signing the enrollment form, the wholesaler-distributor is required to indicate that they understand that TIRF medicines are available only through the TIRF REMS and that they will comply with the program requirements. The TIRF REMS will contact wholesaler-distributors to enroll in the REMS. If you have questions about enrolling in the TIRF REMS, contact the TIRF REMS Call Center at 1-866-822-1483.

How can enrolled wholesaler-distributors access a list of pharmacies that participate in the TIRF REMS?

Wholesaler-distributors can access the current list of certified pharmacies by:

- Utilizing the website (www.TIRFREMSaccess.com/Public/Home/VerifyShippingDestination).
- Calling the TIRF REMS call center at 1-866-822-1483.