

Using Opioids in the
Management of Chronic
Pain Patients: Challenges
and Future Options



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Introduction

It is estimated that more than 50 million Americans currently live with chronic nonmalignant pain,¹ and that the annual costs associated with this pain (e.g., missed work days, inability to work, visits to medical professionals) are in the range of \$85 billion to \$90 billion.² The impact of chronic pain on a patient's life may include the following:

- Sleep disturbance
- Effects on mood
- Restriction of the ability to do household chores
- Restriction of social activities
- Job change due to pain
- Job loss due to pain³

Using opioids to treat patients who have chronic pain can be a difficult decision. Many family physicians are hesitant to prescribe these medications because of concerns regarding the potential for misuse, abuse and addiction. Regulatory requirements that could leave the prescribing physician vulnerable to legal action or sanctions by federal and state authorities are also cause for concern. These and other concerns have sometimes led to undertreatment of chronic pain. For example, according to a 2005 survey, 19 percent of American adults reported suffering from chronic pain, and 34 percent reported recurrent pain.⁴ Only 31 percent of these respondents reported complete relief from pain, and 21 percent reported little to no relief. In another study, only 17.8 percent of responding managed care organizations systematically used clinical practice guidelines for pain management.²

Opioids can be effective for chronic pain relief when used according to published guidelines as part of a comprehensive approach to treatment. For some patients who require daily medication, opioids that are prescribed and monitored appropriately may pose less risk of associated morbidity than other pain medications (e.g., non-steroidal anti-inflammatory medicines).⁵

While opioids can effectively reduce pain severity, they should not be expected to also address the complex psychosocial factors and disability that are frequently comorbid with chronic pain. In order to achieve meaningful improvement of pain and pain-related impairments, opioids should be used in conjunction with a more comprehensive pain management program that will directly address functional impairment and psychosocial factors.⁶

Focusing on the treatment of

nonmalignant chronic pain, this publication will do the following:

- Define terms often associated with opioid use, including misuse, abuse and addiction;
- Briefly review the possible side effects of opioids;
- Describe guidelines for the use of opioid therapy in patients who have chronic nonmalignant pain, including risk management strategies useful for family physicians;
- Talk about the proper disposal of unused opioid medications;
- Discuss the U.S. Food and Drug Administration's (FDA's) Risk Evaluation and Mitigation Strategies (REMS) plan, which is currently open for comment; and
- Discuss the development of abuse-deterrent and abuse-resistant opioid formulations.

Definitions

Prescriptions for opioids have increased substantially during the past 20 years, as have the misuse of opioids and associated mortality.⁶ Family physicians must be able to explain the risks associated with the use of opioids. *Table 1*

Table 1
Definitions

Term	Definition
Aberrant drug-related behavior	A behavior outside the boundaries of the agreed-on treatment plan which is established as early as possible in the doctor-patient relationship.
Abuse	Any use of an illegal drug, or the intentional self-administration of a medication for a nonmedical purpose, such as altering one's state of consciousness (for example, getting high).
Addiction	Characterized by behaviors that include one or more of the following: impaired control over drug use; compulsive use; continued use despite consequences; and craving.
Diversion	The intentional transfer of a controlled substance from legitimate distribution and dispensing channels.
Misuse	Use of a medication (for a medical purpose) other than as directed or indicated, whether willful or unintentional, and whether harm results or not.
Physical dependence	A state of adaptation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.
Tolerance	A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time.

Adapted with permission from Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 2009;10:113-30.

defines a number of relevant terms. When talking with patients about the risks of opioid use, it is important to clearly differentiate these terms. Patients need to understand the potential for addiction, and they also need to know about other risks associated with opioid use.

Side Effects

Before initiating opioid therapy, family physicians should describe the various side effects patients may experience. While side effects are often dose-dependent, they may also depend on the particular drug that is prescribed. In addition, there are certain side effects that are common to opioids as a medication class. The most common adverse side effect experienced by patients on opioid therapy is constipation, followed by fatigue, nausea, sleep disturbances and loss of appetite.^{1,6} Patients who are on daily opioid therapy are more likely to experience these adverse effects than those who take the drugs intermittently.¹ Other possible side effects include depression, sexual dysfunction, hypogonadism, hyperalgesia and rash.^{1,6} For patients who are prescribed methadone, a prolonged QT interval is a possible concern and should be monitored. Patients who are prescribed daily opioid therapy should be placed on an appropriate bowel regimen. This can include increased fluid and fiber intake, and the use of stool softeners and laxatives.⁶ Patients should also be routinely assessed for depression and sexual dysfunction.¹

Risk Factors for Aberrant Behaviors

Certain patient populations are at greater risk for manifesting aberrant behaviors or experiencing harm due to opioid use. *Table 2* lists the most prevalent risk factors. The greatest risk factors for aberrant behaviors are a personal or family history of drug abuse, younger age and a history of psychiatric disorders.⁶ It is important to recognize, however, that aberrant behaviors can also develop in patients who lack these risk factors. All patients who are prescribed opioids must be monitored vigilantly.

Guidelines for Use of Opioids

Recently, the American Pain Society (APS) and the American Academy of Pain Medicine (AAPM) issued guidelines on using opioid therapy to treat patients who have chronic nonmalignant pain.⁶ These guidelines can help the family physician select patients who are good candidates for opioid therapy and document the treat-

Table 2

Risk Factors for Aberrant Behaviors/Harm

Biological	Psychiatric	Social
Age ≤ 45 years	Substance use disorder	Prior legal problems
Female gender	Preadolescent sexual abuse (in women)	History of motor vehicle accidents
Family history of prescription drug or alcohol abuse	Major psychiatric disorder (e.g., personality disorder, anxiety or depressive disorder, bipolar disorder)	Poor family support
Cigarette smoking		Involvement in a problematic subculture

Information from Katz NP, Adams EH, Bennayan JC, Birnbaum HG, Budman SH, Buzzeo RW, et al. Foundations of opioid risk management. Clin J Pain 2007;23:103-18; Manchikanti L, Giordano J, Boswell MV, Fellows B, Manchukonda R, Pampati V. Psychological factors as predictors of opioid abuse and illicit drug use in chronic pain patients. J Opioid Manag 2007;3:89-100; and Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med 2005;6:432-42.

ment and management of these patients, which can lower any liability the physician may incur. The guidelines are comprehensive and cover the following:

- Patient selection and risk stratification
- Informed consent and opioid management plans
- Initiation of chronic opioid therapy
- Methadone
- Monitoring
- Dosage and discontinuation of therapy
- Use of psychotherapeutic cointerventions
- Patient safety
- Identification of a medical home (i.e., the physician responsible for managing a patient's opioid prescriptions)
- Opioid policies

Patient Selection and Risk Stratification

Opioid treatment is not appropriate for all patients. It is important for the physician to order appropriate diagnostic tests to evaluate a patient's underlying pain condition. The physician should consider whether nonopioid therapy is likely to be effective. Patients who have moderate to severe pain that has not responded to nonopioid therapies are most likely to be candidates for opioid therapy.^{7,8}

All patients being considered for opioid therapy should provide a thorough history, including family history and disclosure of any psychosocial risk factors (see *Table 2*). The patient must also undergo a physical examination and appropriate testing. In every case, this testing must include a thorough assessment and stratification of the patient's risk of substance misuse, abuse or addiction.

There are several different screening questionnaires that can be used in clinical practice to assess a patient's potential risk for abuse and addiction, including the

Screener and Opioid Assessment for Patients with Pain (SOAPP®) Version 1 (available online at: <http://www.painedu.org/soapp.asp> [registration required]), the revised SOAPP (SOAPP-R), the Opioid Risk Tool (ORT) and the Diagnosis, Intractability, Risk, Efficacy (DIRE) instrument. The SOAPP and ORT tools are both brief, patient-administered screening instruments used to assess the risk of aberrant drug-related behaviors in patients who have chronic pain. The DIRE tool is administered by the physician and can assess the potential efficacy and potential harms of opioid therapy. These tools should be used as part of a comprehensive education, documentation and informed consent process.

When using a screening tool, the physician must keep in mind that not all patients will be able to comprehend all of the questions. For example, the grade level at which the questions are written may be challenging for some patients.⁹ Average Americans read at the sixth- to eighth-grade level,¹⁰ and most of the screening tools include statements or questions written at the twelfth-grade level.⁹ It is important to gauge each patient's literacy level and make time to explain the various questions and statements, if necessary.

These screening tools can help identify some patients who are at the highest risk for abusing opioids, but they are not perfect. In some cases, the screening tools may give a false sense of security because even patients who score low on risk assessments may go on to misuse or abuse opioids. Therefore, it is important for physicians to be vigilant whenever they prescribe opioid therapy, even when the patient seems to be at lower risk of abuse. For patients who are identified as having a high risk for aberrant drug-related behaviors, including those who have a history of drug abuse or psychiatric issues, it is appropriate to consider consulting with, cotreating the patient with, or referring the patient to a mental health or addiction specialist.

Informed Consent and Opioid Management Plans

Informed consent is an integral part of the opioid prescribing process and should be obtained for all patients undergoing long-term treatment with these drugs. Such consent should also be obtained for patients undergoing short-term opioid therapy who are at high risk for abuse.¹¹ Patients must understand the risks and benefits associated with chronic opioid therapy before it is initiated. In addition, physicians should periodically review the risks and benefits of opioid therapy with patients who are taking opioids. Informed consent requires counseling about the potential for common adverse effects (e.g., constipation, fatigue) and the serious risks of abuse and addiction. It is strongly recommended that the physician document this discussion and have the patient sign an informed consent form.

Perhaps the most important document a physician

and patient can develop before initiating ongoing opioid therapy is the opioid management plan (also known as a medical agreement or opioid contract). This agreement should be tailored to each individual patient. It describes the treatment plan, including the responsibilities of both the patient and the physician, and the rules by which opioid treatment will be provided. The agreement should include a detailed written description of the appropriate and safe use of opioids, such as obtaining prescriptions for these drugs from only one prescriber and filling prescriptions at one designated pharmacy. Information about safe storage of opioid medications should also be included (e.g., mentioning the possibility that opioids may be stolen if they are kept in an unlocked medicine cabinet).

If they are used, opioids should be part of a comprehensive pain management program, rather than the only treatment given to reduce pain. Both the physician and the patient must understand that the primary goal of opioid therapy is to reduce disability. Clear, specific goals that focus on function and quality of life should therefore be established as part of the opioid management plan. Ask the patient to describe how his or her daily functions are affected by chronic pain. Then set goals identifying functional outcomes that can be measured over a specific period of time. For example, a patient's desired outcome could be one of the following: increasing daily ambulation by a defined amount; being able to sit through an entire movie in a theater; or, being able to sit and work at a computer for several hours. While the patient is on opioid therapy, monitor these functional outcomes carefully. If the patient is not meeting his or her goals, the treatment plan should be revisited.

The opioid management plan should clearly describe why the patient is being given a particular medication.¹² The plan should also describe the following:

- Exactly how opioids will be prescribed and taken;
- How often the patient will return for follow-up and monitoring;
- The use of random urine drug testing and pill counting;
- Alternatives to chronic opioid therapy for patients who may not respond to such treatment;
- Additional therapies that may be used during chronic opioid therapy; and
- Reasons for the discontinuation of opioid therapy (e.g., failure to adhere to the agreement, failure to reach therapeutic goals, intolerable adverse effects, serious aberrant behaviors).

It is important to provide the patient with documentation of his or her management plan. Patients often cannot absorb everything that is discussed during an office visit. Giving patients their plan in writing reinforces everything that is required of them while they are on opioid therapy. It also makes it easier to communicate with family members, friends or other caregivers who will be involved in the patient's treatment, including other physicians.

Initiation of Chronic Opioid Therapy

The APS/AAPM guidelines emphasize that initial treatment with opioids should be regarded as a therapeutic trial to determine whether such treatment is appropriate. Outcomes of treatment should be monitored closely, particularly with respect to the goals agreed upon in the patient's management plan. For patients who experience mild or moderate adverse effects from opioid treatment, a longer trial may be needed to determine whether the adverse effects will lessen with time.

While the guidelines point out that short-acting opioids are safer for initial therapy because they are associated with a lower risk of inadvertent overdose, long-acting opioids may be better for patients who have chronic pain. When short-acting opioids are dosed as needed, patients who have chronic pain experience cycles of increased pain as the level of the previous dose in their blood falls and they must wait for the subsequent dose to take effect. Short-acting medications produce substantial peak-to-trough drug level variations, in which the drug level increases rapidly (peak) and decreases a few hours later (trough). Patients who have frequent disabling pain episodes or nearly constant disabling pain may take short-acting medications four to six times per day to try to minimize times of drug trough levels. To combat this, chronic pain patients who have disabling pain may be prescribed sustained-release, long-acting opioids to maintain more consistent opioid levels.¹³ Short-acting opioids may be used occasionally in these patients for acute exacerbations of pain or breakthrough pain.

Methadone

The use of methadone has increased in recent years.¹⁴ Any physician prescribing methadone must be familiar with its clinical pharmacology, its risks and its potential for causing adverse events, including death. Due to its long and variable half-life, which has been estimated at anywhere from 15 to 120 hours,¹⁵ methadone should be started at low doses and titrated slowly.⁶ The APS/AAPM guidelines recommend starting at a safe dose of 2.5 mg every eight hours and increasing doses no more than weekly. In older patients, or patients who have renal or hepatic comorbidities, the guidelines recommend less frequent dosing and more cautious dose titration.

In opioid-tolerant patients, the guidelines recommend cautious conversion to methadone. Matching the dose ratios for methadone relative to

other opioids can be difficult — morphine equivalents can range from 0.1 percent to 10 percent. In patients who are taking lower doses of other opioids, safe starting doses of methadone can be similar to those used in patients who have never received opioids. In patients who are transitioning from a different opioid to methadone, the guidelines recommend that, in general, starting methadone doses should not exceed 30 mg a day, even if the patient was already on higher doses of the other opioid. The guidelines also recommend that methadone should not be used to treat breakthrough pain or as an as-needed medication.⁶

Monitoring

Regular monitoring of all patients on chronic opioid therapy is a vital component of the overall management strategy for these patients. While patients who are at higher risk for opioid misuse and abuse should be monitored extremely closely, all patients who are taking opioids must be seen and monitored on a regular basis. Monitoring should consist of documenting the patient's pain intensity and level of functioning, assessing progress toward the functional outcomes agreed upon in the management plan, discussing adverse effects, and evaluating adherence to prescribed therapies. In addition, monitoring should include pill counts, interviews with family members and/or caregivers, and use of prescription monitoring program data, if available. *Table 3* describes one possible approach to monitoring.

Table 3

Six A's for Monitoring Patients who have Chronic Nonmalignant Pain Taking Controlled Substances

Analgesia	Record patient's pain intensity at baseline and at all subsequent visits. Learn how to handle breakthrough pain.
Activities of daily living	Patient must show a benefit in their daily lives and psychosocial functioning. Note a patient's typical day when beginning opioid therapy, and revise the schedule during subsequent visits.
Adverse events	The goal must be to achieve high analgesia with the most benign side effect profile. Know the typical side effects of the opioid prescribed and all available countermeasures.
Aberrant behavior	Any behaviors suggestive of drug abuse, such as "losing" multiple prescriptions or unauthorized dose escalation.
Assessment	Evaluate the patient's mood on a regular basis. Also evaluate patients at all points for possible signs of abuse or tolerance, and ensure that you know of any adverse events they may experience.
Action plan	Ensure that you have a signed treatment plan in place that details the expectations of therapy, including concrete, measurable outcomes, as well as the consequences of any misuse or abuse of opioid drugs prescribed.

Information from Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. Adv Ther 2000;17:70-83.

Monitoring can help identify patients who are benefiting from opioid therapy, as well as those who may benefit from a different treatment, a different opioid, or additional services, such as treatment for addiction. It can also identify patients for whom the harm of chronic opioid therapy outweighs the benefit. To determine efficacy and tolerability of treatment, patients should be monitored monthly for at least the first three months after beginning opioid therapy. Once patients are on a stable regimen, the APS/AAPM guidelines recommend that patients at low risk for adverse outcomes should be monitored at least once every three to six months. Those at higher risk should be monitored more frequently. For those at highest risk for adverse outcomes, weekly monitoring may be a reasonable strategy.

Periodic random urine drug testing is recommended for all patients on ongoing opioid therapy. It should be conducted more often in patients who are at higher risk for misuse or abuse, and in patients who exhibit possible aberrant drug-taking behaviors (*Table 4*). It is necessary to order a specific type of urine toxicology screen for hydrocodone; tests that screen for morphine or heroin will not necessarily find evidence of hydrocodone.¹⁶ Patients whose urine screenings show an absence of prescribed opioids or the presence of unprescribed opioids or illicit drugs should be tested more thoroughly for misuse or abuse. Physicians should keep in mind that urine drug tests are open to false positive and false negative results, so one screening should never be considered definitive proof that a patient is misusing, abusing or diverting a drug. Targeted urine drug screening may also miss some patients who are engaging in aberrant behaviors.

Dosage and Discontinuation of Therapy

The new APS/AAPM guidelines recommend reassessment of chronic opioid therapy in patients who require repeated dose escalations. Such escalations can improve symptoms and may be a sign that patients are tolerating the treatment well. They also may signal a substance abuse disorder or diversion of prescription medications. Experts on the guideline panel defined high-dose opioid therapy as more than 200 mg daily of morphine or equivalent. For patients who require such high doses of opioids, more frequent and intense monitoring is appropriate. This monitoring can help guide the decision of whether or not to continue opioid therapy. A patient may require therapy restructuring if monitoring indicates that any of the following are true:

- Despite dose escalations, the patient's analgesia, function or quality of life is reduced.
- The patient exhibits aberrant drug-related behaviors.
- The patient is experiencing intolerable adverse effects.

For these patients, opioid rotation, or switching from one opioid to another, is a potential approach, although there is currently insufficient evidence to guide specific

recommendations on this approach. Weaning and discontinuation of chronic opioid therapy are other options.

Use of Psychotherapeutic Cointerventions

Patients who experience chronic nonmalignant pain often have comorbidities that can include psychological disturbances.⁶ The most common are depression, anxiety and sleep disorders. For these patients, chronic opioid therapy usually works best as part of a multimodal treatment approach. Integrating therapies such as cognitive-behavioral therapy, progressive relaxation or biofeedback into a chronic pain patient's treatment can lead to better results than using pharmacologic therapy alone.⁶ Interdisciplinary pain management approaches can also benefit these patients. These approaches involve coordinating care with physical, occupational or vocational therapists, as well as psychologists, and may involve an exercise or activity program and psychological therapy. An interdisciplinary approach requires the participation of at least two health care professionals with different clinical backgrounds. Studies have shown that this interdisciplinary approach can result in improved outcomes for chronic pain patients.¹⁷

Patient Safety

The use of opioid medications requires physicians to counsel patients on certain safety issues. Opioids can cause somnolence, clouded mentation, decreased concentration, and slower reflexes or lack of coordination. This is especially true immediately after therapy is initiated, during dose escalations, or when opioids are taken with other drugs or substances that can affect the central nervous system. Any of these effects can substantially affect a patient's ability to drive or work safely. It is important to counsel all patients who are beginning opioid therapy not to drive or engage in any dangerous work while they may be impaired. Patients who have been stabilized on opioids and are taking a tolerable dose can generally drive safely.⁶ There are additional regulations and laws regulating the use of opioids for patients whose occupations depend on them driving or flying (e.g., bus drivers, pilots). When working with such patients, physicians should be sure they know the applicable laws and regulations and advise patients accordingly. In addition, it is vital to document conversations with the patient about safety issues in his or her medical record.

Identifying a Medical Home

It is important for chronic pain patients who are on opioid therapy to have continuous access to a primary care physician who is in charge of their comprehensive medical care. These patients tend to use health care services more frequently and have more comorbidities than

Table 4
Aberrant Drug-Taking Behaviors

Illegal or Criminal Behavior

Diversion (sale or provision of opioids to others)

Prescription forgery

Stealing or “borrowing” drugs from others

Dangerous Behavior

Motor vehicle crash /arrest related to opioid or illicit drug or alcohol intoxication or effects

Intentional overdose or suicide attempt

Aggressive/threatening/belligerent behavior in the clinic

Behavior that suggests addiction

Use of prescription medications in an unapproved or inappropriate manner (such as cutting time-release preparations, injecting oral formulations, and applying fentanyl topical patches to oral or rectal mucosa)

Obtaining opioids outside of medical settings

Concurrent abuse of alcohol or illicit drugs

Repeated requests for dose increases or early refills, despite the presence of adequate analgesia

Multiple episodes of prescription “loss”

Repeatedly seeking prescriptions from other clinicians or from emergency rooms without informing prescriber, or after warnings to desist

Evidence of deterioration in the ability to function at work, in the family, or socially, which appears to be related to drug use

Repeated resistance to changes in therapy despite clear evidence of adverse physical or psychological effects from the drug

Positive urine drug screen—other substance use

Aberrant behavior that requires attention

Aggressive complaining about needing more of the drug

Drug hoarding during periods of reduced symptoms

Requesting specific drugs

Openly acquiring similar drugs from other medical sources

Unsanctioned dose escalation or other noncompliance with therapy on one or two occasions

Unapproved use of the drug to treat another symptom

Reporting psychic effects not intended by the clinician

Resistance to a change in therapy associated with “tolerable” adverse effects, with expressions of anxiety related to the return of severe symptoms

Missing appointment(s)

Not following other components of the treatment plan (physical therapy, exercise, etc.)

Reprinted from Department of Veterans Affairs and Department of Defense. VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain. Washington, D.C.: Department of Veterans Affairs and Department of Defense; 2003. Available at: http://www.ihp.gov/nonmedicalprograms/nc4/documents/chronic_painguidelinesva2003.pdf.

patients who do not have chronic pain.^{18,19} Additionally, these patients often need to make use of services outside of their medical home. In such cases, the family physician can coordinate the patient’s care, consulting with other professionals and facilitating the patient’s access to their expertise, while also ensuring the follow-up and continuity the patient requires.

Opioid Policies

One concern many family physicians express about prescribing opioid therapy is that they may be subject to legal action and federal and state sanctions if their patients are overtreated. In reality, this type of sanction is exceptionally rare; according to one study, only approximately 0.1 percent of practicing physicians have faced sanctions for offenses related to prescribing opioid analgesics.²⁰ The primary sanctioning bodies are the U.S. Drug Enforcement Agency (DEA) and state medical boards. The APS/AAPM guidelines stress that physicians should be aware of current federal and state laws, regulatory guidelines and policy statements that govern the medical use of opioid therapy for chronic nonmalignant pain. For example, the Federation of State Medical Boards (FSMB) has written a policy regarding the use of controlled substances for the treatment of pain that is used by many state medical boards as their model.²¹ The policy provides information about the responsibilities of physicians who prescribe opioids. It stresses documentation of all facets of the patient’s care, from initial evaluation through monitoring and all reviews of the treatment plan. Presently, 24 states have adopted all or part of the FSMB guidelines.²¹ Most of the recommendations in the FSMB policy overlap with the guidelines presented in this publication. For family physicians who prescribe controlled substances to their patients, it is imperative to have a good working knowledge of the FSMB policy, and any other applicable regulations and laws specific to the state in which they practice.

Disposal of Unused Opioids

Unfortunately, most patients follow no uniform guidelines or protocols for safe and effective disposal of unused opioids.²²

In October 2009, the Office of National Drug Control Policy (ONDCP) issued federal guidelines on the proper disposal of prescription drugs.²³ In these guidelines, the ONDCP states that prescription drugs should not be flushed down the toilet or drain unless the label or accompanying patient information specifically gives instruction to do so. The FDA Web site (see: <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm>) includes a list of drugs that should be flushed, including many opioid medications, such as fentanyl, morphine, methadone and oxymorphone.²⁴ However, many environmental groups discourage flushing any medication into the sewage system because it could reach the water table, polluting drinking water and other water that people use (see: <http://www.SmaRxTDisposal.net>).

The U.S. Department of Justice prohibits consumers, patients and long-term care facilities from returning unused opioids and other controlled substances to pharmacists and physicians for destruction or possible reuse.²² Some communities have initiated pilot programs to take back controlled substances from consumers. In these communities, law enforcement agencies accept the substances from consumers, document what is collected, seal the substances in plastic bags and store them at a secure location until they can be incinerated.²² Contact your state law enforcement agency to determine whether this type of program is available in your practice area. They are not common, and most patients will not have access to them.

Another way to dispose of unused opioids is to put them in the trash. However, to ensure the safety of others (e.g., children) who may be able to get hold of these medications, the ONDCP recommends that the drugs be taken out of their original containers, mixed with undesirable substances (e.g., cat litter, used coffee grounds), and put into a disposable container with a lid or into a sealable bag before being put into the trash. The ONDCP also recommends concealing or removing any personal information on empty prescription containers by covering the information with black permanent marker or duct tape, or by scratching it off.²³

Risk Evaluation and Mitigation Strategies

In February of 2009, the FDA notified manufacturers of certain opioid drug products that these products will be required to have a Risk Evaluation and Mitigation Strategy (REMS). The affected drugs include long-acting and extended-release brand name and generic products formulated with the active ingredients fentanyl, hydromorphone, methadone, morphine, oxycodone and oxymorphone.²⁵ The REMS is intended to ensure that the benefits of these opioid drugs outweigh the risks of misuse, abuse and overdose.

Table 5

Possible Components of FDA Risk Evaluation and Mitigation Strategies (REMS)

- Required training (possibly certification) by physicians and pharmacists on the best use of opioid analgesics
- Increased use and details of physician-patient opioid agreements
- Increased patient education on the risks of opioid therapy
- Designation of certain pharmacies from which patients may get their opioid prescriptions
- Required education of patients on the appropriate use of opioids
- Registration of patients taking opioids
- Requirement of written patient consent prior to opioid therapy
- Required laboratory and pregnancy testing prior to initiation of opioid therapy
- Continuing education about opioid therapy for health care workers
- Development of tools to assess the impact and effectiveness of the REMS program

Information from Sloan PA. Opioid risk management: understanding FDA mandated risk evaluation and mitigation strategies (REMS). J Opioid Manag 2009;5:131-3.

At the time of publication, the FDA was still obtaining input on the proposed REMS. Possible components include the following:

- Medication guides
- Patient package inserts
- A communication plan for health care providers
- Elements to assure safe use, including requirements for those who prescribe, dispense or use opioid medications
- A timetable for submission of assessments of the REMS

Currently, there is no timetable for release of the REMS, but it will be vital for all health care workers to understand its components once the comment period ends and the final rule is released. Possible components of the REMS program are detailed in *Table 5*.

New Opioid Formulations Designed to Deter Abuse

Formulations designed to deter abuse have the potential to reduce the misuse, abuse and illegal use of opioid analgesics. One approach is to make it more difficult for an abusable portion of the active opioid to be extracted by

common methods such as chewing or crushing the opioid, or dissolving it in water or alcohol. Another approach involves formulations that contain an opioid antagonist (e.g., naltrexone, naloxone) in an attempt to blunt the euphorogenic effects of the opioid.²⁶ When the opioid is taken as prescribed, the antagonist remains unavailable. However, if the medication is crushed, chewed or dissolved, the antagonist becomes available. Other opioid formulations include a substance (e.g., capsaicin, niacin) that produces an unpleasant effect if the drug is taken improperly.²⁷ Prodrugs, which require activation in the gastrointestinal tract for the opioid to become active, are also under consideration.²⁷

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