Taking a look at pain in the United States

Large national surveys have found that chronic pain is a common and serious problem in the United States, and its incidence appears to be increasing (Figure 1). Pain can arise from a variety of common causes, including musculoskeletal pain, cancer pain, neuropathic pain, postsurgical pain, and visceral pain. According to the 2009 National Center for Health Statistics survey of noninstitutionalized civilian adults, the percentages of adults who reported experiencing various types of musculoskeletal pain within the previous 3 months was as follows: severe headache or migraine, 16.1%; low back pain, 28.1%; neck pain, 15.1%; knee pain, 19.5%; shoulder pain, 9.0%; finger pain, 7.6%; and hip pain, 7.1%.

Patients with chronic pain report that it has a substantial impact on their ability to perform activities of daily living (Table 1).

Institute of Medicine report on pain and call to action

To better assess the impact of pain in the United States, the Department of Health & Human Services directed the Institute of Medicine (IOM) to develop a report “to increase recognition of pain as public health problem in US” as required by the Affordable Care Act of 2010. The resulting report, Relieving pain in America: A blueprint for transforming prevention, care, education and research, was released in June 2011.

The IOM report provides a comprehensive review of the growing public health problem of under- and untreated pain and the challenges of pain management. It does not provide clinical recommendations for managing pain. Instead, it describes the scope of the problem of pain and provides an overview of needs for care, education, and research. The IOM report echoes recommendations from the public health initiative, Healthy People 2020, which included an objective to “increase the safe and effective treatment of pain.”

The IOM report highlighted several facts that illustrate the substantial burden of chronic pain in the United States:

- A total of 116 million adults experience chronic pain, which is greater than the number of adults with heart disease, diabetes, and all types of cancer combined.

Learning objectives

At the conclusion of this knowledge-based activity, the pharmacist will be able to:

- Discuss the findings and recommendations of the Institute of Medicine’s report, Relieving pain in America: A blueprint for transforming prevention, care, education and research.
- Explain the components of the REMS (risk evaluation and mitigation strategy) for long-acting and extended-release opioids and its impact on pharmacists.
- Describe the characteristics of medications recently approved for the management of pain.
- Discuss the clinical impact of recent published data describing the risks and benefits of analgesics.
The prevalence of chronic pain is expected to increase as the population ages, and increasing obesity rates produce increasing rates of musculoskeletal pain conditions and diabetes-related pain conditions.

Chronic pain results in $560 to $635 billion in added health care costs and lost productivity.

Millions of people receive inadequate pain management, resulting in unnecessary human suffering.

Preassessment questions
1. The Institute of Medicine report provided which of the following types of recommendations to improve pain management?
   a. Clinical practice recommendations for the 20 most common chronic pain conditions
   b. Specific guidance on assessing patients with pain for the risk of misuse, abuse, and/or diversion
   c. An overview of the need for pain care, education, and research
   d. An evidence-based review of all medications available in the United States that have a pain management indication

2. According to an April 2011 FDA announcement, which of the following elements to assure safe use is required for the risk evaluation and mitigation strategy for long-acting and extended-release opioids?
   a. The drug is dispensed to patients with evidence or documentation of safe use conditions (e.g., urine drug screens).
   b. Physicians who prescribe and/or pharmacists who dispense the medications must enroll in a registry.
   c. Each patient who uses one of the medications must be enrolled in a registry.
   d. Training is provided to prescribers of these medications, and patient education materials that providers can use when counseling patients are developed by the manufacturer.

3. What do pharmacists most commonly report as their initial concern when presented with an early refill request for an opioid?
   a. The patient is abusing or diverting the medication.
   b. The patient’s pain is not being adequately managed.
   c. The patient has not received proper education on how to use the medication.
   d. The patient might be cognitively impaired and not managing his or her medications properly.

   Answer locations: 1, TAKING A LOOK AT PAIN IN THE UNITED STATES; 2, REMS FOR OPIOIDS; 3, case studies section.

The IOM report supported the position that “in many cases, chronic pain is a disease in its own right.” Such an understanding of pain calls for increased attention to the treatment of pain by the health care system and in health professionals’ education. The report calls for pain treatment and research “with the same vigor expended on other serious and disabling chronic conditions.”

The IOM report issued a call to action for a cultural transformation in the manner in which pain is researched and managed on a systematic and individual level. Although many of the recommendations must be addressed on a systematic level, pharmacists can engage in many activities to improve the management of patients with pain. The report recommends a comprehensive, population-level strategy and provides a blueprint for moving forward. Key elements of the blueprint include:

- Reducing legal, regulatory, reimbursement, and cultural barriers to access.
- Educating the public about the prevention, treatment, and self-management of pain.
- Improving professional education across the spectrum of disciplines and throughout the continuum of undergraduate, graduate, and continuing health professions training.
- Focusing pain research efforts at the National Institutes of Health and coordinating that research with other government agencies and the private sector to speed development of new therapies, foster interdisciplinary approaches, increase longitudinal research of people in pain, and increase the number of pain researchers.

The IOM recommended that continuing education and training for health professionals address gaps in knowledge and competencies related to pain assessment and management, cultural attitudes about pain, negative and ill-informed attitudes about people with pain, and stereotyping and biases.

Table 1. Impact of pain on activities of daily living

<table>
<thead>
<tr>
<th>Type of pain</th>
<th>Difficulty with basic actions (%)</th>
<th>Complex activity limitation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe headache or migraine</td>
<td>31.0</td>
<td>33.5</td>
</tr>
<tr>
<td>Low back pain</td>
<td>51.6</td>
<td>55.0</td>
</tr>
<tr>
<td>Neck pain</td>
<td>30.2</td>
<td>34.4</td>
</tr>
<tr>
<td>Knee pain</td>
<td>37.3</td>
<td>38.6</td>
</tr>
<tr>
<td>Shoulder pain</td>
<td>17.7</td>
<td>21.4</td>
</tr>
<tr>
<td>Finger pain</td>
<td>14.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Hip pain</td>
<td>15.0</td>
<td>18.4</td>
</tr>
</tbody>
</table>

*Defined as having difficulties in one or more of the following areas: movement, emotional, seeing, hearing, or cognition.

*Defined as having limitations in one or more of the following areas: self-care, social, or work.

Source: Reference 2.
most effective analgesics and are also associated with abuse and diversion “a conundrum.” The misuse and abuse of opioids is a growing and important public health problem with a number of serious consequences. For example, the number of deaths associated with opioid overdoses has risen dramatically during the previous decade (Figure 2). Thus, the needs of patients in pain must be carefully balanced with the need to prevent inappropriate use of these agents.

Several strategies have been advanced that attempt to ensure that analgesics are available for patients who benefit from them while reducing their risks. A recent systemwide development has been the action by FDA to create a REMS for all long-acting and extended-release opioids. Improper use of any opioid can result in serious consequences. However, FDA stated that the proposed REMS did not focus on immediate-release products because a long-acting or extended-release opioid product may result in even greater risk than an immediate-release opioid product if used by a person for whom it was not prescribed or if used improperly. The increased risk occurs because the amount of opioid contained in an extended-release tablet can be much greater than the amount of opioid contained in an immediate-release product and because long-acting opioids can take much longer to be cleared out of the body. The list of opioid products that are

<table>
<thead>
<tr>
<th>Issue</th>
<th>Findings</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>Pain as a public health challenge</td>
<td>(1) Pain is a public health problem. (2) More consistent data on pain are needed. (3) A population-based strategy for reducing pain and its consequences is needed</td>
<td>(1) Improve the collection and reporting of data on pain. (2) Create a comprehensive population-level strategy for pain prevention, treatment, management, and research.</td>
</tr>
<tr>
<td>Care of people with pain</td>
<td>(1) Pain care must be tailored to each person’s experience. (2) Critical barriers to adequate pain care exist.</td>
<td>(1) Promote and enable self-management of pain. (2) Develop strategies for reducing barriers to pain care. (3) Provide education opportunities in pain assessment and treatment in primary care. (4) Support collaboration between pain specialists and primary care clinicians, including referral to pain centers when appropriate. (5) Revise reimbursement policies to foster coordinated and evidence-based pain care. (6) Provide consistent and complete pain assessments.</td>
</tr>
<tr>
<td>Education challenges</td>
<td>(1) Education is a central part of the necessary cultural transformation of the approach to pain.</td>
<td>(1) Expand and redesign education programs to transform the understanding of pain. (2) Improve curriculum and education for health professionals. (3) Increase the number of health professionals with advanced expertise in pain care. (Pharmacists are included in this recommendation.)</td>
</tr>
<tr>
<td>Research challenges</td>
<td>Research to translate advances into effective therapies is a continuing need.</td>
<td>(1) Designate a lead institute at the National Institutes of Health responsible for moving pain research forward, and increase the support for and scope of the Pain Consortium. (2) Improve the process for developing new agents for pain control. (3) Increase support for interdisciplinary research in pain. (4) Increase the conduct of longitudinal research in pain. (5) Increase the training of pain researchers.</td>
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that contribute to disparities in pain care.

The report recommends increasing the number of health professionals with advanced expertise in pain care and specifically calls for pharmacists to receive advanced training. The IOM’s findings and recommendations are grouped by issues in Table 2.

**New developments in managing pain**

A number of developments occurred in 2011 and early 2012 that affect pain management, including development of a risk evaluation and mitigation strategy (REMS) program for long-acting and extended-release opioid analgesics, new research about the risk versus benefit equation for analgesics, and the entry of several new agents into the market.

**REMS for opioids**

A major issue facing the pain management community is that although effective pain-relieving agents exist, their use is limited by their risks. Among the most prominent risks are the cardiovascular and gastrointestinal risks associated with NSAIDs, risk of hepatotoxicity associated with acetaminophen, and risks of misuse, abuse, and diversion with opioids.

The IOM report calls the fact that opioids are among the most effective analgesics and are also associated with abuse and diversion “a conundrum.” The misuse and abuse of opioids is a growing and important public health problem with a number of serious consequences. For example, the number of deaths associated with opioid overdoses has risen dramatically during the previous decade (Figure 2). Thus, the needs of patients in pain must be carefully balanced with the need to prevent inappropriate use of these agents.

Several strategies have been advanced that attempt to ensure that analgesics are available for patients who benefit from them while reducing their risks. A recent systemwide development has been the action by FDA to create a REMS for all long-acting and extended-release opioids.

Improper use of any opioid can result in serious consequences. However, FDA stated that the proposed REMS did not focus on immediate-release products because a long-acting or extended-release opioid product may result in even greater risk than an immediate-release opioid product if used by a person for whom it was not prescribed or if used improperly. The increased risk occurs because the amount of opioid contained in an extended-release tablet can be much greater than the amount of opioid contained in an immediate-release product and because long-acting opioids can take much longer to be cleared out of the body. The list of opioid products that are
required to have a REMS can be found at www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm251735.htm.

In April 2011, FDA announced the specific elements that will be required: All manufacturers of long-acting and extended-release opioids must ensure that training is provided to prescribers of these medications and develop information that prescribers can use when counseling patients about the risks and benefits of opioid use. Prescriber education will include information on weighing the risks and benefits of opioid therapy, choosing patients appropriately, managing and monitoring patients, and counseling patients on the safe use of these drugs. In addition, prescribers will receive training to recognize evidence of and potential for opioid misuse, abuse, and addiction. According to FDA, the REMS program is focused on prescriber education because it is intended to reduce the potential for serious adverse outcomes resulting from inappropriate prescribing and misuse, abuse, and diversion while ensuring that patients with legitimate need for these drugs continue to have appropriate access to them.

The REMS will include educational materials that prescribers can provide to patients on how to use and store these products safely. Prescribers will be educated to properly counsel patients on safe use and the responsibilities associated with using these products, and patients will receive medication guides when they pick up their prescriptions. (Medication guides are designed to provide information in patient friendly language about the medication’s risks and how to use the medication safely.)

FDA notes that several factors were considered when developing the requirements for the REMS. Designing the REMS in a way that it does not steer prescribers away from the long-acting and extended-release opioids to medications that are less appropriate for patients (such as immediate-release opioids that are not covered by the REMS) is important. Ensuring that patient access to needed medications is maintained while the REMS is being implemented is also critical. The REMS is designed so that if properly implemented, it can help improve patient care by improving communication.

FDA is implementing the REMS in a stepwise fashion to minimize the impact and burden on the health care system and patients. At this time, the education program is voluntary for health care providers. FDA is working with lawmakers with the goal of adding an education requirement to the DEA licensure process. If such a requirement is implemented, it would be mandatory for licensure and would circumvent the need to create a separate registration system.6

Understanding REMS
The Food and Drug Administration Amendments Act of 2007 (FDAAA) authorized FDA to require REMSs for medications or medication classes with known serious risks. The law gave FDA the authority to determine whether a REMS is necessary to ensure that the benefits of a drug or biological product outweigh its risks. REMSs replaced the previously existing risk management programs called Risk Minimization Action Plans (RiskMAPs). An important distinction between the two programs is that FDA did not have authority to require or enforce a RiskMAP after product approval. Under FDAAA, FDA has the authority to require a REMS as part of the approval process for a new medication or postapproval if the agency becomes aware of new safety information about serious risks associated with the use of the medication after it is on the market.

As defined by the law, a REMS may include a medication guide, a patient package insert, a communication plan, and other elements to assure safe use (ETASUs). ETASUs, which must include goals to mitigate a specific serious risk listed in the labeling of the drug, may include the following requirements:

- Health care providers who prescribe the drug have particular training or experience or are specially certified.
- Pharmacies, practitioners, or health care settings that dispense the drug are specially trained and/or certified.
- The drug is dispensed to patients only in certain health care settings, such as hospitals (i.e., through a restricted distribution program).
- The drug is dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results.
- Each patient using the drug is subject to certain monitoring.
- Each patient using the drug is enrolled in a registry.
- Physicians who prescribe and/or pharmacists who dispense the drug are enrolled in a registry.

If FDA deems that a REMS is necessary, the agency directs manufacturers to create a REMS with specific elements and the manufacturers are required to comply. REMS programs vary from one another to address the specific issues for each medication, although brand and generic companies generally use a single, shared system. Manufacturers are responsible for implementing the system and working with FDA to assess and monitor outcomes of the system. FDA maintains a list of currently approved REMS at www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatient-sandProviders/ucm111350.htm.

Taking another look at the risk: Benefit equation for NSAIDs
Although NSAIDs are generally well demonstrated to be associated with risk of gastrointestinal and renal adverse events, evidence surrounding the cardiovascular safety of these agents has been evolving. Selective nonsteroidal agents (i.e., the cyclooxygenase [COX]-2 inhibitors) have been shown to be associated with adverse cardiovascular events, which led to the removal of rofecoxib from the market in 2004 and valdecoxib in 2005. Some but not all studies have found celecoxib to have a slightly elevated risk, but it has remained on the market. Questions have remained about the cardiovascular safety of nonselective NSAIDs such as ibuprofen and naproxen.
A 2011 systematic review looked at controlled studies published between 1985 and 2010 and reported on the cardiovascular risks associated with NSAID use. This review concluded that the impact of NSAIDs on cardiovascular risk varies from medication to medication. Naproxen (all doses) and low-dose ibuprofen were found to have the lowest cardiovascular risk, whereas rofecoxib and diclofenac had the highest risk. The risk associated with ibuprofen rose with increasing dosages. Etoricoxib, etodolac, and indomethacin were also found to have somewhat elevated risk. The review found that the level of risk associated with each NSAID remained constant regardless of patient background regarding cardiovascular risk.

Other research has found that patients with established cardiovascular risk (older patients with hypertension and coronary artery disease) who use NSAIDs chronically for pain are at significantly increased risk of cardiovascular events. For example, one study that followed more than 22,000 patients for 2.7 years found that the risk of cardiovascular death was doubled in patients using NSAIDs chronically (compared with both intermittent users and never users).

Questions remain regarding the comparative risks of various NSAIDs in different populations. The ongoing trial PRECISION (Prospective Randomized Evaluation of Celecoxib Integrated Safety versus Ibuprofen Or Naproxen) will hopefully provide more information on this issue. The study is designed to assess cardiovascular risk in patients at high risk who receive chronic treatment with a COX-2 inhibitor or a nonselective NSAID.

New drug products for pain management
Several new pain management medications were approved in 2011 and early 2012.

Two nonoral formulations of NSAIDs that were previously on the market were approved in 2011. Ketorolac tromethamine nasal spray (Sprix—Luitpold) was approved for short-term treatment of moderate to moderately severe pain. It is the first intranasal NSAID to be approved in the United States. Sprix should not be used concomitantly with intramuscular/intravenous or oral ketorolac, aspirin, or other NSAIDs or with probenecid or pentoxyfileline. The dosage is 31.5 mg (one spray in each nostril) every 6 to 8 hours, up to 126 mg/day, for the shortest duration possible, up to 5 days total. (If other dosage forms of ketorolac are used sequentially, the total length of treatment with ketorolac should not exceed 5 days.)

Diclofenac sodium 1.5% topical solution (Pennsaid—Mallinckrodt) was approved for the treatment of signs and symptoms of osteoarthritis of the knees. The dosage is 40 drops per knee four times per day. This topical formulation of diclofenac is associated with a lower risk of gastrointestinal adverse events and abnormal laboratory parameters than oral diclofenac.

Two long-acting gabapentin products were recently approved. Gabapentin enacarbil extended-release 600 mg (Horizant—GlaxoSmithKline) was approved for treating restless leg syndrome in 2011 and received approval for the treatment of postherpetic neuralgia in June 2012. This medication should be taken in the evening with food. Gabapentin extended release (Gralise—Depomed) 300 and 600 mg was approved for the treatment of postherpetic neuralgia. It is the first once-daily medication approved for this indication. This medication can be titrated upward as needed.

Tapentadol extended release (Nucynta ER—Janssen) was approved for moderate to severe chronic pain. Tapentadol is the second combination mu-opioid receptor agonist and monoamine reuptake inhibitor to be approved. (Tramadol was the first drug in this class.) This medication is administered twice daily and is available in several dosages: 50, 100, 150, 200, and 250 mg.

The morphine product Embeda (King), which included a naltrexone core that would be released if the product was crushed, chewed or dissolved, was voluntarily recalled from the market in 2011 as a result of stability issues. It remains uncertain if or when the product will be marketed again.

Two new formulations of fentanyl were approved in 2011, fentanyl sublingual tablets (Abstral—ProStrakan) and fentanyl nasal spray (Lazanda—Archimedes), and in January 2012, a sublingual spray formulation of fentanyl (Subsys—INSYS Therapeutics) was approved. All three products are used to manage breakthrough cancer pain in patients who are already using another opioid around the clock. None of these products should be used by patients who are not opioid tolerant.

Reformulated versions of immediate-release oxycodone (Oxecta—King) and extended-release oxycodone (OxyContin—Purdue) were released. The reformulated versions form a gelatinous mass if crushed, which prevents injection and snorting of the product. Available data indicate that abuse of these products has decreased significantly following the release of the reformulations.

An extended-release formulation of hydromorphone (Exalgo—Mallinckrodt) was released. This product fills the void left by the withdrawal of Palladone (extended-release hydromorphone; Purdue), which was removed from the market because coadministration with alcohol resulted in immediate release of the entire hydromorphone dose. Exalgo is available in 8, 12, and 16 mg tablets and is administered once daily.

A buprenorphine transdermal patch (Butrans—Purdue) was recently approved for managing moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. This agent is a partial mu agonist, weak kappa antagonist, agonist at delta opioid receptors, and a partial agonist at nociceptin (ORL-1) receptors. This receptor binding profile may help prevent the development of hyperalgesia. Butrans patches are available in 5, 10, and 20 mcg/hour formulations and are applied once every 7 days. Dosages above 20 mcg/hour have been associated with increased risk of QT prolongation. It takes 3 days for the medication to reach steady state; thus, a gap of at least 3 days should be allowed between dosage adjustments.

Communicating with patients
Because medications are widely used in pain management and proper care requires consistent monitoring of analgesic...
efficacy balanced with monitoring for potential for adverse events, it is natural that pharmacists, the “medication experts” on the health care team, should be involved in pain management. Regardless of practice setting, informed pharmacists who understand how to assess pain, are familiar with the treatment options for pain, and are adept at monitoring response to treatment can play a critical role in managing pain.

Pharmacists can play an active role in implementing recommendations from the IOM, including the following:

- Promote and enable self-management of pain: Pharmacists can work with and educate their patients to empower them to be informed health care consumers.
- Develop strategies for reducing barriers to pain care: Pharmacists can assess their practices to identify pain care barriers and devise and implement strategies to address these barriers.
- Support collaboration between pain specialists and primary care clinicians, including referral to pain centers when appropriate: For patients whose pain care team includes both primary care providers and specialists, pharmacists can work to facilitate communication among the providers and share information so that all members of the team have information about the patient’s current prescription regimen. In addition, pharmacists can identify patients whose pain is not being adequately managed and provide recommendations to current prescribers or make referrals when appropriate.
- Provide consistent and complete pain assessments: Pharmacists can include regular assessments of patients’ responses to therapy as part of the ongoing monitoring that they perform when patients present at the pharmacy for their prescriptions.
- Pharmacists can play an important role in ongoing monitoring of patients with chronic pain because they typically see patients face to face on a monthly basis. Current research suggests that pharmacists could take a more proactive role in managing patients receiving medications for pain. A recent survey of patients with chronic pain in a community pharmacy found that although patients often do not discuss issues related to the use of analgesics with their pharmacists, they would like to. In addition, they reported that they would like the pharmacist to have more communication with their prescribers (Figure 3).

Although few pharmacists currently have advanced training in pain care, open-ended questions can be used to briefly assess patients and uncover issues that require further intervention. (Open-ended questions are those that cannot be answered with “yes” or “no.”) Such questions can include: How well are you doing with your pain medications? Are you having any problems with constipation or sleepiness? How is your pain right now? Where do you hurt? What makes the pain better? What makes the pain worse? What drugs have worked in the past? And how often do you think you need pain medication?

Although pain rating scales (e.g., asking patients to rate their pain on a scale from 0 to 10) can have a role in assessing pain, questions that assess a patient’s function are likely to yield greater insight regarding the value of a treatment for the patient. If a patient’s functionality and ability to perform activities of daily living does not improve as a result of treatment, then other interventions should be explored. Considering a number of possible explanations for the poor response to treatment, including the need to switch medications, the need to increase dosage, the possibility that the patient is misusing/abusing the medication, and the possibility that the patient has developed opioid-induced hyperalgesia is important.

Pharmacists are encouraged to educate patients so that they understand risks associated with pain management medications and how to use these products safely. In a 2008 survey of individuals reporting nonmedical use of pain relievers, 56% reported receiving the medication free from a friend or relative. Another 9% bought the medication from a friend or relative, and 5% took it from a friend or relative without asking. Patients who receive controlled substances should be instructed to never share the medication and to store the medication in a place where others will not have access to it. Many experts recommend storing the medications in a safe or lock box. Pharmacists should also review the risks of the medication, including the potential for addiction, and requirements for safe use of the medication.

Finally, pharmacists can investigate and work to resolve pain-related medication problems when providing medication therapy management (MTM). They can be active participants on interdisciplinary pain care teams, by sharing drug therapy knowledge and providing recommendations and support to resolve problems identified during MTM services.

**Case 1**

You are counseling a 70-year-old woman regarding her diabetes. Today, the patient tells you that in addition to her controlled-release hydromorphone 16 mg, two tablets daily, she is taking approximately 12 ibuprofen 200 mg tablets to help ease her burning foot pain and arthritis pain.

Which of the following actions would be most appropriate for this patient?
1. Change ibuprofen to celecoxib
2. Start immediate release hydromorphone for breakthrough pain
3. Reassess appropriateness of regimen for diabetic neuropathy
4. Increase dosage of controlled-release hydromorphone

The correct answer is choice 3. The appropriateness of the current treatment should be reassessed. Although patients with diabetic neuropathy may respond to opioid therapy, mechanistically, NSAIDs will likely provide little benefit. An adjuvant analgesic that is indicated for the treatment of neuropathic pain should be considered. Treatment guidelines released in 2011 state that pregabalin is established as effective for the treatment of painful diabetic neuropathy. Other agents considered “probably effective” include venlafaxine, duloxetine, amitriptyline, gabapentin, valproate, capsaicin, and the opioids morphine, tramadol, and controlled-release oxycodone.

While choice 3 is the most correct answer, the other options should also receive consideration. Because of the patient’s age, she is at risk for gastrointestinal adverse events from ibuprofen. Potential appropriate changes to the regimen would be to replace the ibuprofen with celecoxib and/or add an immediate-release version of hydromorphone for breakthrough pain. However, because the patient reports pain that appears to be neuropathic in nature, adding an agent such as a gabapentinoid that is effective for neuropathic pain may be more appropriate before increasing the dosage of the controlled-release hydromorphone.

Case 2
A 37-year-old man reporting low back pain routinely brings in a new prescription for controlled-release oxycodone 5 to 6 days before his previous prescription should be finished. What is the best strategy for addressing this situation?
1. Refill the prescription
2. Call the prescriber
3. Call police
4. Assess pain

The correct answer is choice 4, although choice 2 could also be considered, depending on the relationship with the patient. Many pharmacists report that their initial concern when presented with an early refill request for a controlled substance is that the patient is abusing or diverting the medication, and pharmacists may question the legitimacy of the prescription. However, the underlying reasons for the early refill request should be explored with the patient before proceeding with another course of action. Managing early refills for controlled substances can be challenging and time consuming. However, discussing the situation with the patient is important; each patient’s situation is unique, and exploring the issue with the patient can help uncover the underlying issue, whether it relates to uncontrolled pain, misuse abuse or diversion of the substance, or some other issue (e.g., a patient taking the medication too quickly because of a misunderstanding of dosing instructions).

Conclusion
The 2011 IOM report, Relieving pain in America: A blueprint for transforming prevention, care, education, and research, issued a call to action for a cultural transformation to improve pain management in the United States. Many of the report’s recommendations included activities that pharmacists can implement in their current practice settings.

One of the primary challenges that pharmacists must address in their pain management activities is balancing the need to effectively relieve pain with the need to manage the risks of analgesic medications. New tools and information to manage these risks continually become available. In addition to familiarizing themselves with the latest data regarding the risks associated with analgesic medications, pharmacists can partake in the provider education program through the class-wide REMS for long-acting and extended-release opioids.

Finally, several new analgesic agents were approved in 2011. Pharmacists can familiarize themselves with the characteristics of these agents so that they are prepared to educate both patients and other members of the health care team regarding appropriate use. By taking these steps and working to inform and educate themselves, their patients, and other health care providers, pharmacists can play a critical role in driving the transformation of pain care called for by the IOM.

References


CPE assessment

Instructions: This exam must be taken online; please see “CPE information” for further instructions. There is only one correct answer to each question. This CPE activity will be available online at www.pharmacist.com between August 15, 2012, and March 11, 2015.

1. Which of the following was a fact reported in the Institute of Medicine (IOM) report, Relieving pain in America?
   a. More adults experience chronic pain than those who have heart disease or all types of cancer combined.
   b. Chronic pain results in approximately $100 billion in added health care costs and lost productivity.
   c. The prevalence of chronic pain has decreased during the previous decade.
   d. Severe headache or migraine is the most common form of musculoskeletal pain.

2. As stated in the IOM report, what percentage of patients with low back pain have difficulty with basic actions (i.e., difficulty in one or more of the following areas: movement, emotional, seeing, hearing, cognition)?
   a. 17.5%
   b. 30.2%
   c. 37.3%
   d. 51.6%

3. The IOM report indicated that in many cases, chronic pain should be considered:
   a. A disease in its own right.
   b. A precursor for abuse and addiction.
   c. An indicator of the presence of psychological problems.
   d. A consequence for poor health choices.

4. The IOM report provided which of the following types of recommendations to improve pain management?
   a. Clinical practice recommendations for the 20 most common chronic pain conditions
   b. Specific guidance on assessing patients with pain for the risk of misuse, abuse, and/or diversion
   c. An overview of the need for pain care, education, and research
   d. An evidence-based review of all medications available in the United States that have a pain management indication

5. Which of the following was associated with the highest number of unintentional overdose deaths in 2007?
   a. Cocaine
   b. Heroin
   c. Opioid analgesics
   d. Other illicit substance

6. Which law authorizes FDA to require risk evaluation and mitigation strategies (REMSs)?
   a. The Affordable Care Act of 2010
   b. The Food and Drug Administration Amendments Act of 2007
   c. The Prescription Drug User Fee Act IV of 2007
   d. The Federal Food Drug and Cosmetic Act of 1938

7. According to the law, elements to ensure safe use (ETASUs) for a REMS must be:
   a. Based on recommendations from the product’s manufacturer.
   b. Designed to mitigate a specific serious risk listed in the labeling of the drug.
   c. Selected based on the results of randomized clinical trials assessing their efficacy for mitigating a known risk.
   d. Submitted as part of the approval process for all new molecular entities.

8. What reason did FDA provide for requiring a REMS for long-acting and extended-release opioids but not for immediate-release opioids?
   a. Immediate-release opioids are more widely prescribed, and it would be more burdensome to implement a REMS for these agents.
   b. Immediate-release opioids are less likely to be abused.
   c. The risks are greater with long-acting and extended-release opioids than they are with immediate-release opioids because of the greater amount of opioid contained in the products and increased time to clear the products.
   d. FDA did not provide a rationale for this decision.

9. According to an April 2011 FDA announcement, which of the following ETASUs is required for the REMS for long-acting and extended-release opioids?
   a. The drug is dispensed to patients with evidence or documentation of safe use conditions (e.g., urine drug screens).
   b. Physicians who prescribe and pharmacists who dispense the medications must enroll in a registry.
   c. Each patient who uses one of the medications must be enrolled in a registry.
   d. Training is provided to prescribers of these medications, and patient education material that providers can use when counseling patients are developed by the manufacturer.

10. Based on a review of current published evidence, which NSAIDs have the lowest cardiovascular risk?
    a. Rofecoxib and valdecoxib
    b. Diclofenac and indomethacin
    c. Etoricoxib and etodolac
    d. Naproxen and low-dose ibuprofen
11. Which of the following NSAIDs was approved in a non-oral formulation in 2011?
   a. Indomethacin
   b. Diclofenac
   c. Naproxen
   d. Celecoxib

12. Which of the following medications was approved in 2011 with an indication for treating postherpetic neuralgia?
   a. Buprenorphine transdermal patch
   b. Fentanyl nasal spray
   c. Gabapentin extended release
   d. Tapentadol extended release

13. Which of the following pain management medications was withdrawn from the market in 2011?
   a. Morphine and naltrexone (Embeda)
   b. Hydromorphone extended release (Exalgo)
   c. Buprenorphine transdermal patch (Butrans)
   d. Fentanyl nasal spray (Lazanda)

14. Which of the following medications is both a mu-opioid receptor agonist and a monoamine reuptake inhibitor?
   a. Buprenorphine
   b. Fentanyl
   c. Hydromorphone
   d. Tapentadol

15. Which of the following medications requires 3 days to reach steady state?
   a. Buprenorphine transdermal patch
   b. Extended-release oxycodone
   c. Extended-release hydromorphone
   d. Extended-release tapentadol

16. According to a recent survey by Swick et al., what percentage of patients with chronic pain do not currently discuss their adherence to pain management medications with their pharmacist but would like to?
   a. 32%
   b. 41%
   c. 53%
   d. 58%

17. Which of the following questions is likely to be most helpful to pharmacists when assessing a patient’s response to a pain medication?
   a. How well are you doing with this pain medication?
   b. Are you having any problems with this medication?
   c. Do you think this medication is helping you?
   d. Are you following the directions for using this medication?

18. Among individuals who report nonmedical use of pain relievers, how do the majority obtain the medication?
   a. Obtaining and filling fraudulent prescriptions
   b. Purchasing the medications from individuals whom they do not know
   c. Given the medications by a family member or friend
   d. Stealing the medications

19. According to treatment guidelines released in 2011, which medication has “established efficacy” for the treatment of painful diabetic neuropathy?
   a. Amitriptyline
   b. Duloxetine
   c. Pregabalin
   d. Venlafaxine

20. What do pharmacists most commonly report as their initial concern when presented with an early refill request for an opioid?
   a. The patient is abusing or diverting the medication.
   b. The patient’s pain is not being adequately managed.
   c. The patient has not received proper education on how to use the medication.
   d. The patient might be cognitively impaired and not managing his or her medications properly.