CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-272

LABELING

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OXYCONTIN® safely and effectively. See full prescribing information for OXYCONTIN.

OxyContin® (oxycodone hydrochloride controlled-release) Tablets CII
Initial U.S. Approval: 1982

WARNING: IMPORTANCE OF PROPER PATIENT SELECTION AND POTENTIAL FOR ABUSE

See full prescribing information for complete boxed warning.

- **OxyContin contains oxycodone which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.** (9)
- **OxyContin is indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.** (1)
- **OxyContin is NOT intended for use on an as-needed basis.** (1)
- **OxyContin 60 mg and 80 mg Tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in opioid-tolerant patients to avoid fatal respiratory depression.** (2.7)
- **Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids.** (2.2)
- **OxyContin tablets must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved which can lead to rapid release and absorption of a potentially fatal dose of oxycodone.** (2.1)
- **The concomitant use with cytochrome P450 3A4 inhibitors such as macrolide antibiotics and protease inhibitors may result in an increase in oxycodone plasma concentrations and may cause potentially fatal respiratory depression.** (7.2)

----------INDICATIONS AND USAGE----------

OxyContin is an opioid agonist indicated for:

- Management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. (1)
- Not for use on an as-needed basis or in the immediate post-operative period. (1)

----------DOSAGE AND ADMINISTRATION----------

- Use low initial doses in patients who are not already opioid-tolerant, especially those who are receiving concurrent treatment with muscle relaxants, sedatives, or other central nervous system (CNS) active medications. (2.2)
- For patients already receiving opioids, use standard conversion ratio estimates. (2.2)
- Tablets must be swallowed whole and are not to be cut, broken, chewed, crushed, or dissolved (risk of potentially fatal dose). (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

- Controlled-Release Tablets: 10 mg, 15 mg, 20 mg , 30 mg, 40 mg, 60 mg and 80 mg (3)

----------CONTRAINDICATIONS----------

- in patients who have significant respiratory depression (4)
- in patients who have or are suspected of having paralytic ileus (4)
- in patients who have acute or severe bronchial asthma (4)
- in patients with known hypersensitivity to oxycodone (4)

----------WARNINGS AND PRECAUTIONS----------

- Must be swallowed whole (5.1)
- May cause somnolence, dizziness, alterations in judgment and alterations in levels of consciousness, including coma. (5.2)
- Additive CNS effects are expected when used with alcohol, other opioids, or illicit drugs. (5.1, 5.3, 7.3)
- Use with caution in patients who are receiving other CNS depressants. (5.1, 5.3, 7.3)
- May cause respiratory depression, use with extreme caution in patients at risk of respiratory depression, elderly and debilitated patients (5.4)
- May aggravate convulsions in patients with convulsive disorders, and may induce or aggravate seizures in some clinical settings. (5.5)
- May worsen increased intracranial pressure and obscure its signs, such as level of consciousness or pupillary signs. (5.6)
- May cause hypotension, use with caution in patients at increased risk of hypotension and in patients in circulatory shock. (5.7)
- Concomitant use of CYP3A4 inhibitors may increase opioid effects (5.8)
- Mixed agonist/antagonist analgesics may precipitate withdrawal symptoms. (5.9)
- Use with caution in patients with biliary tract disease, including acute pancreatitis. (5.10)
- Use with caution in patients at risk for ileus. Monitor for decreased bowel motility in postoperative patients. (5.10)
- Tolerance may develop. (5.11)
- Use with caution in alcoholism; adrenocortical insufficiency; hypothyroidism; prostatic hypertrophy or urethral stricture; severe impairment of hepatic, pulmonary or renal function; and toxic psychosis. (5.12)
- May impair the mental and physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. (5.13)
- No approved use in the treatment of addiction. (5.14)
- Not every urine drug test for "opioids" or "opiates" detects oxycodone reliably. (5.15)

----------ADVERSE REACTIONS----------

Most common adverse reactions (>5%) are constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, asthenia, and sweating.

To report Suspected Adverse Reactions, contact Purdue Pharma L.P. at 1-888-726-7535 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------DRUG INTERACTIONS----------

- OxyContin may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression. (7.1)
- The CYP3A4 isoenzyme plays a major role in the metabolism of OxyContin, drugs that inhibit CYP3A4 activity may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations. (7.2)
- Concurrent use of other CNS depressants may cause respiratory depression, hypotension, and profound sedation or coma. (7.3)
- Mixed agonist/antagonist analgesics may reduce the analgesic effect of oxycodone and may precipitate withdrawal symptoms in these patients. (7.4)

----------USE IN SPECIFIC POPULATIONS----------

- Labor and Delivery: Not recommended for use in women immediately prior to and during labor and delivery; (8.2)
- Nursing Mothers: Nursing should not be undertaken while a patient is receiving OxyContin. (8.3)
- Pediatrics: Safety and effectiveness in pediatric patients below the age of 18 have not been established. (8.4)
- Geriatrics: The initial dose may need to be reduced to 1/3 to ½ of the usual doses. (8.5)
- Hepatic impairment: Initiate therapy at 1/3 to 1/2 the usual doses and titrate carefully. (8.6)
- Renal impairment: Dose initiation should follow a conservative approach. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.
Revised: April 2010

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FULL PRESCRIBING INFORMATION

WARNING: IMPORTANCE OF PROPER PATIENT SELECTION AND POTENTIAL FOR ABUSE

OxyContin contains oxycodone which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine. (9)

OxyContin 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. (9.2)

OxyContin is a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. (1)

OxyContin is not intended for use on an as-needed basis. (1)

Patients considered opioid tolerant are those who are taking at least 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for one week or longer.
OxyContin 60 mg and 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in opioid-tolerant patients, as they may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory-depressant or sedating effects of opioids. (2.7)

Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse, abuse and addiction. (2.2)

OxyContin must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved. Taking cut, broken, chewed, crushed or dissolved OxyContin tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone. (2.1)

The concomitant use of OxyContin with all cytochrome P450 3A4 inhibitors such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir) may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse effects and may cause potentially fatal respiratory depression. Patients receiving OxyContin and a CYP3A4 inhibitor should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted (7.2).

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1 INDICATIONS AND USAGE

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

Limitations of Usage

OxyContin is not intended for use on an as-needed basis.

OxyContin is not indicated for the management of pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the pain is mild, or not expected to persist for an extended period of time. OxyContin is indicated for postoperative use following the immediate post-operative period only 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. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.)

OxyContin is not indicated for pre-emptive analgesia (preoperative administration for the management of postoperative pain).

OxyContin is not indicated for rectal administration.

2 DOSAGE AND ADMINISTRATION

2.1 Safe Administration Instructions

OxyContin tablets must be swallowed whole and must not be cut, broken, chewed, crushed or dissolved. Taking cut, broken, chewed, crushed or dissolved OxyContin tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone.

Selection of patients for treatment with OxyContin should be governed by the same principles that apply to the use of similar opioid analgesics. Physicians should individualize treatment using a progressive plan of pain management such as outlined by the World Health Organization, Federation of State Medical Boards Model Policy, and the American Pain Society. Healthcare professionals should follow appropriate pain management principles of careful assessment and ongoing monitoring.

2.2 Initiating Therapy with OxyContin

It is critical to initiate the dosing regimen for each patient individually. Attention should be given to:

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