**DRUG FORMULARY COMMISSION**

**Drugs for Formulary Inclusion:**

**DRAFT Monograph**

1. **Introduction**

Generic name: Oxycodone hydrochloride

Trade name: OxyContin

Manufacturer: Purdue Pharma

Classification[[1]](#endnote-1): Type 4 – Type of ADF technology

1. **Preliminary Review**

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| --- | --- | --- | --- |
|   | *Preliminary Review of Individual Drug Product* |  |  |
| **Question** |  | **Result** | **Result** |
| 1 | *Does the drug have FDA abuse deterrent labeling or an abuse deterrent property?* | ***YES*** | NO |

1. **Executive Summary**

The FDA has approved abuse-deterrent labeling for OxyContin in 2013.1 The purpose of this drug monograph is to evaluate this medication, which was reformulated in 2010. OxyContin is a widely-used opioid analgesic commonly used in the management of moderate to severe pain.2 Due to the addictive nature of opioid medications, there are many concerns with adulteration and abuse of OxyContin, among many other opioid analgesics. The new, reformulated OxyContin is more difficult to crush, due to a fused-polymer, plastic-like coating, which in turn makes nasal inhalation (“snorting”) more difficult.3 Furthermore, when mixing with liquid, this formulation becomes viscous and poses challenges regarding administration via syringe. Therefore, OxyContin is still as effective as its original formulation and gains the added benefit of abuse deterrence.

1. **Monograph Content**
	1. **Reference Data**

OxyContin is a semisynthetic opioid analgesic.2 This medication works as an agonist at the µ (OP3) opiate receptor, which is a G-protein coupled receptor. It alters the perception of pain in the spinal cord and higher levels of the central nervous system, resulting in an analgesic effect. OxyContin is administered orally as a tablet, and it is an extended-release formulation of oxycodone. In contrast to the immediate-release formulation, OxyContin has a longer duration of action and can be dosed less frequently (every 12 hours). Other similar semisynthetic opiates include hydrocodone, hydromorphone, and oxymorphone.4 There are also natural alkaloids, such as morphine and codeine, and synthetic opioids, such as methadone and fentanyl.

* 1. **Therapeutic Indications/Efficacy**

The primary indication for OxyContin is moderate to severe pain.2 There is one off-label indication, which is diabetic neuropathic pain, but there is a low level of evidence for this indication. The new, abuse-deterrent formulation of OxyContin has been shown to be bioequivalent to the original formulation.3 Additionally, this new formulation has been shown to prevent adulteration of the product, therefore reducing injection via syringe, and it has been associated with a decrease in reported deaths.5,6

* 1. **Pharmacokinetics**

After oral administration, OxyContin is 60–87% bioavailable and approximately 45% protein bound.2 Food does not seem to affect the extent of absorption, and the release of the medication is independent of pH. Plasma concentrations reach steady state within 24–36 hours. OxyContin undergoes distribution to the skeletal muscle, liver, intestines, lungs, spleen, central nervous system, and has even been present in breast milk. This medication is metabolized in the liver by cytochrome P450 enzymes, specifically CYP3A4 and CYP2D6, to weaker metabolites such as noroxycodone, noroxymorphone, and oxymorphone. It is then excreted in the urine. The half-life of this extended-release formulation is approximately 4.5 hours. Hepatic insufficiency results in higher drug concentrations and longer half-life, and renal insufficiency results in decreased drug clearance. There may be only minimal differences in geriatric and pediatric populations.

* 1. **Dosage Forms**

OxyContin is an extended-release formulation of oxycodone that comes in a tablet dosage form.2 Strengths of OxyContin, on the market, include the following: 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, and 80mg. This medication should not be crushed or chewed, and it should be stored at room temperature.

* 1. **Dosage Range**

Dosing of OxyContin is individualized and differs from one patient to another.2 The 60mg and 80mg extended-release tablets should only be provided to opioid-tolerant patients. Furthermore, total daily doses that are greater than 80 mg should only be used in opioid-tolerant patients. For opioid-naive patients, an initial dose of 10 mg every 12 hours may be administered. Dosage strength may be titrated up gradually every few days, if necessary, as the patient begins to tolerate side effects. OxyContin can be used in the geriatric population and in children of the age 11 or older. Requirements for prescribing OxyContin for children include opioid exposure for at least 5 consecutive days and a minimum of 20 mg per day of oxycodone for 2 days immediately prior to starting OxyContin. In the presence of hepatic or renal insufficiency, patients should start with a low dose and titrate up carefully, since plasma concentrations of this drug may be increased. OxyContin is administered every 12 hours, so it may be taken in the morning and in the evening. It may be taken with or without food, and patients should avoid alcohol consumption. Since it is metabolized by CYP3A4, medications that induce CYP3A4 can decrease the efficacy of OxyContin, while inhibitors of CYP3A4 can increase its plasma concentration and increase risk of side effects. Therefore, presence of these enzyme inducers or inhibitors may warrant dose adjustments.

# Adverse Effects

The common adverse effects of OxyContin tend to be gastrointestinal in nature, including nausea, vomiting, stomach upset, and abdominal pain.2 Constipation is also a common side effect of this medication and other opiates. This constipation may be avoided or relieved by increasing fiber intake, staying hydrated, staying active, and using laxatives as needed. OxyContin may also cause miosis, also referred to as pinpoint pupils. A serious adverse reaction to OxyContin is respiratory depression, so it is suggested that this medication be avoided in those with pulmonary diseases. Since this is an opioid medication, addiction and dependence can occur. Dependence may be physical or psychological in nature. Fortunately, the new formulation of OxyContin supports prevention of medication abuse.

# Contraindications

# OxyContin should be avoided in patients with gastrointestinal obstruction or decreased GI motility, since this medication can further contribute to these conditions.2 Due to the black box warning concerning respiratory depression, this medication should also be avoided in patients with pulmonary diseases or those with acute or severe asthma. Caution should be taken when dosing and titrating doses for opioid-naive patients. Another important precaution is overdose, especially because of the abuse potential and dependence associated with this medication.

* 1. **Toxicities**

The FDA has categorized OxyContin as a pregnancy category B medication.2 Congenital defects have not been reported, but there have been no well-controlled human studies in pregnant women regarding this medication. However, it is suggested that this medication should be avoided in high doses close to labor, since it could increase risk of respiratory depression in the newborn. Neonatal opioid withdrawal syndrome is also a concern in the presence of prolonged exposure to opiates during pregnancy. Due to its distribution into breast milk, OxyContin is not recommended in nursing mothers. If a mother is taking this medication, discontinuation of breast-feeding may lead to withdrawal symptoms in the child.

# Drug Interactions

# OxyContin is metabolized in the liver by cytochrome P450 enzymes, specifically CYP3A4 and CYP2D6.2 Therefore, it is susceptible to interactions with drugs that either induce or inhibit these enzymes. Inducers of these enzymes may cause this medication to be less effective, while inhibitors of these enzymes may result in an increase in the action of this medication and higher risk of toxicity/adverse effects. Avoid concurrent use of OxyContin with other opioids, sedating medications, or antidiarrheal medications, since this may increase the risk and/or amplify the side effects of this medication. Alcohol consumption should be avoided while taking this medication. Grapefruit juice should also be avoided or limited while taking this medication, since it can act as an inhibitor of CYP3A4.

* 1. **Patient Monitoring Guidelines**

Monitoring parameters regarding the effectiveness of OxyContin do not include laboratory values.2 Instead, effectiveness is measured based on the reduction in pain reported by the patient. The patient may report any nausea, vomiting, stomach upset, or abdominal pain. Patients may monitor constipation by tracking the duration between bowel movements. Any changes in breathing or symptoms of withdrawal/dependence should be reported immediately. Since OxyContin is an extended-release medication that is dosed every 12 hours, confirm that the patient is not taking it more than prescribed.

* 1. **Cost Effectiveness**

There are some other medications recently approved for abuse-deterrent labeling by the FDA. Some other examples include medications such as Embeda and Hysingla.7,8 When compared with OxyContin, these medications cost around the same price. All of these extended-release formulations tend to be more costly than immediate-release medications, given their convenient dosing schedule. However, OxyContin is still a widely prescribed medication and is readily accessible and available in the pharmacy.

* 1. **Data**

As previously stated, OxyContin is a widely used medication. Figures regarding this medication and its usage in the United States in 2013 demonstrate that 283,311 patients were taking this medication, 145,494 prescribers were prescribing it, there were approximately 1.92 million Medicare Part D claims, and the retail cost was approximately $945 million.9 OxyContin is commonly prescribed for a one month supply, which is a quantity of 60 pills due to its twice per day dosing schedule. Prescription monitoring programs (PMPs) are very important in regard to OxyContin, since it is a Schedule II controlled substance.10 PMPs are useful in the prevention of multiple prescriber episodes, cutting down on the number of patients who receive multiple prescriptions for controlled substances from multiple different prescribers.

1. **References**

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1. This is the table that corresponds to the “Classification” designation contained within this section.

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| **Classification System** |
| *By Chemical Type* |
| **Type** | **Definition** |
| 1 | New molecular entity not marketed in U.S. |
| 2 | New salt, ester, or other derivative of another drug marketed in the U.S. |
| 3 | New ADF formulation of a drug marketed in U.S. |
| 4*7By Therapeutic Potential* | Type of ADF technology |
| 58  | Manufacturer Post-Marketing data if available |
| 6 | Additional references |

 [↑](#endnote-ref-1)