# Setting the Record Straight on Reuters

*June 28, 2019*

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Purdue Pharma strongly rejects the claims made by Reuters in its article titled “How judges added to the grim toll of opioids” (June 25, 2019) both about the use of protective orders in litigation and about the effectiveness of OxyContin’s 12-hour dosing schedule.

Since the FDA first approved OxyContin® (oxycodone HCl) extended-release tablets CII in 1995, the medicine has been deemed safe and effective for 12-hour dosing. Since then, the FDA-approved label for OxyContin has been updated more than 30 times, and at no point has the FDA requested a change to 12-hour dosing.

The FDA has had multiple opportunities to revise or update its guidance on the 12-hour dosing of OxyContin. On each occasion, after reviewing the latest scientific data and medical expert testimony, the FDA has maintained the 12-hour labeling.

Purdue has always sold OxyContin in a variety of doses that allow doctors the ability to titrate the dose up or down to find the appropriate dose for pain relief and minimize adverse reactions in a particular patient. This is in line with accepted medical practice that a physician and patient individualize therapy and that physicians continually reevaluate patients for maintenance of pain control, signs and symptoms of opioid withdrawal, adverse reactions, and for the development of addiction, abuse and misuse.

Any claim that Purdue has used court-ordered document protective orders to somehow withhold from the FDA relevant information about the safety or efficacy of OxyContin is not only without any basis in fact, but also is wildly misleading and recklessly inflammatory. In fact, Reuters has on numerous occasions sought on its own behalf court orders to prevent discovery or maintain the secrecy of its documents produced in discovery.

Purdue continues to fulfill its regulatory requirements to share information with the FDA about the safety and efficacy of its medicines.

**CLAIM: Judges routinely allow Purdue and other companies to keep information pertinent to public health and safety under wraps during litigation, “robbing consumers of the chance to make informed choices and regulators of opportunities to improve safety.”**

**FACT:** Protective orders are standard and accepted practice in US litigation that permit the forthright disclosure of massive amounts of information during the discovery process. Protective orders such as those entered into by Purdue and certain plaintiffs enable the easy exchange of vast quantities of information. They are essential to ensuring that the discovery process is not abused and are specifically provided for in applicable court rules, including Federal Rule of Civil Procedure 26(c)(1)(g).

This is a standard practice routinely taken by parties in complex litigation (including Reuters in cases in which it has been a party). It is intended to protect confidential business information and is agreed to by the parties and the judge presiding over the case. In the opioid litigation, attorneys general and plaintiffs’ attorneys have repeatedly agreed to such protective orders.

To permit millions of communications to be publicly disclosed simply because a lawsuit has been filed would undermine existing American jurisprudence and its foundation of liberal discovery.

Implying that an adverse inference should be drawn from the existence of routine protective orders is both misinformed and irresponsible, inaccurately suggesting that the protective order process deliberately withheld certain information from our regulators. Purdue regularly provides FDA scientific information about the safety and efficacy of its medications, as part of ongoing, periodic reporting as well as on an ad-hoc basis in the case of certain serious adverse events.

**CLAIM: OxyContin is not effective for 12-hour dosing.**

**FACT:** This is an old allegation that was discredited many years ago. The FDA-approved labeling for OxyContin has always recognized the importance of individualized treatment and dosing for each patient. The Dosage and Administration section of the labeling includes the statement, “Initiate the dosing regimen for each patient individually; taking into account the patient’s severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.” Furthermore, this section of the label states to “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, signs and symptoms of opioid withdrawal, and adverse reactions, as well as monitoring for the development of addiction, abuse and misuse.”

Over a decade ago, the FDA rejected a 2004 petition from Connecticut Attorney General Richard Blumenthal that sought to revise OxyContin labeling to include additional warnings about the risk of taking the drug at more frequent intervals. In doing so, the Agency reinforced the 12-hour labeling for OxyContin. As part of the response, the FDA noted that “while a 12-hour dosing schedule would be expected to be

optimal for most patients, it is possible that some patients will require a more or less frequent dosing schedule to account for individual pharmacokinetic and pharmacodynamic differences." It ultimately concluded that the petition "failed to provide sufficient information to demonstrate an association between dosing OxyContin more frequently than q12h and an increased risk of developing side effects and potentially serious adverse reactions."

As it relates to dosing, the FDA prohibits pharmaceutical companies from promoting their products for uses not approved by the Agency. Given the FDA has not approved OxyContin for dosing more frequently than 12 hours, we do not recommend dosing other than every 12 hours to prescribers. The FDA-approved label for OxyContin has been updated more than 30 times, including after allegations regarding 8-hour dosing had been raised publicly and by the Attorney General of Connecticut, and at no point has the FDA requested a change from 12-hour dosing. In fact, the label clearly states that "There are no well-controlled clinical studies evaluating the safety and efficacy with dosing more frequently than every 12 hours." And as the FDA-approved Medication Guide for OxyContin states, "Take your prescribed dose every 12 hours at the same time every day. Do not take more than your prescribed dose in 12 hours. If you miss a dose, take your next dose at your usual time."

**CLAIM: OxyContin was a catalyst for the opioid epidemic.**

**FACT:** Opioid abuse is a subset of drug abuse in the United States, and the opioid addiction crisis is a complex societal problem that involves a number of different stakeholders, including manufacturers, prescribers, distributors, pharmacies, insurance companies, and governments at all levels. Attempts to pin blame on one party undermines the efforts of those tasked with understanding and addressing the crisis.

OxyContin constitutes an exceedingly small percentage of the prescription opioids prescribed in the United States (less than 2%), and its share of this market was never more than 4%.

Today's opioid addiction crisis is driven primarily by illegal opioids, such as illicit fentanyl and heroin. According to the Centers for Disease Control and Prevention (CDC)[1], the top five drugs involved in US overdose deaths in 2016 were fentanyl and heroin, followed by cocaine, methamphetamine, and alprazolam. While the percentage of overdose deaths involving oxycodone decreased from 13.5% in 2011 to 9.7% in 2016, the percentage of deaths involving fentanyl and heroin increased during that time from 4% to 28.8% and 11.1% to 25%, respectively. Together, fentanyl and heroin are now involved in over 53% of drug overdose deaths.[2]

**CLAIM: Purdue withheld important materials from the FDA as part of a lawsuit filed by Patricia Gwen Kiser.**

**FACT:** While it is true that Purdue opposed Ms. Kiser's motion to lift a protective order entered by the judge in her case regarding 21 confidential Purdue documents, the insinuation that by doing so Purdue somehow withheld from the FDA valuable safety information regarding OxyContin is utterly false.

First, the federal district judge overseeing the case duly considered and denied Ms. Kiser's motion.

Second, the FDA was aware of those documents. Purdue previously disclosed all or most of those documents in connection with a lengthy federal government investigation, in which the FDA participated, and Ms. Kiser described them in her petition to the FDA. The FDA ruled on that petition without requesting the documents from Purdue. That is unsurprising given that the documents do not contain the type of scientific information upon which the Agency usually relies in rendering decisions.

Third, Purdue appropriately discloses relevant safety information about OxyContin to the FDA.

**CLAIM: David Egilman, an expert witness in a lawsuit against Purdue, was wrongly denied access to company materials in response to a petition he filed in 2008.**

**FACT:** In June 2008, Dr. Egilman brought a lawsuit against the Attorney General for the Commonwealth of Massachusetts ("OAG") seeking to obtain documents Purdue produced to the OAG in 2005 and 2006 pursuant to a Civil Investigative Demand and subject to assurances of confidentiality. The OAG resisted Egilman's request for disclosure on the grounds that the records were exempt from disclosure by statute and Egilman filed a lawsuit in response. In 2011, after his action lay dormant for several years, Egilman resurfaced and begun pressing his lawsuit against the OAG. Purdue moved to intervene in order to protect its documents from public disclosure. Egilman did not oppose the motion to intervene and the motion was granted. Shortly thereafter, Judge Giles dismissed the case.

In 2007, Egilman paid $100,000 for participating in a scheme to leak to the press confidential documents in violation of a protective order in a case involving another pharmaceutical company.

**CLAIM: A 2016 Los Angeles Times investigation found that Purdue sold OxyContin as a 12-hour drug, "even**

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1 Centers for Disease Control. U.S. Opioid Prescribing Rate Maps. Accessed March 30, 2019. https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html

2 Center for Disease Control and Prevention. Drugs most frequently involved in drug overdose deaths: United States, 2011–2016. National Vital Statistics Reports. Hedegaard H, et al. 2018;67(9). Accessed Mar 15, 2019. https://www.cdc.gov/nchs/data/nvsr/nvsr67/nvsr67_09-508.pdf

**though the company knew it often didn't last that long" based on documents kept under seal by judges.**

**FACT:** Any documents maintained under seal were so designated pursuant to a court issued protective order intended to enable the easy exchange of vast quantities of information during discovery and agreed to by attorneys general and plaintiffs' attorneys.

As Purdue stated at the time of the article's publication, we spent more than a dozen hours with the Los Angeles Times in briefings and discussions regarding the clinical evidence supporting OxyContin's 12-hour dosing and the regulatory requirement to promote it as such. Unfortunately, the paper disregarded this information, relying instead on anecdotal evidence to resurrect a long-discredited theory.

Over a decade ago, the FDA formally cited a lack of evidence when it rejected the claim that patients receiving OxyContin extended-release tablets at dosing intervals more frequent than 12 hours are at increased risk of developing side effects and serious adverse reactions.

The FDA-approved label for OxyContin has been updated more than 30 times, and at no point has the FDA requested a change from 12-hour dosing. In fact, the label clearly states that "There are no well-controlled clinical studies evaluating the safety and efficacy with dosing more frequently than every 12 hours."

The FDA prohibits pharmaceutical companies from promoting their products for uses, including dosing, not approved by the Agency. Given the FDA has not approved OxyContin for dosing more frequent than every 12 hours, we do not recommend that dosing to prescribers.

**CLAIM: Purdue sales reps marketed OxyContin as a 12-hour drug because "insurers would balk at paying top dollar for a pain reliever that was little different from cheaper alternatives."**

**FACT:** Because the FDA approved OxyContin to be administered to patients every 12 hours, Purdue is permitted to promote its medication to be dosed at that frequency. In contrast, less expensive generic versions of branded immediate-release opioids such as Percocet® and Vicodin® are approved to be dosed every 4 to 6 hours. A medication dosed every 12 hours is able to be taken less frequently – twice a day.

**CLAIM: Per the amended complaint brought against Purdue by the Massachusetts Attorney General, the company conducted a "deadly and illegal scheme to deceive doctors and patients."**

**FACT:** We vigorously deny the allegations brought against Purdue by the State of Massachusetts, seeking to blame the company for the entire opioid addiction crisis in court of public opinion rather than the justice system. Such a serious allegation demands clear evidence linking the conduct alleged to the harm described, but Massachusetts fails to show such causation and offers little evidence to support its sweeping legal claims.

**CLAIM: Per the Massachusetts amended complaint, "Purdue sought to boost prescriptions for bigger doses, even though a 2012 internal analysis acknowledged that the more potent pills 'very likely' carried heightened 'dose-related overdose risk.'**

**FACT:** This claim is a mischaracterization of the 2012 document. Far from an "internal analysis," the document is a memo referencing and discussing limitations of certain published studies.

*Please read the OxyContin Full Prescribing Information, including Box Warning and additional Important Safety Information on the following page.*

## IMPORTANT SAFETY INFORMATION

**WARNING: ADDICTION, ABUSE AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS**

**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 and conditions *[see Warnings and Precautions (5.1)]*.**

**Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)**
**To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products *[see Warnings and Precautions (5.2)]*.**

**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 (5.3)]*.**

**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 (5.3)]*.**

**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 (5.4)]*.**

**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 (5.5), Drug Interactions (7), Clinical Pharmacology (12.3)]*.**

**Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants**
**Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death *[see Warnings and Precautions (5.6), Drug Interactions (7)]*.**

- **Reserve concomitant prescribing of OXYCONTIN and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

## CONTRAINDICATIONS

OxyContin is contraindicated in patients with:

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Hypersensitivity (e.g., anaphylaxis) to oxycodone.

## WARNINGS AND PRECAUTIONS

### Addiction, Abuse, and Misuse

- OxyContin contains oxycodone, a Schedule II controlled substance. OxyContin exposes users to the risks of opioid addiction, abuse, and misuse. Because extended-release products such as OxyContin deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of oxycodone present.
- Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed OxyContin. Addiction can occur at recommended doses and if the drug is misused or abused.
- Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing OxyContin, and monitor all patients receiving OxyContin for the development of these behaviors and conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as OxyContin, but use in such patients necessitates intensive counseling about the risks and proper use of OxyContin along with intensive monitoring for signs of addiction, abuse, and misuse.

- Abuse or misuse of OxyContin by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of oxycodone and can result in overdose and death.
- Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing OxyContin. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug.

**Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)**

- To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to do all of the following:
- complete a REMS-compliant education program,
- counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,
- emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and
- consider other tools to improve patient, household, and community safety.
- To obtain further information on the opioid analgesic REMS and for a list of accredited REMS CME/CE, call 1-800-503-0784, or log on to www.opioidanalgesicrems.com. The FDA Blueprint can be found at www.fda.gov/OpioidAnalgesicREMSBlueprint

**Life-Threatening Respiratory Depression**

- Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended, and if not immediately recognized and treated, may lead to respiratory arrest and death.
- While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of OxyContin, the risk is greatest during the initiation of therapy or following a dosage increase. Closely monitor patients for respiratory depression, especially within the first 24-72 hours of initiating therapy with and following dosage increases of OxyContin.
- To reduce the risk of respiratory depression, proper dosing and titration of OxyContin are essential. Overestimating the OxyContin dosage when converting patients from another opioid product can result in a fatal overdose with the first dose.
- Accidental ingestion of even one dose of OxyContin, especially by children, can result in respiratory depression and death due to an overdose of oxycodone.

**Neonatal Opioid Withdrawal Syndrome**

- Prolonged use of OxyContin during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

**Risks of Concomitant Use or Discontinuation of Cytochrome P450 3A4 Inhibitors and Inducers**

- Concomitant use with a CYP3A4 inhibitor, such as macrolide antibiotics, azole-antifungal agents, and protease inhibitors, particularly when an inhibitor is added after a stable dose of OxyContin is achieved, and discontinuation of a CYP3A4 inducer, such as rifampin, carbamazepine, and phenytoin, may increase plasma concentrations of oxycodone and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression. Monitor patients closely at frequent intervals and consider dosage reduction of OxyContin until stable drug effects are achieved. Concomitant use of OxyContin with CYP3A4 inducers or discontinuation of a CYP3A4 inhibitor could decrease oxycodone plasma concentrations, decrease opioid efficacy or, possibly, lead to a withdrawal syndrome in a patient who had developed physical dependence to oxycodone. Monitor patients closely at frequent intervals and consider increasing the opioid dosage if needed to maintain adequate analgesia or if symptoms of opioid withdrawal occur.

**Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants**

- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of OxyContin with benzodiazepines or CNS depressants (e.g., non-benzodiazepines sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
- If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

- Advise both patients and caregivers about the risks of respiratory depression and sedation when OxyContin is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs.
- The use of OxyContin in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated. OxyContin-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of OxyContin.

**Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients**

- Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients.
- Monitor such patients closely, particularly when initiating and titrating OxyContin and when OxyContin is given concomitantly with other drugs that depress respiration. Alternatively, consider the use of non-opioid analgesics in these patients.

**Adrenal Insufficiency**

- Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers.

**Severe Hypotension**

- OxyContin may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or after concurrent administration of certain CNS depressants drugs (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension after initiating or titrating the dosage of OxyContin. In patients with circulatory shock, OxyContin may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of OxyContin in patients with circulatory shock.

**Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness**

- In patients who may be susceptible to the intracranial effects of CO2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), OxyContin may reduce respiratory drive, and the resultant CO2 retention can further increase intracranial pressure. Monitor those patients for signs of sedation and respiratory depression, particularly when initiating therapy with OxyContin. Opioids may obscure the clinical course in a patient with a head injury. Avoid the use of OxyContin in patients with impaired consciousness or coma.

**Difficulty in Swallowing and Risk for Obstruction in Patients at Risk for a Small Gastrointestinal Lumen**

- There have been post-marketing reports of difficulty swallowing OxyContin tablets. These reports include choking, gagging, regurgitation, and tablets stuck in the throat. Instruct patients not to pre-soak, lick or otherwise wet OxyContin tablets prior to placing in the mouth, and to take one tablet at a time with enough water to ensure complete swallowing immediately after placing in the mouth.
- There have been rare post-marketing reports of cases of intestinal obstruction, and exacerbations of diverticulitis, some of which have required medical intervention to remove the tablet. Patients with underlying GI disorders such as esophageal cancer or colon cancer with a small gastrointestinal lumen are at greater risk of developing these complications. Consider use of an alternative analgesic in patients who have difficulty swallowing and patients at risk for underlying GI disorders resulting in a small gastrointestinal lumen.

**Risks of Use in Patients with Gastrointestinal Conditions**

- OxyContin is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus. The oxycodone in OxyContin may cause spasm of the sphincter of Oddi. Opioids may cause increases in the serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis.

**Increased Risk of Seizures in Patients with Seizure Disorders**

- The oxycodone in OxyContin may increase the frequency of seizures in patients with seizure disorders, and may increase the risk of seizures occurring in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during OxyContin therapy.

**Withdrawal**

- Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving a full opioid agonist analgesic, including OxyContin. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms. When discontinuing OxyContin, gradually taper the dosage. Do not abruptly discontinue OxyContin.

**Risks of Driving and Operating Machinery**

- OxyContin may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of OxyContin and know how they will react to the medication.

**Laboratory Monitoring**

- Not every urine drug test for "opioids" or "opiates" detects oxycodone reliably, especially those designed for in-office use. Further, many laboratories will report urine drug concentrations below a specified "cut-off" value as "negative." Therefore, if urine testing for oxycodone is considered in the clinical management of an individual patient, ensure that the sensitivity and specificity of the assay is appropriate, and consider the limitations of the testing used when interpreting results.

**ADVERSE REACTIONS**

- OxyContin may increase the risk of serious adverse reactions such as those observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, or shock.
- The most common adverse reactions (> 5%) reported by adult patients in clinical trials comparing OxyContin with placebo are constipation, nausea, somnolence, dizziness, pruritus, vomiting, headache, dry mouth, asthenia, and sweating.

**Please read Full Prescribing Information, including Boxed Warning.**