

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 extended-release tablets), for oral use, CII

Initial U.S. Approval: 1950

WARNING: ADDICTION, ABUSE and MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and CYTOCHROME P450 3A4 INTERACTION

See full prescribing information for complete boxed warning.

- OXYCONTIN exposes users to risks of addictions, abuse and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing and monitor regularly for development of these behaviors and conditions. (5.1)
- Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow OXYCONTIN tablets whole to avoid exposure to a potentially fatal dose of oxycodone. (5.2)
- Accidental ingestion of OXYCONTIN, especially in children, can result in a fatal overdose of oxycodone. (5.2)
- Prolonged use of OXYCONTIN during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.3)
- Initiation of CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of oxycodone from OXYCONTIN. (5.14)

RECENT MAJOR CHANGES

Boxed Warning	04/2014
Indications and Usage (1)	04/2014
Dosage and Administration (2)	04/2014
Warnings and precautions (5)	04/2014

INDICATIONS AND USAGE

OXYCONTIN is an opioid agonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. (1)

Limitations of Use

- Because of the risks of addiction, abuse and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release formulations, reserve OXYCONTIN for use in patients for whom alternative treatment options (e.g. non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. (1)
- OXYCONTIN is not indicated as an as-needed (prn) analgesic. (1)

DOSAGE AND ADMINISTRATION

- 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 patients in whom tolerance to an opioid of comparable potency has been established. (2.1)
- For opioid-naïve and opioid non-tolerant patients, initiate with 10 mg tablets orally every 12 hours. (2.1)
- Do not abruptly discontinue OXYCONTIN in a physically dependent patient. (2.4)
- Tablets must be swallowed intact and are not to be cut, broken, chewed, crushed, or dissolved (risk of potentially fatal dose). (2.5, 5.1)
- OXYCONTIN tablets should be taken one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth. (2.5, 5.9, 17)

FULL PRESCRIBING INFORMATION: CONTENTS*

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1 INDICATIONS AND USAGE

2 DOSAGE FORMS AND STRENGTHS

Extended-release tablets: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg (3)

CONTRAINDICATIONS

- Significant respiratory depression (4)
- Acute or severe bronchial asthma (4)
- Known or suspected paralytic ileus and GI obstruction (4)
- Hypersensitivity to oxycodone (4)

WARNINGS AND PRECAUTIONS

- Interactions with CNS depressants: Concomitant use may cause profound sedation, respiratory depression and death. If coadministration is required, consider dose reduction of one or both drugs. (5.4)
- Elderly, cachectic, debilitated patients, and those with chronic pulmonary disease: Monitor closely because of increased risk for life-threatening respiratory depression. (5.5, 5.6)
- Hypotensive effects: Monitor during dose initiation and titration. (5.7)
- Patients with head injury or increased intracranial pressure: Monitor for sedation and respiratory depression. Avoid use of OXYCONTIN in patients with impaired consciousness or coma susceptible to intracranial effects of CO₂ retention. (5.8)
- Use with caution in patients who have difficulty swallowing or have underlying GI disorders that may predispose them to obstruction. (5.9)
- Concomitant use of CYP3A4 inhibitors may increase opioid effects. (5.14)

ADVERSE REACTIONS

Most common adverse reactions (>5%) are constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, asthenia, and sweating. (6.1)

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

- Mixed agonist/antagonist and partial agonist opioid analgesics: Avoid use with OXYCONTIN because they may reduce analgesic effect of OXYCONTIN or precipitate withdrawal symptoms. (7.4)

USE IN SPECIFIC POPULATIONS

- Nursing mothers: Oxycodone has been detected in human milk. Closely monitor infants of nursing women receiving OXYCONTIN. (8.3)
- Geriatrics: The initial dose may need to be reduced to 1/3 to 1/2 of the usual doses. (8.5)
- Hepatic impairment: Initiate therapy at 1/3 to 1/2 the usual doses and titrate carefully. (8.6)

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Revised: 04/2014

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FULL PRESCRIBING INFORMATION

WARNING: ADDICTION, ABUSE and MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and CYTOCHROME P450 3A4 INTERACTION

Addiction, Abuse, and Misuse

OXYCONTIN[®] exposes patients and other users to the risks of opioid addiction, abuse and misuse, which can lead to overdose and death. Assess each patient’s risk prior to prescribing OXYCONTIN and monitor all patients regularly for the development of these behaviors or conditions [see Warnings and Precautions (5.1)].

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of OXYCONTIN. Monitor for respiratory depression, especially during initiation of OXYCONTIN or following a dose increase. Instruct patients to swallow OXYCONTIN tablets whole; crushing, chewing, or dissolving OXYCONTIN tablets can cause rapid release and absorption of a potentially fatal dose of oxycodone [see Warnings and Precautions (5.2)].

Accidental Ingestion

Accidental ingestion of even one dose of OXYCONTIN, especially by children, can result in a fatal overdose of oxycodone [see Warnings and Precautions (5.2)].

Neonatal Opioid Withdrawal Syndrome

Prolonged use of OXYCONTIN during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available [see Warnings and Precautions (5.3)].

Cytochrome P450 3A4 Interaction

The concomitant use of OXYCONTIN with all cytochrome P450 3A4 inhibitors may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in oxycodone plasma concentration. Monitor patients receiving OXYCONTIN and any CYP3A4 inhibitor or inducer [see Warnings and Precautions (5.14) and Clinical Pharmacology (12.3)].

1 INDICATIONS AND USAGE

OXYCONTIN is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve OXYCONTIN for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- OXYCONTIN is not indicated as an as-needed (prn) analgesic

2 DOSAGE AND ADMINISTRATION

2.1 Initial Dosing

OXYCONTIN should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.

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 patients in whom tolerance to an opioid of comparable potency has been established. Patients considered opioid tolerant are those receiving, for one week or longer, 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.

Initiate the dosing regimen for each patient individually, taking into account the patient's prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse [see Warnings and Precautions (5.1)]. Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy with OXYCONTIN [see Warnings and Precautions (5.2)].

OXYCONTIN tablets must be taken whole, one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth [see Patient Counseling Information (17)]. Crushing, chewing, or dissolving OXYCONTIN tablets will result in

uncontrolled delivery of oxycodone and can lead to overdose or death [see Warnings and Precautions (5.1)].

Use of OXYCONTIN as the First Opioid Analgesic

Initiate treatment with OXYCONTIN with one 10 mg tablet orally every 12 hours.

Use of OXYCONTIN in Patients who are not Opioid Tolerant

The starting dose for patients who are not opioid tolerant is OXYCONTIN 10 mg orally every 12 hours. Patients who are opioid tolerant are those receiving, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, or an equianalgesic dose of another opioid.

Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression.

Conversion from other Oral Oxycodone Formulations to OXYCONTIN

Patients receiving other oral oxycodone formulations may be converted to OXYCONTIN by administering one-half of the patient's total daily oral oxycodone dose as OXYCONTIN every 12 hours.

Conversion from other Opioids to OXYCONTIN

Discontinue all other around-the-clock opioid drugs when OXYCONTIN therapy is initiated.

There are no established conversion ratios for conversion from other opioids to OXYCONTIN defined by clinical trials. Discontinue all other around-the-clock opioid drugs when OXYCONTIN therapy is initiated and initiate dosing using OXYCONTIN 10 mg orally every 12 hours.

It is safer to underestimate a patient's 24-hour oral oxycodone requirements and provide rescue medication (e.g., immediate-release opioid) than to overestimate the 24-hour oral oxycodone requirements which could result in adverse reactions. While useful tables of opioid equivalents are readily available, there is substantial inter-patient variability in the relative potency of different opioid drugs and products.

Conversion from Methadone to OXYCONTIN

Close monitoring is of particular importance when converting from methadone to other opioid agonists. The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure. Methadone has a long half-life and can accumulate in the plasma.

Conversion from Transdermal Fentanyl to OXYCONTIN

Eighteen hours following the removal of the transdermal fentanyl patch, OXYCONTIN treatment can be initiated. Although there has been no systematic assessment of such conversion, a conservative oxycodone dose, approximately 10 mg every 12 hours of OXYCONTIN, should be initially substituted for each 25 mcg/hr fentanyl transdermal patch. Follow the patient closely during conversion from transdermal fentanyl to OXYCONTIN, as there is limited documented experience with this conversion.

2.2 Titration and Maintenance of Therapy

Individually titrate OXYCONTIN to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving OXYCONTIN to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as monitoring for the development of addiction, abuse and misuse. Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initial titration. During chronic therapy, periodically reassess the continued need for the use of opioid analgesics.

Patients who experience breakthrough pain may require a dose increase of OXYCONTIN or may need rescue medication with an appropriate dose of an immediate-release analgesic. If the level of pain increases after dose stabilization, attempt to identify the source of increased pain before increasing the OXYCONTIN dose. Because steady-state plasma concentrations are approximated in 1 day, OXYCONTIN dosage may be adjusted every 1 to 2 days. If unacceptable opioid-related adverse reactions are observed, the subsequent dose may be reduced. Adjust the dose to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

There are no well-controlled clinical studies evaluating the safety and efficacy with dosing more frequently than every 12 hours. As a guideline, the total daily oxycodone dose usually can be increased by 25% to 50% of the current dose, each time an increase is clinically indicated.

2.3 Patients with Hepatic Impairment

For patients with hepatic impairment, start dosing patients at 1/3 to 1/2 the usual starting dose followed by careful dose titration [*see Clinical Pharmacology (12.3)*].

2.4 Discontinuation of OXYCONTIN

When the patient no longer requires therapy with OXYCONTIN tablets, use a gradual downward titration of the dose to prevent signs and symptoms of withdrawal in the physically dependent patient. Do not abruptly discontinue OXYCONTIN.

2.5 Administration of OXYCONTIN

Instruct patients to swallow OXYCONTIN tablets intact. The tablets are not to be crushed, dissolved, or chewed due to the risk of rapid release and absorption of a potentially fatal dose of oxycodone [*see Warnings and Precautions (5.1)*].

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