Successful Pain Management for the Recovering Addicted Patient

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Successful pain management in the recovering addict provides primary care physicians with unique challenges. Pain control can be achieved in these individuals if physicians follow basic guidelines such as those put forward by the Joint Commission on Accreditation of Healthcare Organizations in their standards for pain management as well as by the World Health Organization in their stepladder approach to pain treatment. Legal concerns with using pain medications in addicted patients can be dealt with by clear documentation of indication for the medication, dose dosing interval, and amount provided. Terms phy sicians need to be familiar with include physical dependence, tolerance, substance abuse, and active versus recovering addiction. Treatment is unique for 3 different types of pain: acute, chronic, and end of life. Acute pain is treated in a similar fashion for all patients regardless of addiction history. However, follow-up is important to prevent relapse. The goal of chronic pain treatment in addicted patients is the same as individuals without addictive disorders-to maximize functional level while providing pain relief. However, to minimize abuse potential, it is important to have 1 physician provide all pain medication prescriptions as well as reduce the opioid dose to a minimum effective dose, be aware of tolerance potential, wean periodically to reassess pain control, and use nonpsychotropic pain medications when possible. Patients who are at the end of their life need to receive aggressive management of pain regardless of addiction history. This management includes developing a therapeutic relationship with patients and their families so that pain medications can be used without abuse concerns. By following these strategies, physicians can successfully provide adequate pain control for individuals with histories of addiction.

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roviding pain control for the 5% to 17% of the U.S. population with a substance abuse disorder of some type¹ presents primary care physicians with unique challenges. When these individuals experience pain, they are less likely to receive adequate pain management than individuals in the general population.² While relapse in a recovering individual may occur in spite of appropriate use of opioids and psychotropic medications required for effective pain management, inadequate pain relief is also a significant risk factor for relapse.³ Some of the challenges that physicians face include distinguishing between seeking pain relief and seeking drugs for the euphoric effects and identifying predictable neuroadaptations such as tolerance and physiologic dependence that can be misinterpreted as drug seeking or relapse behavior.⁴ In addition, comorbid psychiatric and medical illnesses may complicate effective pain management.⁵

This article will address 5 areas related to successful pain management in the recovering addict: (1) basic principles, (2) legal concerns, (3) substance abuse terminology, (4) active addiction versus recovery, and (5) management strategies for acute, chronic, and end-of-life pain. This information will provide physicians with a better understanding of the unique challenges of providing pain control in these individuals.

CASE VIGNETTES

The following vignettes describing 2 actual patients* highlight some of the issues that can confront primary care physicians in their daily practice:

John is dead. He committed suicide last week. Until a year ago, he was a successful physician enjoying 5 years of recovery from addiction to hydrocodone and alcohol. He was doing well until he fell and fractured his distal ulnar (styloid process) and experienced associated mild-to-moderate pain. Like his primary care physician, the orthopedic physician who evaluated John knew that he was in recovery from "drugs" and prescribed the nonscheduled pain reliever tramadol. Significant pain

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^{*}Patients' names are fictitious, to protect the anonymity of the individuals.

was resolved after 1 week. John had his cast removed 4 weeks later and was released to the care of his primary care physician. Although John subsequently did follow up with his primary care physician regarding his fracture and had several office evaluations for different medical problems, the issue of his addiction was never readdressed. Drug testing at the time of his death revealed the presence of hydrocodone.

Ben enjoyed 22 years in recovery from addiction to alcohol, was gainfully employed, and had an active and stable family life with his wife and 2 children before suffering a back injury in an auto accident 3 years ago that resulted in a moderately severe pain syndrome. At the time of his accident, the emergency room physician successfully managed his initial pain with a combination of bed rest, cyclobenzaprine, and oxycodone. A week later as instructed, Ben followed up with his primary care physician, who continued his bed rest and scheduled him for magnetic resonance imaging (MRI) of his lumbosacral spine. Due to concerns related to Ben's addiction history, his primary care physician changed his pain medication at that time to tramadol, a nonscheduled pain medication. Ben called back 2 days later to report a marked increase in pain, so his physician changed his medication to hydrocodone. When Ben called again in another days, he asked to be given oxycodone, saying that the hydrocodone was not providing the pain relief he needed. He also reported not being able to get his MRI because of the incapacitating pain he was experiencing. Ben's noncompliance related to obtaining the MRI and his request for a specific, stronger narcotic suggested to his physician that Ben was seeking drugs rather than pain relief. His physician became worried about relapse for Ben and the possible legal consequences for himself of "inappropriate" prescribing of narcotics and refused to change the prescription. Ben subsequently began selfmedicating his pain with his drug of choice, alcohol. His alcohol use continued to escalate, causing significant consequences including the loss of his job and family.

BASIC PRINCIPLES

Regardless of substance abuse history, there are several basic principles in pain management.⁶ The first principle is to provide effective pain management, and this requires certain strategies. First, medications should be chosen on the basis of their ability to afford adequate pain relief. There are multiple medications and delivery routes that supply health care providers with a variety of pain relief strategies. An important principle is to use the level of pain the patient is experiencing in determining the strength of pain medication that may be warranted and as a guide for effectiveness of pain management. As discussed in the preceding vignettes, while John's physician appropriately prescribed tramadol for his mild-to-

Pain Level	Drug	Dose
1. Mild pain	Acetaminophen	
(nonnarcotic drugs)	Nonsteroidal anti-inflammatory	
	drugs	
	COX-2 inhibitors	
Moderate pain	Codeine	15–60 mg every 6 h
(weak opioids used in addition to those in step 1)	Hydrocodone	5–7.5 mg every 4 h
3. Severe pain (strong	Morphine	10-20 mg every 4-6 h
opioids used in	Oxycodone	5–30 mg every 4 h
addition to those	Hydromorphone	2-4 mg every 3-8 h
in step 1)	Methadone	2.5-20 mg every 3-4 h
	Extended-release oxycodone	10 mg every 12 h ^b
	Extended-release morphine	15-30 mg every 8-12 h

Table 1. Pain Management Strategies Based on the World

COX-2 = cyclooxygenase-2.

^bIn opiate-tolerant patients, 80–160 mg may be needed.

moderate pain, Ben's physician failed to adequately address his more severe level of pain. Considerable inconsistency has been found when assessments of pain intensity are compared between primary care physicians and their patients, with primary care physicians tending to rate patients' pain much lower than the patients.⁷ The Joint Commission on Accreditation of Healthcare Organizations recommends a numerical scale for adults⁸ because of the ease of implementing the scale, the ease of understanding it, and its reproducibility. An example would be a scale of 1 to 10 where 10 represents severe pain. Perhaps the use of a simple tool such as this would have allowed Ben's physician to deal more effectively with Ben's pain.

A second strategy is to provide pain relief around the clock. Pain medications that are used strictly on an as-needed basis allow pain to escalate and require more medication for pain control. The use of around-the-clock dosing suppresses the pain and will provide better comfort for patients. This schedule is frequently best accomplished by continuous use of long-acting opioids with the p.r.n. addition of short-acting opioids for breakthrough pain. Opioids should be titrated to a level that provides adequate pain control (Table 1). Most opioids have no dose ceiling, and large doses have not been shown to suppress respirations or decrease life expectancy if patients are in pain.¹⁰

When choosing pain medication, the emphasis should be on using medications that provide adequate pain relief. Attempting to use "less addicting" narcotics may result in inadequate pain relief, which may actually precipitate relapse by forcing recovering individuals to self-medicate their pain. This appears to have been the case in Ben's situation, with his former drug of choice—alcohol being used to help manage unresolved pain.

The choice of pain medication is based on the World Health Organization's stepladder approach for mild, moderate, and severe pain.9 Step 1, mild pain, can be treated with acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and cyclooxygenase-2 (COX-2) inhibitors. Step 2, moderate pain, can be treated with the same agents with the addition of a weak opioid such as codeine or hydrocodone. Step 3, severe pain, should be treated with strong opioids such as morphine, oxycodone, hydromorphone, or methadone. Meperidine should be avoided because of its short length of effectiveness and its tendency to induce euphoria. Propoxyphene and its combinations should also be avoided because they provide minimal analgesia with a high abuse potential. Agonistantagonist drugs such as pentazocine, nalbuphine, and butorphanol should be avoided in treating addicts who are actively abusing narcotics and those on opioid maintenance programs (i.e., methadone maintenance) because the agonist-antagonist drugs can precipitate an opioid withdrawal syndrome.

The second principle is that acute pain is a medical emergency and should be treated as such. If not treated aggressively, the pain can escalate, making it increasingly difficult to control. Finally, addiction concerns for those without an addictive disorder, although real, are frequently overrated, given that only approximately 3% to 5% of individuals with pain treated with opioids experience subsequent problems with addiction.⁶

LEGAL ISSUES

Many physicians have a fear of using opioids in adequate amounts to relieve pain ("opiophobia").¹¹ This is in part due to fear of legal repercussions for overprescribing narcotics. Even if Ben's physician had correctly assessed his level of pain, the fear of "possible legal consequences" may still have resulted in the prescription of inadequate pain medication.

Through the Uniform Controlled Substances Act of 1970, federal law regulates the use of narcotics only when used for purposes of opioid detoxification and/or maintenance; it does not regulate the use of narcotics for pain relief. The Psychotropic Substances Act, a 1978 amendment to the Controlled Substances Act, specifically prohibits restrictions on opioid prescription for pain relief. Individual state regulations usually follow the federal guidelines. It is, therefore, the responsibility of individual practitioners to treat patients for legitimate medical purposes in accordance with generally accepted medical standards,¹² such as those outlined by the Joint Commission on Accreditation of Healthcare Organizations in their standards of pain management⁸ and the World Health Organization stepladder approach to determining the medication to be used.9 Of utmost importance is clear documentation in the medical record of the need for narcotic

Table 2. Substance Abuse Terminology		
Term	Definition	
Physical dependence	Normal physiologic event (neuroadaptation): defined by development of withdrawal syndrome on abrupt dose reduction	
Tolerance	Normal physiologic event (neuroadaptation): decreasing pharmacologic effect of drug's pain-relieving properties	
Substance abuse	Use of any illicit drug. Unsanctioned use of licit drug or inappropriate use of alcohol	
Active addiction	Presence of maladaptive behavior Loss of control Compulsive use Preoccupation Continued use despite harm	

analgesia, for both clinical and potential legal purposes. This documentation includes the indication for narcotic use, medication provided with the dosage, dosing interval, and amount provided. It is also important to document the timing for the next medication refill that is agreed on by the patient and the physician.

SUBSTANCE ABUSE TERMINOLOGY

To understand treatment strategies for recovering addicted patients, physicians need to understand substance abuse terminology (Table 2). The terms physical dependence and tolerance have been inappropriately used in the past to define the term addiction. Physical dependence is defined as development of a physical withdrawal syndrome following abrupt dose reduction. Its presence does not indicate the presence of addiction, but rather is a normal physiologic consequence of chronic use of many psychotropic medications. Tolerance likewise is not indicative of addiction and can be defined as a normal physiologic response at the cellular level to chronic use of many psychotropic medications that results in requiring more drug to elicit the same physiologic response. Physical dependence and tolerance to opioids are normal and predictable physiologic events that are natural consequences of chronic opioid use. Their development can be expected after extended use of these drugs (several days to 2 weeks) and does not imply the presence of substance abuse or an addictive disorder.13

Substance abuse is defined as use of any illegal drug (marijuana, cocaine, heroin) or inappropriate use of a controlled substance. In addition to the procuring of medications through nonmedical sources (e.g., buying drugs "on the streets"), another example of substance abuse would be the use of an opioid left over from a previous prescription for relief of a subsequently developed emotional pain.

In this article, the term *addiction* refers to the condition of both someone who is currently active in their addiction ("active addiction") and someone who is in recovery

Table 3. Maladaptive Behaviors Suggestive of Active Addiction^a

Selling drugs Prescription forgery Stealing or borrowing drugs from others Requesting specific drugs Drug hoarding during periods of reduced symptoms Losing medication Patient looking for pain medication at first visit to a new physician Using multiple physicians to obtain medication Obtaining prescription drugs from nonmedical sources Using multiple pharmacies Seeking medication for new sources of pain or unapproved use of the drug to treat other symptoms Unsanctioned dose escalation Continued dosing in spite of significant side effects or consequences that are due to the drug and not to the pain or the condition causing the pain (eg, alienation of friends and/or family, inability to work) Injecting oral medications Unapproved use of other psychotropic drugs during opioid therapy Concurrent abuse of alcohol Unwillingness to comply with full treatment plan (eg, utilization of nonopioid pain management techniques) Evidence of use of illegal drugs (cocaine, marijuana, heroin) Overwhelming concerns about the continued availability of the opioid being used Risk-taking behaviors while using psychotropic medications Frequent signs of intoxication: significant impairment of physical, mental, or social skills

^aAdapted from Portenoy,² Sees and Clark,¹³ and Passik et al.¹⁴

from their addiction ("recovery"). The presence of active addiction may be difficult for the physician to determine. Active addiction is frequently characterized by the presence of potentially maladaptive, drug-seeking behaviors (Table 3).¹⁴ Physicians should familiarize themselves with these behaviors, because the presence of these behaviors can be instrumental in differentiating between drug-seeking individuals and pain relief–seeking individuals. Most important is the presence of a pattern of behaviors rather than the isolated presence of a behavior.¹⁴

However, adding to the already difficult task of determining the presence of active addiction is a phenomenon called "pseudoaddiction," which may mimic active addiction. Out of fear of not receiving adequate pain medication, individuals may hoard medication or ask for amounts that seem out of proportion to their pain.¹⁵ This behavior may be particularly evident in individuals who have previously experienced the prescribing of inadequate amounts of pain medication by physicians who fear using opioids in patients with substance abuse disorders.¹³

ACTIVE ADDICTION VERSUS RECOVERY

Active addiction can pose clinical problems distinct from those encountered with patients in drug-free recovery and those in methadone maintenance programs. Attempts to provide compassionate treatment to these challenging individuals may be skillfully subverted by patients seeking to obtain narcotics for purposes other than pain relief.¹⁶ Addicts, especially opioid addicts, often require larger opioid doses and more frequent dosing intervals than nonaddicted patients to adequately control their pain. Ben's need for what seemed to his physician to be excessive pain medication may have been due to a similar increased opioid requirement to relieve his pain.

Narcotic withdrawal symptoms can interfere with attempts to control pain. The time for detoxification is not when pain management is needed but rather when opioids are no longer medically indicated. For acute pain situations, opioids should be administered in doses adequate to prevent withdrawal and afford effective pain relief. The best analgesia is achieved when withdrawal states and anxiety related to inadequate pain relief are prevented. One way of controlling opioid withdrawal symptoms while maintaining effective pain control is the use of methadone, 15–20 mg/day, to control withdrawal symptoms, while additional opioids can be given for control of pain at their usual therapeutic doses.³

Methadone maintenance patients should be given their usual daily dose of methadone in addition to the opioids required for effective pain management. Methadone may also be used in increased doses (10–20 mg every 3–4 hours) for pain management in these individuals; however, the dosing intervals are adjusted for effective pain control because the pain-relieving effect of methadone may last only 4 to 6 hours. Because of the potential to precipitate an acute withdrawal syndrome, a mixed antagonist-agonist opioid such as pentazocine, nalbuphine, or butorphanol should never be given to anyone on a methadone maintenance program or to individuals in active opioid addiction.¹⁷

MANAGEMENT STRATEGIES

In a recovering individual, the fear of experiencing withdrawal symptoms can be a substantial block to successful discontinuation of narcotic medication when no longer needed for pain control. While continued use of opioids is warranted in patients experiencing tolerance, continued pain syndrome, or pseudoaddiction, patients who are physically dependent on opioids may continue their use despite resolution of pain solely to avoid withdrawal. Such use does not necessarily reflect addiction. Successful management of these concerns may be accomplished by slowly tapering medications over several days under close supervision. In certain cases, short-term admission to a detoxification unit may be necessary.

Colloquial definitions of addiction and dependence used by individuals with substance abuse disorders can be helpful in making this determination. Dependence is frequently defined as "I can't quit" because the individual is unwilling to experience withdrawal symptoms. Active

Table 4. Guidelines for Directing Effective Acute Pain Management^a

Avoid opioid agonist-antagonist in known or suspected active opioid addicts

Maintain structured control of access

Focus endpoint of treatment on effectiveness of pain relief

Put less emphasis on maintaining maximum level of function

Prescribe pain medication and other psychotropic medications in sufficient doses

Institute more frequent dosing intervals when necessary

Change to nonopioid and nonpsychotropic medications when possible Use opioids with a long half-life when pain management may be prolonged

Inpatient management when necessary

Encourage the individual in recovery to enhance his or her recovery program

Educate patient and family on the goal of the pain management program

Ensure that comorbid psychiatric disorders are effectively managed Ensure that comorbid medical disorders are effectively managed Ensure that underlying pain-producing disorder is effectively managed ^aAdapted from Savage,³ Agency for Health Care Policy and Research,¹⁸ Passik et al.,¹⁴ and Portenoy,¹⁹

addiction is defined as "I can't *stay* quit," which is the result of reinstituting opioid use for reasons other than pain control after their appropriate use has been successfully discontinued. Such was the case for John. While tramadol is a pain reliever with a relatively low addiction potential for the general public, it has greater potential harm for the recovering addict because the mild "high" it produces can trigger the need for an even stronger "high" and subsequent relapse. Reserving the term *addict* for this second group of individuals can help limit the inappropriate labeling of every individual seeking pain medication as an addict and improve the diagnostic value of the term by putting the emphasis on the need for long-term rather than short-term monitoring for relapse when managing pain in individuals with addictive disorders.

Pain management with opioids for recovering addicts should include a pretreatment agreement for random, witnessed drug screens 1 month, 3 months, and 6 months after pain management has been discontinued. Any failure to follow through with the drug screen when a drug screen is called for is considered a positive screen. Once relapse is suspected, management includes offering medical intervention. Perhaps if John's physician had established a screening schedule at the beginning of treatment, this extra level of accountability could have encouraged John to remain abstinent or detected his substance abuse in time to reinitiate treatment.

Acute Pain

The goal of acute pain management is effective pain relief, with elimination of pain as a reasonable endpoint.⁶ Maintaining functional levels of physical, social, and cerebral activity is generally a secondary concern. Nonopioid and nonpsychotropic pain relief treatment options should be utilized whenever possible to provide effective pain

Table 5. Measures That Enhance the Recovery Program

Being active in recovery-related support systems (ie, aftercare, outpatient treatment programs, 12-step programs) Having an active sponsor Actively participating in a spiritual program Maintaining stability in the workplace Maintaining stability at home Maintaining medical and psychiatric support Avoiding sleep deprivation and hunger (chronic pain) Maintaining an active exercise program (chronic pain)

relief. However, when effective pain management cannot be achieved by these measures alone, use of opioids and other psychotropic medications is warranted (Table 4).¹⁹ Physicians may need to overcome their fear that prescribing narcotics and other psychotropic medications for an addict will necessarily result in relapse.¹¹

If tolerance to opioids develops, more frequent analgesic dosing may be needed.¹⁷ A change should be made to nonopioid, nonpsychotropic medications such as acetaminophen, NSAIDs, and COX-2 inhibitors only when it does not sacrifice adequate pain relief. Because the "high" that addicts achieve from psychotropic drugs is directly proportional to the rate at which the concentration of the drug rises in the blood, long-acting opioids are used when possible.¹⁴ Use of opioid agonist-antagonists in known or suspected active opioid addicts is absolutely contraindicated because they can precipitate an acute withdrawal syndrome.¹⁴

The presence of a psychiatric disorder such as depression can significantly hinder treatment initiation and limit treatment effectiveness if not adequately addressed. John's suicide could have reflected the presence of a clinical depression that may have contributed to his relapse.

Structured control of medication access can decrease the chance for relapse.¹⁸ Such control may be achieved by giving the medication at fixed intervals and by arranging distribution of the medication by someone other than the patient. Giving medication at fixed intervals may also help minimize conflict between patients and caregivers. As previously noted, inadequate pain relief may encourage addicts to seek pain relief through self-medicating, thereby increasing the chance for relapse.³

Risk of relapse is also related to the quality of a patient's substance abuse recovery and support program.²⁰ Active involvement in a recovery support program should be initiated or intensified during a period of pain management.²¹ Additional suggestions for enhancing recovery are listed in Table 5.

Chronic Pain

The goal of chronic pain management is to obtain reasonable pain relief while maintaining a maximum level of function.¹³ When possible, opioid treatment should improve occupational and social functioning while

minimizing any decrease in cerebral function. Physical rehabilitation is appropriate to help restore patients as much as possible to their premorbid levels of physical and social functioning.

Addiction and chronic pain may reinforce each other.³ However, while requests for increased amounts of opioids may initially appear to be drug-seeking behavior, such requests may also reflect the presence of pseudoaddiction or suggest the development of physiologic tolerance. In addition, an increased need for pain medication may be indicative of an exacerbation of the underlying disease process causing the pain or heralding the presence of an undiagnosed or ineffectively treated comorbid medical or psychiatric disorder. Prior to any increase in pain medication, patients should be evaluated for the possible development of new disorders or exacerbation of existing disorders. Physicians should be alert for lowered pain thresholds and subsequent increase in pain perception resulting from emotional pain, sleep deprivation, and fear of inadequate pain relief.22

When possible, pain should be specified as being inflammatory, neurogenic, muscular, etc., and medication directed at those specific sources should be used.²³ Nonpsychotropic drugs should be used when they do not sacrifice adequate pain control or level of physical functioning. Comorbid emotional discomfort can be managed with nonpsychotropic medications, disorder-specific psychotropic medications, and counseling.⁵

Factors that contribute to effective chronic pain management include the following: (1) having only 1 physician prescribe *all* pain medications, (2) encouraging maintenance of stability at home and at the workplace, (3) periodically weaning the patient from the pain medication to assess the pain syndrome and level of function, (4) reducing opioid use to the minimum dose necessary to effectively relieve pain while maintaining an effective level of function, (5) using nonpsychotropic pain management options when possible without sacrificing effective pain relief or level of function, and (6) being aware that increased doses may be required to maintain effective pain relief and/or level of function due of the development of drug tolerance or the progression of the underlying disease.

End-of-Life Pain

One of the common concerns patients have at the end of life is control of symptoms, with pain identified as their biggest fear.²⁴ Despite advances in pain management and increased awareness of the need for pain control during the terminal phase of life, patients still suffer from under-treated or untreated pain.^{25–27} This failure to adequately treat pain causes a significant amount of stress.²⁷

As stated earlier, good pain control can be achieved for most patients, and acute pain should be considered a medical emergency. Escalation of pain could represent a progression of patients' terminal disease or an increased pain perception secondary to nonphysical causes such as psychosocial or spiritual issues.

When providing pain management, opioids are not the only option for providing pain relief. In fact, in certain cases such as bone pain, opioids are usually unable to provide adequate analgesia. In situations where musculoskeletal or bone pain is present, first-line therapy consists of nonsteroidal anti-inflammatory agents or corticosteroids. There are 2 distinct types of neuropathic pain. The first is continuous dysesthesias, which are characterized by continuous burning, electrical, or other abnormal sensations. The second is chronic lancinating or paroxysmal pain, described as sharp, stabbing, shooting, knifelike pain that often has a sudden onset. The current first-line treatment recommendation for the continuous dysesthesia type of pain is tricyclic antidepressants such as amitriptyline. For lancinating or paroxysmal neuropathic pain, first-line treatment options are the anticonvulsants, with gabapentin representing the best choice in this class.

In pain management at the end of life, addiction should not be an issue. The philosophy of providing comfort during this time period is the same regardless of any current or past history of addiction. The mechanism for pain management, however, does differ. The recovering or active addict may require more opioids to control pain because of increased opioid tolerance than those who do not have a history of addiction. Another concern is whether escalation of opioid requirements for pain control is related to disease progression or a sign of substance abuse. This escalation can be controlled to some extent by providing only a specific amount and number of pain medications with strict dosage instructions and establishing a contract with the patient and family concerning these issues. If substance abuse or diversion of controlled substances does occur, a frank discussion concerning these issues needs to be performed with the understanding that these behaviors are not acceptable. Pain control is obtainable in patients with addictions, but it needs to be a collaborative effort between physicians and patients.

SUMMARY

Successful pain management, while complicated by substance abuse activity or history, can generally be accomplished in primary care settings. Recognition and attention to withdrawal concerns, relapse triggers, and comorbid conditions are essential, as is proactive support for long-term recovery.

Drug names: amitriptyline (Elavil, Endep, and others), butorphanol (Stadol and others), cyclobenzaprine (Flexeril and others), gabapentin (Neurontin), hydrocodone (Lortab and others), hydromorphone (Dilaudid and others), meperidine (Demerol and others), nalbuphine (Nubain and others), oxycodone (Percocet and others), pentazocine (Talwin and others), propoxyphene (Darvon and others), tramadol (Ultram).

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