**Primlev 1143A00**

### Tablets, USP

**Mechanism of Action**

(*10 mg oxycodone hydrochloride is equivalent to 8.9637 mg oxycodone*)

White to off-white fine crystalline powder. The molecular formula for oxycodone hydrochloride is C$_{18}$H$_{21}$NO$_4$•HCl and the drug plays a role in the analgesic effects of this drug.

**Accidental Ingestion**

Primlev is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

**Drug Interactions**

The combination of oxycodone hydrochloride and acetaminophen has not been evaluated for mutagenicity.

Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.

### Absorption and Distribution

Oxycodone in Primlev is given to achieve absorption by the gastrointestinal tract. The clinical profile of the drug is not the same as other opioid analgesics.

**Overdose**

Furosemide, reducing fluid volume, may be given to patients with overdose in whom hypotensive or fluid volume-compromised conditions are present.

**DOSAGE AND ADMINISTRATION**

Oxycodone in Primlev is given to achieve absorption by the gastrointestinal tract. The clinical profile of the drug is not the same as other opioid analgesics.

### Contraindications

Primlev is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

**WARNINGS**

Due to additive pharmacologic effect, the concomitant use of benzodiazepines and other CNS depressants such as alcohol or other sedatives/hypnotics is not recommended. Primlev is given to achieve absorption by the gastrointestinal tract. The clinical profile of the drug is not the same as other opioid analgesics.

### PRECAUTIONS

Serum amylase levels may increase approximately 2-6 days after the use of Primlev, and persist for up to 5 days after discontinuation of Primlev. Psychiatric patients may have a significant increase in agitation and delirium and should be monitored for signs and symptoms of an opioid overdose.

### ADVERSE REACTIONS

### Instruct patients on...
**Teratogenic Effects**

Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An apparent increase in the incidence of neonatal respiratory depression in the newborn infant has been observed when a mother has been dependent on opioids. The effect of oxycodone on the human neonate is unknown.

**Animal and Prenatal Studies**

Published studies in rodents report that oral acetaminophen treatment of male animals at doses that are 1.2 times the human therapeutic dose did not produce evidence of fetal harm. It has been estimated that the potential for a drug to produce teratogenic effects in man is dependent on its effect on the animal fetal skeletal development. The highest dose of acetaminophen that produced skeletal variations in the fetal rat was 262 mg/kg/day. Because oxycodone is eliminated via the feces and not via the milk of nursing mice and rats, there was no opportunity to determine whether oxycodone could cause opiate withdrawal syndrome in the nursing neonate.

**Neonatal opioid withdrawal syndrome** presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, muscle floccaretion, yawning, vomiting, diarrhea, and hypothermia. Opioid withdrawal in the neonate may also be accompanied by increases in blood pressure and heart rate. The withdrawal syndrome can be prevented by gradual tapering of the opioid dosage in pregnant women treated with an opioid to relieve their pain.

**Hepatic Impairment**

Because oxycodone is extensively metabolized in the liver, its clearance may decrease in patients with hepatic impairment. Care should be exercised in dosing when the patient is hepatically impaired.

**Renal Impairment**

Dose adjustment is recommended for patients with severe renal impairment. In addition, care should be exercised in patients with severe renal impairment when titrating the dose or increasing the frequency of administration. Plasma concentrations of oxycodone in patients with severe renal impairment may be increased and the dosing interval should be increased to achieve an appropriate balance between management of pain and opioid-related adverse reactions.

**Elderly**

Elderly patients (aged 65 years or older) may have increased sensitivity to acetaminophen and oxycodone, and should be monitored closely for adverse effects such as respiratory depression, sedation, and hypotension [see Clinical Pharmacology]. The use of all opioids, including acetaminophen and oxycodone, in the elderly population is supported by a clinical study of postoperative pain control in elderly patients 70 years and older. Pain control was better in elderly patients than in younger patients treated with acetaminophen. Elderly patients 70 years and older may require lower doses of acetaminophen and oxycodone because of increased sensitivity to adverse effects such as respiratory depression, sedation, and hypotension. Care should be exercised in dosing when the patient is elderly.

**Nursing Mothers**

Oxycodone is excreted in breast milk in low concentrations, and there have not been reports of adverse effects in nursing infants. In case of maternal overdose, the possibility of an opioid withdrawal syndrome in the infant should be considered. Use of opioids to maintain a neonate who is physically dependent on a synthetic opioid such as oxycodone at birth should be considered. If a woman is dependent on an opioid drug, she should be managed according to the principles of medical management of opioid dependence and the principles of neonatal opioid withdrawal syndrome [see Clinical Pharmacology]. It is not known whether oxycodone is excreted in breast milk following administration of oral or rectal oxycodone. The risk of opioid withdrawal syndrome in the nursing infant should be carefully considered when a woman who is receiving an opioid drug is breast feeding.

**Acetaminophen**

Acetaminophen is not recommended for use in pregnant women during or immediately prior to labor, when the use of an opioid analgesic is not indicated or when the risk outweighs the potential benefits. Upon delivery of the neonate, injections of a drug to act primarily on the central nervous system or to produce local muscle relaxation are not indicated, asphyxia is rarely due to a lack of respiratory stimulation at birth. However, because of the risk of neonatal withdrawal syndrome, consider the use of acetaminophen to control opioid withdrawal syndrome in the neonate when the risk of the withdrawal syndrome outweighs the potential benefits of acetaminophen. Acetaminophen should not be used for postoperative pain in the immediate postoperative period, as the administration of opioid analgesics or other means of pain control is recommended. Acetaminophen should not be used to treat the fever associated with the common cold or flu. A dose of acetaminophen up to 40 mg/kg/day for a maximum of 5 days is recommended in the treatment of fever due to common viral infections such as the common cold. Acetaminophen should not be used when the underlying cause of fever is not known or cannot be otherwise treated (e.g., in patients with a suspected infectious etiology). Acetaminophen, like other analgesics, should not be used to treat fever in neonates younger than 2 weeks of age. The use of acetaminophen for the treatment of fever in these patients has not been studied. The safety and efficacy of acetaminophen for the treatment of fever in neonates younger than 2 weeks of age are unknown.

**Opioids**

**Drug-seeking** behavior is very common in persons with substance use disorders. Drug-seeking tactics include doctor shopping and the use of multiple prescription sites to obtain opioids, use of fraudulent or falsified identification, and the use of social media and electronic means to obtain opioids. Drug-seeking tactics also include the use of coercion, force, or the threat of violence to obtain opioids. Drug-seeking behavior may be associated with the use of other substances, including alcohol and other psychoactive substances. Drug-seeking behavior is a manifestation of substance use disorder and implies the need for a comprehensive treatment program. Drug-seeking behavior may be severe and can result in serious harm to patients and others.

**Adverse Reactions**

**Central Nervous System**

- Dizziness, fall, impaired concentration, increased sedation, seizures,
- Tiredness, sleepiness, or somnolence

**Respiratory System**

- Respiratory depression, bradypnea

**Cardiovascular System**

- Nausea, vomiting, diarrhea

**Gastrointestinal System**

- Dry mouth, flatulence, gastro-intestinal disorder

**Hepatic System**

- Hepatitis, jaundice

**Renal System**

- Enuresis, interstitial nephritis, papillary necrosis, proteinuria

**Endocrine System**

- Diabetes mellitus, hypoglycemia

**Skin and Appendage System**

- Rash, urticaria

**Other**

- Altered mental status, allergic reactions

**Drug Interactions**

**Acetaminophen**

- An increase in plasma levels of acetaminophen with concomitant administration of drugs that are known to cause hepatitis (e.g., isoniazid, ethambutol, or isoniazid plus rifampin) can result in the enhancement of acetaminophen toxicity. Concomitant administration of acetaminophen with other hepatotoxic agents can also result in the enhancement of acetaminophen toxicity. Acetaminophen toxicity may be enhanced by concomitant administration with drugs that induce or inhibit CYP2E1, an enzyme that catalyzes the initial reaction in the metabolism of acetaminophen.

**Oxycodone**

- Concomitant use of opioids with other sedative-hypnotics can result in additive effects, including respiratory depression (see Precautions).

**Opiate withdrawal** syndrome occurs with the abrupt discontinuation of opioids in patients physically dependent on opioids. If oxycodone is being withdrawn, a gradual taper is recommended to allow the body to become acclimated to the lack of the opioid. An opioid taper schedule should be employed for patients withdrawing from opioids, as the degree of withdrawal symptoms varies greatly between patients. It is important to monitor patients closely during the tapering process. Administration of a tapering dose of oxycodone as a single daily dose according to the taper schedule may be given for the shortest time needed.

**Precautions**

**Neonatal opioid withdrawal syndrome** presents as irritability, hyperactivity, and abnormal sleep pattern, high pitched cry, tremor, muscle floccaretion, yawning, vomiting, diarrhea, and hypothermia. It is important to carefully monitor the mother for signs of opioid withdrawal as signs of withdrawal in the neonate may not always be present.

**Drug-Induced Liver Injury Network** suggests that the use of acetaminophen in combination with other drugs that are known to cause liver injury (e.g., isoniazid, ethambutol, or isoniazid plus rifampin) can result in the enhancement of acetaminophen toxicity. Acetaminophen toxicity may be enhanced by concomitant administration with drugs that induce or inhibit CYP2E1, an enzyme that catalyzes the initial reaction in the metabolism of acetaminophen.

**Interactions with Alcohol**

- Alcohol increases the CNS depressant effects of opioids and increases the risk of respiratory depression and opioid overdose. Patients who use alcohol should be advised to discontinue alcohol use when opioid therapy is initiated and for the duration of therapy. Patients should be advised to record all alcohol consumption or drug use in a journal to facilitate monitoring of compliance with the dosage regimen.

**Contraindications**

- Drug-seeking behavior is very common in persons with substance use disorders. Drug-seeking tactics include doctor shopping and the use of multiple prescription sites to obtain opioids, use of fraudulent or falsified identification, and the use of social media and electronic means to obtain opioids. Drug-seeking tactics also include the use of coercion, force, or the threat of violence to obtain opioids. Drug-seeking behavior may be severe and can result in serious harm to patients and others.

**Adverse Reactions**

**Central Nervous System**

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- Diabetes mellitus, hypoglycemia

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- Rash, urticaria

**Important Information**