**DRUG USE REVIEW**
**NEWSLETTER**

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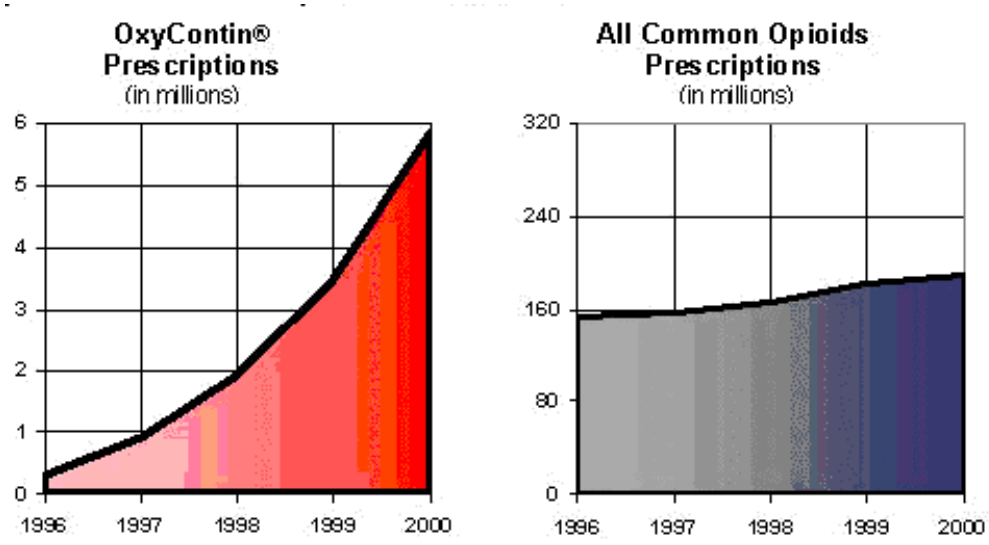
# MISSOURI DUReport

## The Use and Abuse of OxyContin®

OxyContin® was approved by the FDA in 1995 as a controlled-release formulation of oxycodone. It is intended for use in the management of moderate to severe pain when a continuous analgesic is needed for an extended period of time. From 1996 to 2000, the number of OxyContin® prescriptions rose to approximately 5.8 million, becoming one of the most prescribed Schedule II narcotics in the United States. Prescriptions dispensed for all other common opioid analgesics (such as codeine, hydrocodone, morphine and hydromorphone) increased 23% over the same time period (Figure 1).[1]

**Figure 1**



**. FDA Indications (Appropriate Uses):**

OxyContin® is indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.[2]

- OxyContin® is NOT intended for use as a prn analgesic.
- OxyContin® is NOT indicated for pain in the immediate postoperative period (the first 12-24 hours following surgery).
- OxyContin® is NOT for pain that is mild, or not expected to persist for an extended period of time.
- OxyContin® is **ONLY** indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time.[2]

Several clinical trials have been done to compare controlled-release OxyContin® to the immediate-release formulation of oxycodone in different pain settings. The following uses have been studied:

Pain-Osteoarthritis

A double-blind, randomized trial of 107 patients was performed to determine the effects of controlled-release oxycodone (OxyContin®) given every 12 hours and immediate-release oxycodone with acetaminophen given every 4 to 6 hours in relieving moderate to severe osteoarthritis pain and improving quality of sleep. Prior to the clinical trial, both groups were treated with NSAIDs. During the study, NSAID therapy continued and oxycodone doses were individualized according to the patient. The result suggest that the addition of controlled-release or immediate-release oxycodone can benefit patients with osteoarthritis when pain is no longer adequately controlled by regular NSAID doses.[3]

Pain-Lower Back

In a double-blind trial of 57 patients whose lower back pain was not controlled by non-opioid analgesics, 52 (91%) achieved stable analgesia with oxycodone. Both the controlled-release and immediate-release oxycodone were equally efficacious and safe for the treatment of persistent lower back pain. The study concluded that oxycodone is effective in treating persistent lower back pain.[4]

Pain-Cancer

In a 5-day, randomized, double-blind study, 180 patients who had been receiving opioid treatment for cancer pain were given either OxyContin® in 2 equal doses daily or immediate-release oxycodone in 4 equal doses daily. OxyContin® and immediate release oxycodone provided equally effective pain relief for cancer patients. The study concludes that oxycodone is effective for moderate to severe pain in cancer patients with few adverse effects.[5]

A second study fully evaluated 35 cancer patients to determine if patients with chronic pain could be titrated to stable pain control as readily with controlled-release oxycodone as immediate-release formulation. The results showed no difference between controlled-release and immediate-release oxycodone with respect to the percentage of patients achieving pain control, the time to achieve pain control, and the degree of pain control achieved.[6]

Pain-Postoperative

OxyContin® is **ONLY** indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for and extended perios of time.[2] In a randomized, clinical trial to assess postoperative pain, sixty patients undergoing reconstruction of the anterior cruciate ligament (ACL) were evaluated. Patients were randomized into three groups: Immediate-release oxycodone 10 mg every 4 hours as needed, oxycodone 10 mg every 4

hours around the clock, or controlled-release oxydodone 20 mg every 12 hours. Pain was assessed over a 72-hour period. There was a difference in pain scores among the groups (P<0.0001) with less pain in the controlled-release oxycodone group. The study concluded that controlled-release formulation of oxycodone in patients undergoing ACL repair provides significant analgesic benefit over a fixed or as-needed oxycodone regimen.[7]

Pain-Postherpetic Neuralgia

Postherpetic neuralgia (PHN), a chronic pain syndrome, is often refractory to treatment and can last for years. In randomized, controlled clinical trials, the topical lidocaine patch, gabapentin, and controlled-released oxycodone have been shown to provide superior pain relief to placebo. In addition, these therapies have also been shown to be as effective as tricyclic antidepressants in the treatment of PHN. The results of these studies suggest that each of these treatments should be considered early in the course of therapy.[8]

*Opioid naïve patients*—A reasonable initiating dose for patients who are opioid naïve is 10 mg every 12 hours. It can be administered concurrently with nonopioid analgesics such as aspirin, acetaminophen, or NSAIDs.

*Opioid tolerant patients*—The conversion of other opioid therapies to OxyContin® is variable between patients, especially patients receiving large opioid doses. Conversion tables are available from the manufacturer upon request, however physician observation and frequent titration are indicated until patients are stable on OxyContin® therapy.[9]

Recommended Initial Dosing

It is recommended that all physicians initiate an individualized dosing regimen, taking into account the patient's prior opioid and non-opioid analgesic treatment.

**II. Abuse Potential:**
On July 25, 2001, the FDA approved the addition of the following BLACK BOX WARNING.

**WARNING:**

**OxyContin® is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.**

**Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin® in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.**

**OxyContin® Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.**

**OxyContin® tablets are NOT intended for use as a prn analgesic.**

**OxyContin® 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID TOLERANT PATIENTS ONLY. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.**

**OxyContin® (oxycodone hydrochloride controlled-release) TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED OR CRUSHED OxyContin® TABLETS LEADS TO A RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.**

Oxycodone is a pure opioid agonist. The therapeutic effects of oxycodone include analgesia, anxiolysis, and feelings of relaxation. Oxycodone has similar properties to other pure opioid agonists. There is no maximum dose of pure opioid agonists because patients can develop tolerance to such medications. This “no ceiling” effect makes individualized dosing regimens extremely important.[2]

OxyContin® tablets are made with a dual-polymer matrix that is designed to have controlled delivery of oxycodone over a 12-hour period. Potential abuse arises from crushing the controlled-release mechanism, turning the 12-hour controlled dose into a large immediate-release bolus. The crushed tablet is ingested, snorted, or diluted in water to be injected. The euphoria is comparable to that of heroin, and it is often called “poor man’s heroin" despite the high price it commands on the street. OxyContin® can sell from between 50 cents to one dollar per milligram; therefore, the street value of one 40 mg tablet can cost up to 40 dollars.[10]

When OxyContin® is abused by means of crushing the tablet, its effects become highly addictive. This addiction can lead to a “drug-seeking” behavior. Drug-seeking tactics can include emergency calls or visits near the end of office hours and refusal to undergo appropriate examination. Other methods to obtain prescriptions include repeated “loss” of prescriptions, tampering with prescriptions and reluctance to provide prior medical records or contact information from other treating physicians. “Doctor shopping” to obtain additional prescriptions is common among drug abusers and people suffering from untreated addiction.[2]

Prescription drug abuse in America is growing at an alarming rate. “The National Household Survey on Drug Abuse,which is conducted annually by the Substance Abuse and Mental Health Administration SAMHSA), demonstrated that an estimated 1.6 million Americans used prescription-type pain relievers non-medically for the first time during 1998.” This figure rose to 2.6 million in 1999. (The most recent data available (Table 1) is from the Drug Abuse Warning Network (DAWN). Their report shows that the abuse of oxycodone was 108% higher in 2000 than in 1998. DAWN also reports that oxycodone was mentioned in 2% of all emergency department episodes in 2000.[1]

it is important to inform patients that addiction to opioids used for legitimate medical purposes under a qualified physician’s care is rare.[11] Tolerance and physical dependence in pain patients are **NOT** signs of addiction. Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia. Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug, or upon administration of an antagonist. When the patient no longer requires therapy and is receiving 60 mg/day or less, therapy can usually be stopped abruptly without incident. However, higher doses should be tapered over several days to prevent signs and symptoms of withdrawal in the physically dependent patient.[2]



**Please send comments and suggestions regarding this newsletter to Jayne Zemmer,DUR Coordinator, Division of Medical Services, P.O. Box 6500 Jefferson City, MO 65102-6500**

**III. Prevention:**

As part of Purdue's antidiversion efforts, the company has created a 10-point program for prevention and education. This program is outlined with distinct initiatives.[12]

1. **CONTINUING MEDICAL EDUCATION PROGRAMS** are being provided by Purdue Pharma in those regions of the U.S. that have been most affected by prescription pain medication abuse. These non-promotional educational programs teach healthcare professionals how to properly assess and treat patients suffering from real pain and reduce diversion of prescription drugs by abusers.

2. **TAMPER-RESISTANT PRESCRIPTION PADS** are being offered by Purdue Pharma to physicians at no cost in regions with the highest reported incidence of drug abuse. To date these pads have been distributed to physicians in Maine, Virginia, West Virginia, Tennessee, Alabama, Ohio, Pennsylvania and Florida. The pads will also be rolled out in additional states as well.

3. **DRUG PREVENTION AND EDUCATION PROGRAMS FOR MIDDLE SCHOOL STUDENTS** are being created by Purdue Pharma to combat prescription drug abuse at the age when many kids start experimenting with drugs and alcohol. The company is working with the Community Anti-Drug Coalitions of America and other organizations to educate parents, teachers, and students about the social and emotional consequences of prescription drug abuse as well as its physical risks.

4. **OPIOID DOCUMENTATION KITS** are being offered to help physicians assess pain properly and to distinguish between legitimate patients with pain and abusers who pretend to be in pain in order to obtain controlled substances.

5. **ABUSE AND DIVERSION BROCHURES** have been mailed to nearly 500,000 physicians and more than 60,000 pharmacists throughout the country, providing valuable information on how they can help prevent diversion of prescription drugs.

6. **A MAJOR STUDY OF PRESCRIPTION MONITORING PROGRAMS** is being underwritten by Purdue Pharma. Working with the healthcare and law enforcement communities, the study will seek to develop a model prescription monitoring program that would prevent "doctor shopping" by drug abusers and allow legitimate patients to receive appropriate prescription medicines.

7. **EDUCATIONAL PROGRAMS WITH THE LAW ENFORCEMENT COMMUNITY**, including the National Association of Drug Diversion Investigators (NADDI), several State Attorneys General and the National Association of State Controlled Substance Authorities (NASCSA), have been developed to better understand the undertreatment of pain and to combat prescription drug abuse.

8. **RESEARCH** on the prevalence and root cause of the abuse of specific prescription drugs is being collected by Purdue-sponsored researchers so that more effective prevention programs can be developed and evaluated.

9. **CROSS-BORDER SMUGGLING** is being addressed, in cooperation with the DEA, to prevent OxyContin® from being smuggled into the U.S. from Mexico and Canada. Tablets sold in Canada and Mexico will have unique markings to enable law enforcement to identify where the product was dispensed.

10. **ABUSE-RESISTANT MEDICINES** are the number one priority in Purdue's research labs. Purdue is spending tens of millions of dollars to test and develop new forms of pain relievers that would be resistant to abuse while providing legitimate patients with safe and effective pain relief.

The following guidelines have been recommended by Purdue Pharma and the DEA:

- OxyContin® should only be prescribed to patients where use of an opioid is appropriate for moderate to severe pain lasting more than a few days.
- OxyContin® should only be prescribed by physicians who are knowledgeable about the use of opioids in the treatment of pain.
- None of the efforts to reduce abuse and diversion should interfere with the ability of patients in pain to receive OxyContin® for appropriate medical uses.[13]

Purdue Pharmaceuticals is currently working on a new formulation to eradicate the abuse OxyContin®. The new delivery system would combine controlled-release oxycodone with the opioid antagonist, naloxone. When taken as directed, the naloxone should not interfere with the analgesic properties of oxycodone. However, if the tablet is crushed or injected, the naloxone would be released into the blood stream and negate the effects of oxycodone—including euphoria.[14] Ideally, this would minimize the potential for abuse.

**Conclusion:**

There have been many headlines regarding OxyContin® over the past several months. Patients will continue to ask healthcare professionals about the facts and myths regarding OxyContin®. It is important to educate patients with chronic pain that OxyContin® is a safe and effective treatment when used appropriately.

**Missouri Medicaid Statistics**

The DUR Board and Prior Authorization Committee continue to review the utilization of Oxycontin in an attempt to control potential misuse of this product. Suggestions from these advisory groups have focused on eliminating inappropriate prescribing and dispensing, while avoiding interference with legitimate pain therapy for patients who need it. Although no system limitations have been imposed to date on reimbursement for Oxycontin, the Division of Medical Services will continue to scrutinize its utilization and will implement appropriate controls as necessary and as new systems become available.

**Net Change over CY 2001**

| Amount paid for all analgesics | Amount paid for oxycodone | Number of Rx for all analgesics | Number of Rx for oxycodone |
|---|---|---|---|
| +0.89 % | +1.56% | - 0.45 % | +0.36% |

**Totals for CY 2001**

| Total paid for all analgesics | Total paid for oxycodone | Total # of Rx for all analgesics | Total # Rx for oxycodone | Percentage of analgesic use for Oxycontin |
|---|---|---|---|---|
| $72,579,821 | $11,487,922 | 1,937,473 | 63,899 | 3.29% |

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