

**ROXICODONE®** (II)  
(OXYCODONE HYDROCHLORIDE)  
TABLETS USP, ORAL SOLUTION USP,  
AND LIQUID CONCENTRATE

R<sub>x</sub> only

**DESCRIPTION**

Each tablet contains:

Oxycodone Hydrochloride 5 mg

Each 5 mL Oral Solution contains:

Oxycodone Hydrochloride 5 mg

Each mL Liquid Concentrate contains:

Oxycodone Hydrochloride 20 mg

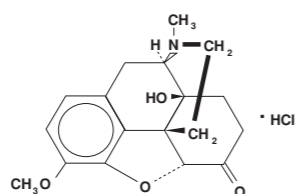
*Inactive Ingredients:*

The tablets contain microcrystalline cellulose and stearic acid.

The oral solution contains alcohol, FD&C Red No. 40, flavoring, glycol, sorbitol, water, and other ingredients.

The liquid concentrate contains citric acid, sodium benzoate, and water.

Oxycodone is 14-hydroxydihydrocodeinone, a white odorless crystalline powder which is derived from the opium alkaloid, thebaine, and may be represented by the following structural formula:



**ACTIONS**

The analgesic ingredient, oxycodone, is a semi-synthetic narcotic with multiple actions qualitatively similar to those of morphine; the most prominent of these involve the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value of oxycodone are analgesia and sedation. Oxycodone is similar to codeine and methadone in that it retains at least one half of its analgesic activity when administered orally.

**INDICATIONS**

For the relief of moderate to moderately severe pain.

**CONTRAINDICATIONS**

ROXICODONE® is contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment) and patients with acute or severe bronchial asthma or hypercarbia. ROXICODONE® is contraindicated in any patient who has or is suspected of having paralytic ileus.

**WARNINGS**

**Respiratory Depression:** Respiratory depression is the chief hazard from all opioid agonist preparations. Respiratory depression occurs most frequently in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

ROXICODONE® should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having

substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression. In such patients, even usual therapeutic doses of ROXICODONE® may decrease respiratory drive to the point of apnea. In these patients alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose.

**Hypotensive Effect:** ROXICODONE®, like all opioid analgesics, may cause severe hypotension in an individual whose ability to maintain blood pressure has been compromised by a depleted blood volume, or after concurrent administration with drugs such as phenothiazines or other agents which compromise vasomotor tone. ROXICODONE® may produce orthostatic hypotension in ambulatory patients. ROXICODONE®, like all opioid analgesics, should be administered with caution to patients in circulatory shock, since vasodilatation produced by the drug may further reduce cardiac output and blood pressure.

**Head Injury and Increased Intracranial Pressure:**

The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

**Drug Dependence:** Oxycodone can produce drug dependence of the morphine type, and therefore, has the potential for being abused. Psychological dependence, physical dependence and tolerance may develop upon repeated administration of this drug, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, this drug is subject to the Federal Controlled Substances Act.

**PRECAUTIONS**

**General:** ROXICODONE® is intended for use in patients who require oral pain therapy with an opioid agonist. As with any opioid analgesic, it is critical to adjust the dosing regimen individually for each patient (see DOSAGE AND ADMINISTRATION).

Use of ROXICODONE® is associated with increased potential risks and should be used only with caution in the following conditions: acute alcoholism; adrenocortical insufficiency (e.g., Addison's disease); convulsive disorders; CNS depression or coma; delirium tremens; debilitated patients; kyphoscoliosis associated with respiratory depression; myxedema or hypothyroidism; prostatic hypertrophy or urethral stricture; severe impairment of hepatic, pulmonary or renal function; and toxic psychosis.

The administration of ROXICODONE® like all opioid analgesics, may obscure the diagnosis or clinical course in patients with acute abdominal conditions. Oxycodone may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings.

**Tolerance and Physical Dependence:** Physical dependence and tolerance are not unusual during chronic opioid therapy. Significant tolerance should not occur in most patients treated with the lowest doses of oxycodone. It should be expected, however, that a fraction of patients will develop some degree of tolerance and require progressively higher dosages of ROXICODONE® to maintain pain control during chronic treatment. The dosage should be selected according to the patient's individual analgesic response and ability to tolerate side effects. Tolerance to the analgesic effects of opioids is usually paralleled by tolerance to side effects except for constipation.

Physical dependence results in withdrawal symptoms in patients who abruptly discontinue the drug or may be precipitated through the administration of drugs with opioid antagonist activity. If ROXICODONE® is abruptly discontinued in a physically dependent patient, an abstinence syndrome may occur. If signs and symptoms of withdrawal occur, patients should be treated by reinstitution of opioid therapy followed by gradual tapered dose reduction of ROXICODONE® combined with symptomatic support.

**Use In Pancreatic/Biliary Tract Disease:**

ROXICODONE® may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis. Opioids like ROXICODONE® may cause increases in the serum amylase level.

**Drug interactions:** Oxycodone is metabolized in part to oxymorphone via the cytochrome p450 isoenzyme CYP2D6. While this pathway may be blocked by a variety of drugs (e.g., certain cardiovascular drugs and antidepressants), such blockade has not yet been shown to be of clinical significance with this agent. However, clinicians should be aware of this possible interaction.

**Neuromuscular Blocking Agents:** Oxycodone, as well as other opioid analgesics, may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.

**CNS Depressants:** Patients receiving narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with ROXICODONE® may exhibit an additive CNS depression. Interactive effects resulting in respiratory depression, hypotension, profound sedation, or coma may result if these drugs are taken in combination with the usual dosage of ROXICODONE®. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

**Mixed Agonist/Antagonist Opioid Analgesics:** Agonist/antagonist analgesics (i.e., pentazocine, nalbuphine, butorphanol and buprenorphine) should be administered with caution to patients who have received or are receiving a course of therapy with a pure opioid agonist analgesic such as ROXICODONE®. In this situation, mixed agonist/antagonist analgesics may reduce the analgesic effect of ROXICODONE® and/or may precipitate withdrawal symptoms in these patients.

**Monoamine Oxidase Inhibitors (MAOIs):** MAOIs have been reported to intensify the effects of at least one opioid drug causing anxiety, confusion and significant depression of respiration or coma. The use of ROXICODONE® is not recommended for patients taking MAOIs or within 14 days of stopping such treatment.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Long-term studies have not been performed in animals to evaluate the carcinogenic potential of ROXICODONE® or oxycodone. The possible effects on male or female fertility have not been studied in animals.

Oxycodone hydrochloride was genotoxic in an *in vitro* mouse lymphoma assay in the presence of metabolic activation. There was no evidence of genotoxic potential in an *in vitro* bacterial reverse mutation assay (*Salmonella typhimurium* and *Escherichia coli*) or in an assay for chromosomal aberrations (*in vivo* mouse bone marrow micronucleus assay.)

**Pregnancy:Category B:** There are no adequate and well controlled studies of oxycodone in pregnant women. ROXICODONE® should be used during pregnancy only if potential benefit justifies the potential risk to the fetus. Neonates whose mothers have taken oxycodone chronically may exhibit respiratory depression and/or withdrawal symptoms, either at birth and/or in the nursery.

**Labor and Delivery:** ROXICODONE® is not recom-

ended for use in women during or immediately prior to labor. Occasionally, opioid analgesics may prolong labor through actions which temporarily reduce the strength, duration and frequency of uterine contractions. Neonates, whose mothers received opioid analgesics during labor, should be observed closely for signs of respiratory depression. A specific narcotic antagonist, naloxone, should be available for reversal of narcotic-induced respiratory depression in the neonate.

**Nursing Mothers:** Oxycodone has been detected in breast milk. Withdrawal symptoms can occur in breast-feeding infants when maternal administration of an opioid analgesic is stopped. Ordinarily, nursing should not be undertaken while a patient is receiving ROXICODONE® since oxycodone may be excreted in milk.

**Pediatric Use:** The safety and efficacy of oxycodone in pediatric patients have not been evaluated.

**Geriatric Use:** Of the total number of subjects in clinical studies of ROXICODONE®, 20.8% (112/538) were 65 and over, while 7.2% (39/538) were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

**Hepatic Impairment:** Since oxycodone is extensively metabolized, its clearance may decrease in hepatic failure patients. Dose initiation in patients with hepatic impairment should follow a conservative approach. Dosages should be adjusted according to the clinical situation.

**Renal Impairment:** Published data reported that elimination of oxycodone was impaired in end-stage renal failure. Mean elimination half-life was prolonged in uremic patients due to increased volume of distribution and reduced clearance. Dose initiation should follow a conservative approach. Dosages should be adjusted according to the clinical situation.

**Ambulatory Patients:** ROXICODONE® may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using this drug should be cautioned accordingly.

**ADVERSE REACTIONS**

Serious adverse reactions that may be associated with ROXICODONE® therapy in clinical use are those observed with other opioid analgesics and include: respiratory depression, respiratory arrest, circulatory depression, cardiac arrest, hypotension, and/or shock (see OVERDOSE, WARNINGS).

The most frequently observed adverse reactions include lightheadedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

**DRUG ABUSE AND DEPENDENCE**

**Controlled Substance**  
**Roxicodone contains oxycodone, a mu-agonist opioid of the morphine type and is a Schedule II controlled substance. Roxicodone, like other opioids used in analgesia, can be abused and is subject to criminal diversion.**

**Abuse**  
Drug addiction is characterized by compulsive use, use for non-medical purposes, and continued use despite harm or risk of harm. Drug addiction is a treatable dis-



ease, utilizing a multi-disciplinary approach, but relapse is common.

“Drug-seeking” behavior is very common in addicts and drug abusers. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing or referral, repeated “loss” of prescriptions, tampering with prescriptions and reluctance to provide prior medical records or contact information for other treating physician(s). “Doctor-shopping” to obtain additional prescriptions is common among drug abusers and people suffering from untreated addiction.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence. In addition, abuse of opioids can occur in the absence of true addiction and is characterized by misuse for nonmedical purposes, often in combination with other psychoactive substances. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests is strongly advised.

**Roxicodone is intended for oral use only. Abuse of Roxicodone poses a risk of overdose and death. The risk is increased with concurrent abuse of alcohol and other substances. Parenteral drug abuse is commonly associated with transmission of infectious diseases such as hepatitis and HIV.**

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

**Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal symptoms.**

#### Dependence

Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist. Physical dependence and tolerance are not unusual during chronic opioid therapy.

The opioid abstinence or withdrawal syndrome is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other symptoms also may develop, including irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate. In general, opioids should not be abruptly discontinued.

#### MANAGEMENT OF OVERDOSAGE

Signs and Symptoms: Serious overdose of oxycodone hydrochloride is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdose, apnea, circulatory collapse, cardiac arrest and death may occur.

Treatment: Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against respiratory depression which may result from overdose or unusual sensitivity to narcotics, including oxycodone. Therefore, an appropriate dose of naloxone (usual initial adult dose: 0.4 mg) should be administered, preferably by the intravenous route, simultaneously with efforts at

respiratory resuscitation. Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration. An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated. Gastric emptying may be useful in removing unabsorbed drug.

#### DOSAGE AND ADMINISTRATION

The usual adult oral dose is 10 to 30 mg every 4 hours as needed for pain or as directed by physician. The dose must be individually adjusted according to severity of pain, patient response and patient size. More severe pain may require 30 mg or more every 4 hours. If the pain increases in severity, analgesia is not adequate or tolerance occurs, a gradual increase in dosage may be required.

For control of severe, chronic pain in patients with certain terminal diseases, this drug should be administered on a regularly scheduled basis, every 4 hours, at the lowest dosage level that will achieve adequate analgesia.

#### HOW SUPPLIED

##### 5 mg white scored tablets (Identified 54 582).

NDC 66479-580-25: Unit dose, 25 tablets per card, (reverse numbered), 4 cards per shipper.

NDC 66479-580-10: Bottles of 100 tablets.

##### 5 mg per 5 mL Oral Solution

NDC 66479-583-05: Unit dose patient cup filled to deliver 5 mL (5 mg Oxycodone Hydrochloride), ten 5 mL patient cups per shelf pack, four shelf packs per shipper.

NDC 66479-583-50: Bottles of 500 mL.

##### 20 mg per mL Liquid Concentrate

NDC 66479-584-03: Bottles of 30 mL with calibrated dropper [graduations of 0.25 mL (5 mg), 0.5 mL (10 mg), 0.75 mL (15mg), and 1 mL (20 mg) on the dropper].

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [See USP Controlled Room Temperature].

#### DEA Order Form Required.

ROXICODONE is a registered trademark of Xanodyne Pharmaceuticals, Inc.

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Marketed by:



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To request medical information or to report suspected adverse events, contact Xanodyne Medical Affairs at 1-877-773-7793.

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