he risks of opioid use and misuse is a growing national epidemic, sparking the government and its agencies to take action (see page xx for more on new CDC guidelines for prescribing). But there is yet another class of medications that presents its own set of challenges for physicians and patients alike.

TIRF (Transmucosal Immediate Release Fentanyl) carries a potentially greater hazard for the inexperienced patient, physician and pharmacist. As a rapid acting opioid, the fentanyl in TIRF products is highly desirable for abuse. Data suggests that the adjusted risks for abuse are greater for these more difficult to obtain fentanyl IR products than would be expected based on lower prescribed volume/availability alone.²

Consequently, a few years ago the FDA introduced a REMS (Risk Evaluation and Mitigation Strategy) program to mitigate the risk of misuse, abuse, addiction, overdose, and serious complications due to medication errors with the use of TIRF medicine.

A Little Background

The TIRF REMS program is an FDA-required program designed to ensure informed risk-benefit decisions before initiating treatment and while patients are taking TIRF to ensure appropriate use of these medicines. TIRF medicines are indicated only for the management of breakthrough pain in adult cancer patients who are already receiving and who are tolerant to around-the-clock opioid therapy. TIRF medicines are contraindicated in opioid non-tolerant patients and in the management of acute or postoperative pain, including headache/migraine and dental pain, or use in the emergency room. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients.

An important objective for the shared TIRF REMS is to reduce the incidence of adverse events associated with accidental exposure and use by opioid naive, non-tolerant individuals. Each prescription is accompanied by a medication guide discussing issues such as proper dosing and administration, as well as appropriate safe storage and disposal of...
unused, used or unneeded medications.

**Role of the Pharmacy**

To ensure access and further enhance the safe use of this class of medications, clinicians and patients have employed the assistance of specialized pharmacies. In addition to regular stocking of TIRF medications, these pharmacies add extra levels of oversight and confirm that the TIRF products are being prescribed only to opioid tolerant patients. They confirm that patient-prescriber agreements are completed and ensure that patients are not only provided with the medication guide(s), but are also universally counseled regarding safe and appropriate use.

Having their oversight also assists with insurance complexities and assures a stable medication supply to provide consistent therapy. This helps patients avoid “running out” of medications, which could lead to painful flares, costly care in the emergency room, and potential inpatient hospital admission.

In our practice, we use a specialized pharmacy with a focus on cancer pain. They are one of a handful of pharmacies in the United States that have started to implement safeguards around the dispensing of all opioids. It is this author’s opinion that when patients are assessed and monitored properly and appropriate treatment algorithms are followed, TIRF products are the least frequently abused prescription opioids. This is in part due to the success of the TIRF REMS program. In order to prescribe these products long term, clinicians must enroll by:

- Reviewing the TIRF REMS Access Education Program
- Successfully completing the Knowledge Assessment with a score of 100%
- Signing the acknowledgement statements on the enrollment form

Considering the inherent risk with TIRF products, having an extra layer of compliance, education, and oversight by specialized pharmacies is a welcomed addition. Logic would dictate that when all interested parties are actively involved—including patients, prescribers, and pharmacies—that safety should improve. Examples of steps taken include questionnaire checklists to vet not only the patients, but the physicians based on variables such as credentials, specialty, board sanctions, enrollment in TIRF REMS, and licensure status.

**How Pharmacy Safeguards Make a Difference: A Brief Case Report**

A specialized pharmacy [Dunn Meadow, Ft. Lee, NJ] received a prescription for a TIRF product from a new patient. On completing their TIRF REMS checklist, and during their clinical assessment, they identified that the patient was not on around-the-clock opioids (a requirement of TIRF), and was being prescribed a TIRF product for severe pain due to kidney stones.

In addition, the prescriber started the patient at a dose higher than the recommended “lowest possible dose.” Through this diligence, the specialized pharmacy deemed that the prescription was not medically necessary, communicated with and educated the prescriber, and potentially ward off a significant adverse event for the patient. Safeguards like this appear to make a clinical difference and, in the case of TIRF prescribing, can be a life-saving intervention.

In a recent interview with *Practical Pain Management*, Dan Weinstein, CEO at Dunn Meadow, explained his pharmacy’s methods and policies: “Along with the help of our retired DEA [Drug Enforcement Agency] consultants and physician-only advisory board, we have created TIRF-REMS specific clinical assessments to control inappropriate prescribing. Prescriptions that do not pass our assessments will not be dispensed.”

Collaboration among the key stakeholders has the potential to improve appropriate prescribing of all opioids while helping to mitigate the risks of abuse and misuse. The list of stakeholders is notable for its breadth and depth: FDA, the DEA, the Centers for Disease Control and Prevention, the Substance Abuse and Mental Health Services Administration,
the Federation of State Medical Boards, individual state and local health-care regulatory and law enforcement agencies, prescribers, pharmacies, patient advocacy groups, and product manufacturers.

The literature supports the need for a comprehensive solution to the complex problems of nonmedical use and overdose with opioids. The new shared TIRF REMS program may be an important first step toward this goal, but it is likely that additional measures will be needed in the future.

Often times, TIRFS are used in an off-label manner for chronic pain not related to cancer, and adding clinical assessments at the pharmacy level may curtail inappropriate use. Having specialized pharmacy oversight adds one extra layer to the safe use of TIRF products. Prescribing clinicians should consider partnering with a local, regional or national specialized pharmacy partner.

References