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

Risk of Medication Errors
Ensure accuracy when prescribing, dispensing, and administering oxycodone hydrochloride and acetaminophen oral solution. Dosing errors due to confusion between mg and mL, and other oxycodone hydrochloride and acetaminophen solutions of different concentrations can result in accidental overdose and death [see WARNINGS, DOSAGE AND ADMINISTRATION].

Addiction, Abuse, and Misuse
Oxycodone hydrochloride and acetaminophen oral solution 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 oxycodone hydrochloride and acetaminophen oral solution, and monitor all patients regularly for the development of these behaviors and conditions [see WARNINGS].

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 REMS for these products [see WARNINGS]. 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
- **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.**

Life-Threatening Respiratory Depression
Serious, life-threatening, or fatal respiratory depression may occur with use of oxycodone hydrochloride and acetaminophen oral solution. Monitor for respiratory depression, especially during initiation of oxycodone hydrochloride and acetaminophen oral solution or following a dose increase [see WARNINGS].

Accidental Ingestion
Accidental ingestion of oxycodone hydrochloride and acetaminophen oral solution, especially by children, can result in a fatal overdose of oxycodone hydrochloride and acetaminophen oral solution [see WARNINGS].

Neonatal Opioid Withdrawal Syndrome
Prolonged use of oxycodone hydrochloride and acetaminophen oral solution 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].

Cytochrome P450 3A4 Interaction
The concomitant use of oxycodone hydrochloride and acetaminophen oral solution with all cytochrome P450 3A4 inhibitors may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse reactions 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 oxycodone hydrochloride and acetaminophen oral solution and any CYP3A4 inhibitor or inducer [see CLINICAL PHARMACOLOGY, WARNINGS, PRECAUTIONS; Drug Interactions].

Hepatotoxicity
Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 mg per day, and often involve more than one acetaminophen-containing product.

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, PRECAUTIONS; Drug Interactions].
- **Reserve concomitant prescribing of oxycodone hydrochloride and acetaminophen oral solution 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.**

DESCRIPTION

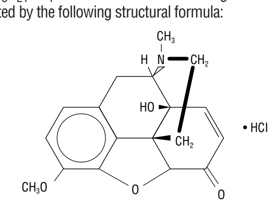
Oxycodone hydrochloride and acetaminophen are available in liquid form for oral administration.

Each 5 mL of oral solution for oral administration contains:

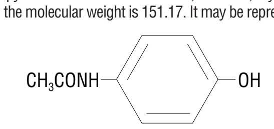
Oxycodone hydrochloride USP... 10 mg*
(*10 mg oxycodone hydrochloride is equivalent to 8.9637 mg oxycodone)
Acetaminophen USP.. 300 mg

Inactive Ingredients
The solution contains: anhydrous citric acid, edetate disodium, fructose, glycerin, polyethylene glycol, potassium sorbate, propylene glycol, purified water, saccharin sodium with FD&C Red #40 as coloring and tropical fruit punch flavoring.

Oxycodone hydrochloride and acetaminophen oral solution contains oxycodone, 14-hydroxydihydrocodeinone, a semisynthetic opioid analgesic which occurs as a white to off-white fine crystalline powder. The molecular formula for oxycodone hydrochloride is $C_{18}H_{21}NO_4 \cdot HCl$ and the molecular weight is 351.82. It is derived from the opium alkaloid, thebaine, and may be represented by the following structural formula:



Oxycodone hydrochloride and acetaminophen oral solution contains acetaminophen, 4'-hydroxyacetanilide, is a non-opiate, non-salicylate analgesic and antipyretic which occurs as a white, odorless, crystalline powder. The molecular formula for acetaminophen is $C_8H_9NO_2$ and the molecular weight is 151.17. It may be represented by the following structural formula:



CLINICAL PHARMACOLOGY

Mechanism of Action
Oxycodone is a full opioid agonist with relative selectivity for the mu-opioid receptor, although it can interact with other opioid receptors at higher doses. The principal therapeutic action of oxycodone is analgesia. Like all full opioid agonists, there is no ceiling effect for analgesia with oxycodone. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug.

The precise mechanism of the analgesic properties of acetaminophen is not established but is thought to involve central actions.

Pharmacodynamics
Effects on the Central Nervous System
Oxycodone produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves a reduction in the responsiveness of the brain stem respiratory centers to both increases in carbon dioxide tension and electrical stimulation.

Oxycodone causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of hemorrhagic or ischemic origins may produce similar findings). Marked mydriasis rather than miosis may be seen due to hypoxia in overdose situations.

Therapeutic doses of acetaminophen have negligible effects on the cardiovascular or respiratory systems; however, toxic doses may cause circulatory failure and rapid, shallow breathing.

Effects on the Gastrointestinal Tract and Other Smooth Muscle
Oxycodone causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone may be increased to the point of spasm, resulting in constipation. Other opioid-induced effects may include a reduction in biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

Effects on the Cardiovascular System
Oxycodone produces peripheral vasodilation which may result in orthostatic hypotension or syncope. Manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes, sweating, and/or orthostatic hypotension.

Effects on the Endocrine System
Opioids inhibit the secretion of adrenocorticotropic hormone (ACTH), cortisol, and luteinizing hormone (LH) in humans [see **ADVERSE REACTIONS**]. They also stimulate prolactin, growth hormone (GH) secretion, and pancreatic secretion of insulin and glucagon.

Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as symptoms as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date [see **ADVERSE REACTIONS**].

Effects on the Immune System
Opioids have been shown to have a variety of effects on components of the immune system. The clinical significance of these findings is unknown. Overall, the effects of opioids appear to be modestly immunosuppressive.

Concentration–Efficacy Relationships
The minimum effective analgesic concentration will vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. The minimum effective analgesic concentration of oxycodone for any individual patient may increase over time due to an increase in pain, the development of a new pain syndrome, and/or the development of analgesic tolerance [see **DOSAGE AND ADMINISTRATION**].

Concentration–Adverse Reaction Relationships
There is a relationship between increasing oxycodone plasma concentration and increasing frequency of dose-related opioid adverse reactions such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation may be altered by the development of tolerance to opioid-related adverse reactions [see **DOSAGE AND ADMINISTRATION**].

Pharmacokinetics
Absorption and Distribution
The mean absolute oral bioavailability of oxycodone in cancer patients was reported to be about 87%. Oxycodone has been shown to be 45% bound to human plasma proteins *in vitro*. The volume of distribution after intravenous administration is 211.9 ±186.6 L.

Absorption of acetaminophen is rapid and almost complete from the GI tract after oral administration. With overdosage, absorption is complete in 4 hours. Acetaminophen is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; only 20% to 50% may be bound at the concentrations encountered during acute intoxication.

Metabolism and Elimination
Oxycodone
In humans, oxycodone is extensively metabolized to noroxycodone by means of CYP3A-mediated N-demethylation, oxymorphone by means of CYP2D6-mediated O-demethylation, and their glucuronides [see **PRECAUTIONS; Drug Interactions**].

Acetaminophen
Acetaminophen is rapidly absorbed from the gastrointestinal tract and is distributed throughout most body tissues. A small fraction (10-25%) of acetaminophen is bound to plasma proteins. The plasma half-life is 1.25 to 3 hours, but may be increased by liver damage and following overdosage. Elimination of acetaminophen is principally by liver metabolism (conjugation) and subsequent renal excretion of metabolites. Acetaminophen is primarily metabolized in the liver by first-order kinetics and involves three principal separate pathways: conjugation with glucuronide; conjugation with sulfate; and oxidation via the cytochrome, P450-dependent, mixed-function oxidase enzyme pathway to form a reactive intermediate metabolite, which conjugates with glutathione and is then further metabolized to form cysteine and mercapturic acid conjugates. The principal cytochrome P450 isoenzyme involved appears to be CYP2E1, with CYP1A2 and CYP3A4 as additional pathways. Approximately 85% of an oral dose appears in the urine within 24 hours of administration, most as the glucuronide conjugate, with small amounts of other conjugates and unchanged drug [see **OVERDOSAGE**] for toxicity information.

INDICATIONS AND USAGE

Oxycodone hydrochloride and acetaminophen oral solution is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations of Use
Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses [see **WARNINGS**], reserve oxycodone hydrochloride and acetaminophen oral solution for use in patients for whom alternative treatment options [e.g., non-opioid analgesics]
- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

CONTRAINDICATIONS

Oxycodone hydrochloride and acetaminophen oral solution is contraindicated in patients with:
- Significant respiratory depression [see **WARNINGS**]
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment [see **WARNINGS**]
- Known or suspected gastrointestinal obstruction, including paralytic ileus [see **WARNINGS**]
- Hypersensitivity to oxycodone, acetaminophen, or any other component of the product (e.g., anaphylaxis) [see **WARNINGS, ADVERSE REACTIONS**]

WARNINGS

Risk of Accidental Overdose and Death due to Medication Errors
Dosing errors can result in accidental overdose and death. Avoid dosing errors that may result from confusion between mg and mL and confusion with oxycodone hydrochloride and acetaminophen oral solutions of different concentrations, when prescribing, dispensing, and administering oxycodone hydrochloride and acetaminophen oral solution. Ensure that the dose is communicated clearly and dispensed accurately. Always use a calibrated measuring device when administering oxycodone hydrochloride and acetaminophen oral solution to ensure the dose is measured and administered accurately.

Addiction, Abuse, and Misuse
Oxycodone hydrochloride and acetaminophen oral solution contains oxycodone, a Schedule II controlled substance. As an opioid, oxycodone hydrochloride and acetaminophen oral solution exposes users to the risks of addiction, abuse, and misuse [see **DRUG ABUSE AND DEPENDENCE**].

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed oxycodone hydrochloride and acetaminophen oral solution. Addiction can occur at recommended dosages and if the drug is misused or abused.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing oxycodone hydrochloride and acetaminophen oral solution, and monitor all patients receiving oxycodone hydrochloride and acetaminophen oral solution 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 oxycodone hydrochloride and acetaminophen oral solution, but use in such patients necessitates intensive counseling about the risks and proper use of oxycodone hydrochloride and acetaminophen oral solution along with intensive monitoring for signs of addiction, abuse, and misuse.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing oxycodone hydrochloride and acetaminophen oral solution. 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 [see **PRECAUTIONS; Information for Patients/Caregivers**]. Contact local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

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 offered by an accredited provider of continuing education (CE) or another education program that includes all the elements of the FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain.
- Discuss the safe use, serious risks, and proper storage and disposal of opioid analgesics with patients and/or their caregivers every time these medicines are prescribed. The Patient Counseling Guide (PCG) can be obtained at this link: www.fda.gov/OpioidAnalgesicREMSPCG.
- Emphasize to patients and their caregivers the importance of reading the Medication Guide that they will receive from their pharmacist every time an opioid analgesic is dispensed to them.
- Consider using other tools to improve patient, household, and community safety, such as patient-prescriber agreements that reinforce patient-prescriber responsibilities. To obtain further information on the opioid analgesic REMS and for a list of accredited REMS CME/CE, call 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. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status [see **OVERDOSAGE**]. Carbon dioxide (CO_2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of oxycodone hydrochloride and acetaminophen oral solution, the risk is greatest during the initiation of therapy or following a dosage increase. Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy with and following dosage increases of oxycodone hydrochloride and acetaminophen oral solution.

To reduce the risk of respiratory depression, proper dosing and titration of oxycodone hydrochloride and acetaminophen oral solution are essential [see **DOSAGE AND ADMINISTRATION**]. Overestimating the oxycodone hydrochloride and acetaminophen oral solution dosage when converting patients from another opioid product can result in a fatal overdose with the first dose.

Accidental ingestion of oxycodone hydrochloride and acetaminophen oral solution, especially by children, can result in respiratory depression and death due to an overdose of oxycodone hydrochloride and acetaminophen oral solution.

Opioids can cause sleep-related breathing disorders including central sleep apnea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper [see **DOSAGE AND ADMINISTRATION**].

Neonatal Opioid Withdrawal Syndrome
Prolonged use of oxycodone hydrochloride and acetaminophen oral solution 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 [see **PRECAUTIONS; Information for Patients/Caregivers, Pregnancy**].

Risks of Concomitant Use or Discontinuation of Cytochrome P450 3A4 Inhibitors and Inducers
Concomitant use of oxycodone hydrochloride and acetaminophen oral solution with a CYP3A4 inhibitor, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir), may increase plasma concentrations of oxycodone hydrochloride and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression [see **WARNINGS**], particularly when an inhibitor is added after a stable dose of oxycodone hydrochloride and acetaminophen oral solution is achieved. Similarly, discontinuation of a CYP3A4 inducer, such as rifampin, carbamazepine, and phenytoin, in oxycodone hydrochloride and acetaminophen oral solution-treated patients may increase oxycodone plasma concentrations and prolong opioid adverse reactions. When using oxycodone hydrochloride and acetaminophen oral solution with CYP3A4 inhibitors or discontinuing CYP3A4 inducers in oxycodone hydrochloride and acetaminophen oral solution-treated patients, monitor patients closely at frequent intervals and consider dosage reduction of oxycodone hydrochloride and acetaminophen oral solution until stable drug effects are achieved [see **PRECAUTIONS; Drug Interactions**].

Concomitant use of oxycodone hydrochloride and acetaminophen oral solution with CYP3A4 inducers or discontinuation of a CYP3A4 inhibitor could decrease oxycodone hydrochloride plasma concentrations, decrease opioid efficacy or, possibly, lead to a withdrawal syndrome in a patient who had developed physical dependence to oxycodone hydrochloride. When using oxycodone hydrochloride and acetaminophen oral solution with CYP3A4 inducers or discontinuing CYP3A4 inhibitors, 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 [see **PRECAUTIONS; Drug Interactions**].

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants
Profound sedation, respiratory depression, coma, and death may result from the concomitant use of oxycodone hydrochloride and acetaminophen oral solution with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine 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.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics [see **PRECAUTIONS; Drug Interactions**].

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 oxycodone hydrochloride and acetaminophen oral solution 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.

Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients
The use of oxycodone hydrochloride and acetaminophen oral solution in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: Oxycodone hydrochloride and acetaminophen oral solution-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 oxycodone hydrochloride and acetaminophen oral solution [see **WARNINGS; Life Threatening Respiratory Depression**].

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 [see **WARNINGS; Life Threatening Respiratory Depression**].

Monitor such patients closely, particularly when initiating and titrating oxycodone hydrochloride and acetaminophen oral solution and when oxycodone hydrochloride and acetaminophen oral solution is given concomitantly with other drugs that depress respiration [see **WARNINGS; Life Threatening Respiratory Depression**]. 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. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. 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. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

Severe Hypotension
Oxycodone hydrochloride and acetaminophen oral solution may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics) [see **PRECAUTIONS; Drug Interactions**]. Monitor these patients for signs of hypotension after initiating or titrating the dosage of oxycodone hydrochloride and acetaminophen oral solution. In patients with circulatory shock oxycodone hydrochloride and acetaminophen oral solution may cause vasodilatation that can further reduce cardiac output and blood pressure. Avoid the use of oxycodone hydrochloride and acetaminophen oral solution with circulatory shock.

Hepatotoxicity
Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product. The excessive intake of acetaminophen may be intentional to cause self-harm or unintentional as patients attempt to obtain more pain relief or unknowingly take other acetaminophen-containing products.

The risk of acute liver failure is higher in individuals with underlying liver disease and in individuals who ingest alcohol while taking acetaminophen.

Instruct patients to look for acetaminophen or APAP on package labels and not to use more than one product that contains acetaminophen. Instruct patients to seek medical attention immediately upon ingestion of more than 4000 milligrams of acetaminophen per day, even if they feel well.

Serious Skin Reactions
Rarely, acetaminophen may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs of serious skin reactions, and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Hypersensitivity/Anaphylaxis
There have been post-marketing reports of hypersensitivity and anaphylaxis associated with use of acetaminophen. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, pruritus, and vomiting. There were infrequent reports of life-threatening anaphylaxis requiring emergency medical attention. Instruct patients to discontinue oxycodone hydrochloride and acetaminophen oral solution immediately and seek medical care if they experience these symptoms. Do not prescribe oxycodone hydrochloride and acetaminophen oral solution for patients with acetaminophen allergy [see **PRECAUTIONS; Information for Patients/Caregivers**].

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 CO_2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), oxycodone hydrochloride and acetaminophen oral solution may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with oxycodone hydrochloride and acetaminophen oral solution.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of oxycodone hydrochloride and acetaminophen oral solution in patients with impaired consciousness or coma.

Risks of Use in Patients with Gastrointestinal Conditions
Oxycodone hydrochloride and acetaminophen oral solution is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

The administration of oxycodone hydrochloride and acetaminophen oral solution, or other opioids may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

The oxycodone in oxycodone hydrochloride and acetaminophen oral solution may cause spasm of the sphincter of Oddi. Opioids may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

Increased Risk of Seizures in Patients with Seizure Disorders
The oxycodone in oxycodone hydrochloride and acetaminophen oral solution 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 oxycodone hydrochloride and acetaminophen oral solution therapy.

Withdrawal
Do not abruptly discontinue oxycodone hydrochloride and acetaminophen oral solution in a patient physically dependent on opioids. When discontinuing oxycodone hydrochloride and acetaminophen oral solution in a physically dependent patient, gradually taper the dosage. Rapid tapering of oxycodone hydrochloride and acetaminophen oral solution in a patient physically dependent on opioids may lead to a withdrawal syndrome and return of pain [see **DOSAGE AND ADMINISTRATION, DRUG ABUSE AND DEPENDENCE**].

Additionally, 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 oxycodone hydrochloride and acetaminophen oral solution. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or precipitate withdrawal symptoms [see **PRECAUTIONS; Drug Interactions**].

PRECAUTIONS

Risks of Driving and Operating Machinery
Oxycodone hydrochloride and acetaminophen oral solution 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 oxycodone hydrochloride and acetaminophen oral solution and know how they will react to the medication [see **PRECAUTIONS; Information for Patients/Caregivers**].

Information for Patients/Caregivers
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Storage and Disposal
Because of the risks associated with accidental ingestion, misuse, and abuse, advise patients to store oxycodone hydrochloride and acetaminophen oral solution securely, out of sight and reach of children, and in a location not accessible by others, including visitors to the home [see **WARNINGS, DRUG ABUSE AND DEPENDENCE**]. Inform patients that leaving oxycodone hydrochloride and acetaminophen oral solution unsecured can pose a deadly risk to others in the home.

Advise patients and caregivers that when medicines are no longer needed, they should be disposed of promptly. Expired, unwanted, or unused oxycodone hydrochloride and acetaminophen oral solution should be disposed of by flushing the unused medication down the toilet if a drug take-back option is not readily available. Inform patients that they can visit www.fda.gov/drugdisposal for a complete list of medicines recommended for disposal by flushing, as well as additional information on disposal of unused medicines.

Medication Errors
Instruct patients how to measure and take the correct dose of oxycodone hydrochloride and acetaminophen oral solution and to always use a calibrated measuring device when administering oxycodone hydrochloride and acetaminophen oral solution to ensure the dose is measured and administered accurately [see **WARNINGS**].

If the prescribed concentration is changed, instruct patients on how to correctly measure the new dose to avoid errors which could result in accidental overdose and death.

Addiction, Abuse, and Misuse
Inform patients that the use of oxycodone hydrochloride and acetaminophen oral solution, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose and death [see **WARNINGS**]. Instruct patients not to share oxycodone hydrochloride and acetaminophen oral solution with others and to take steps to protect oxycodone hydrochloride and acetaminophen oral solution from theft or misuse.

Life-Threatening Respiratory Depression
Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting oxycodone hydrochloride and acetaminophen oral solution or when the dosage is increased, and that it can occur even at recommended dosages [see **WARNINGS**]. Advise patients how to recognize respiratory depression and to seek medical attention if breathing difficulties develop.

Accidental Ingestion
Inform patients that accidental ingestion, especially by children, may result in respiratory depression or death [see **WARNINGS**].

Interactions with Benzodiazepines and Other CNS Depressants
Inform patients and caregivers that potentially fatal additive effects may occur if oxycodone hydrochloride and acetaminophen oral solution is used with benzodiazepines and other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a health care provider [see **WARNINGS, PRECAUTIONS; Drug Interactions**].

Serotonin Syndrome
Inform patients that opioids could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and to seek medical attention right away if symptoms develop. Instruct patients to inform their healthcare providers if they are taking, or plan to take serotonergic medications [see **PRECAUTIONS; Drug Interactions**].

Monoamine Oxidase Inhibitor (MAOI) Interaction
Inform patients to avoid taking oxycodone hydrochloride and acetaminophen oral solution while using any drugs that inhibit monoamine oxidase. Patients should not start MAOIs while taking oxycodone hydrochloride and acetaminophen oral solution [see **PRECAUTIONS; Drug Interactions**].

Adrenal Insufficiency
Inform patients that opioids could cause adrenal insufficiency, a potentially life-threatening condition. Adrenal insufficiency may present with non-specific symptoms and signs such as nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. Advise patients to seek medical attention if they experience a constellation of these symptoms [see **WARNINGS**].

Important Administration Instructions
Instruct patients how to properly take oxycodone hydrochloride and acetaminophen oral solution [see **DOSAGE AND ADMINISTRATION, WARNINGS**].

Advise patients to always use a calibrated oral syringe/dosing cup when administering oxycodone hydrochloride and acetaminophen oral solution to ensure the dose is measured and administered accurately [see **WARNINGS**].

Advise patients never to use household teaspoons or tablespoons to measure oxycodone hydrochloride and acetaminophen oral solution.

Advise patients not to adjust the dose of oxycodone hydrochloride and acetaminophen oral solution without consulting with a physician or other healthcare professional.

If patients have been receiving treatment with oxycodone hydrochloride and acetaminophen oral solution for more than a few weeks and cessation of therapy is indicated, counsel them on the importance of safely tapering the dose as abrupt discontinuation of the medication could precipitate withdrawal symptoms. Provide a dose schedule to accomplish a gradual discontinuation of the medication [see **DOSAGE AND ADMINISTRATION**].

Important Discontinuation Instructions
In order to avoid developing withdrawal symptoms, instruct patients not to discontinue oxycodone hydrochloride and acetaminophen oral solution without first discussing a tapering plan with the prescriber [see **DOSAGE AND ADMINISTRATION**].

Maximum Daily Dose of Acetaminophen
Inform patients to not take more than 4000 milligrams of acetaminophen per day. Advise patients to call their prescriber if they take more than the recommended dose.

Hypotension
Inform patients that oxycodone hydrochloride and acetaminophen oral solution may cause orthostatic hypotension and syncope. Advise patients how to recognize such a reaction and when to seek medical attention [see **CONTRAINDICATIONS, ADVERSE REACTIONS**].

Anaphylaxis
Inform patients that anaphylaxis has been reported with ingredients contained in oxycodone hydrochloride and acetaminophen oral solution. Advise patients how to recognize such a reaction and when to seek medical attention [see **CONTRAINDICATIONS, ADVERSE REACTIONS**].

Pregnancy
Neonatal Opioid Withdrawal Syndrome
Inform female patients of reproductive potential that prolonged use of oxycodone hydrochloride and acetaminophen oral solution during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated [see **WARNINGS, PRECAUTIONS; Pregnancy**].

MEDICATION GUIDE
Oxycodone (ox" i koe' done hye" droe klor' ide) Hydrochloride and Acetaminophen (a seet" a min' oh fen) Oral Solution, CII

Oxycodone Hydrochloride and Acetaminophen Oral Solution is:
- A strong prescription pain medicine that contains an opioid (narcotic) that is used to manage pain, severe enough to require an opioid analgesic and for which alternative treatments are inadequate and when other pain treatments such as non-opioid pain medicines do not treat your pain well enough or you cannot tolerate them.
- An opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death.

Important information about Oxycodone Hydrochloride and Acetaminophen Oral Solution:
- **Get emergency help right away if you take too much Oxycodone Hydrochloride and Acetaminophen Oral Solution (overdose).** When you first start taking Oxycodone Hydrochloride and Acetaminophen Oral Solution, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur. Taking Oxycodone Hydrochloride and Acetaminophen Oral Solution with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.
- Never give anyone else your Oxycodone Hydrochloride and Acetaminophen Oral Solution. They could die from taking it. Selling or giving away Oxycodone Hydrochloride and Acetaminophen Oral Solution is against the law.
- Store Oxycodone Hydrochloride and Acetaminophen Oral Solution securely, out of sight and reach of children, and in a location not accessible by others, including visitors to the home.

Do not take Oxycodone Hydrochloride and Acetaminophen Oral Solution if you have:
- Severe asthma, trouble breathing, or other lung problems.
- A bowel blockage or have narrowing of the stomach or intestines
- Known hypersensitivity to oxycodone, acetaminophen, or any ingredient in Oxycodone Hydrochloride and Acetaminophen Oral Solution

Before taking Oxycodone Hydrochloride and Acetaminophen Oral Solution, tell your healthcare provider if you have a history of:
- Head injury, seizures
- Liver, kidney, thyroid problems
- Problems urinating
- Pancreas or gallbladder problems
- Abuse of street or prescription drugs, alcohol addiction, or mental health problems

Tell your healthcare provider if you are:
- **Pregnant or planning to become pregnant.** Prolonged use of Oxycodone Hydrochloride and Acetaminophen Oral Solution during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated.
- **Breastfeeding.** Oxycodone Hydrochloride and Acetaminophen Oral Solution passes into breast milk and may harm your baby.
- Taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking Oxycodone Hydrochloride and Acetaminophen Oral Solution with certain other medicines can cause serious side effects that could lead to death.

Oxycodone Hydrochloride and Acetaminophen Oral Solution CII
Rx only
Code 1172B00
Rev. 09/2019
FPO

Product Information

Flat Size: 12.25" x 21"
Folded Size: 1.25" x 1.25"
Number of Panels: 170 Panel
Paper Weight: 26# Opaque Offset
Ink: Food Grade Black

When taking Oxycodone Hydrochloride and Acetaminophen Oral Solution:

- Do not change your dose. Take Oxycodone Hydrochloride and Acetaminophen Oral Solution exactly as prescribed by your healthcare provider. Use the lowest dose possible for the shortest time needed.
- Ask your healthcare provider if you have any questions on how to correctly measure your dose. Always use a calibrated measuring device for Oxycodone Hydrochloride and Acetaminophen Oral Solution to correctly measure your dose. A household teaspoon or tablespoon is not an adequate measuring device. Given the inexactitude of the household spoon measure and the possibility of using a tablespoon instead of a teaspoon, which could lead to overdosage, it is strongly recommended that caregivers obtain and use a calibrated measuring device.
- Take your prescribed dose every 6 hours as needed for pain. Do not take more than your prescribed dose. If you miss a dose, take your next dose at your usual time.
- Call your healthcare provider if the dose you are taking does not control your pain.
- If you have been taking Oxycodone Hydrochloride and Acetaminophen Oral Solution regularly, do not stop taking Oxycodone Hydrochloride and Acetaminophen Oral Solution without talking to your healthcare provider.
- Dispose of expired, unwanted, or unused Oxycodone Hydrochloride and Acetaminophen Oral Solution by promptly flushing down the toilet, if a drug take-back option is not readily available. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.

While taking Oxycodone Hydrochloride and Acetaminophen Oral Solution DO NOT:

- Drive or operate heavy machinery, until you know how Oxycodone Hydrochloride and Acetaminophen Oral Solution affects you. Oxycodone Hydrochloride and Acetaminophen Oral Solution can make you sleepy, dizzy, or lightheaded.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with Oxycodone Hydrochloride and Acetaminophen Oral Solution may cause you to overdose and die.

The possible side effects of Oxycodone Hydrochloride and Acetaminophen Oral Solution:

- Constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, abdominal pain. Call your healthcare provider if you have any of these symptoms and they are severe.

Get emergency medical help if you have:

- Trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue, or throat, extreme drowsiness, light-headedness when changing positions, feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.

These are not all the possible side effects of Oxycodone Hydrochloride and Acetaminophen Oral Solution. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. **For more information go to dailymed.nlm.nih.gov.**

Distributed by: FH2 Pharma LLC, Delray Beach, FL 33444

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised: 09/2019
Code 1172B00

Embryo-Fetal Toxicity
Inform female patients of reproductive potential that oxycodone hydrochloride and acetaminophen oral solution can cause fetal harm and to inform the healthcare provider of a known or suspected pregnancy [see **PRECAUTIONS; Pregnancy**].

Lactation
Advise nursing mothers to monitor infants for increased sleepiness (more than usual), breathing difficulties, or limpness. Instruct nursing mothers to seek immediate medical care if they notice these signs [see **PRECAUTIONS; Nursing Mothers**].

Infertility
Inform patients that chronic use of opioids may cause reduced fertility. It is not known whether these effects on fertility are reversible [see **ADVERSE REACTIONS**].

Driving or Operating Heavy Machinery
Inform patients that oxycodone hydrochloride and acetaminophen oral solution may impair the ability to perform potentially hazardous activities such as driving a car or operating heavy machinery. Advise patients not to perform such tasks until they know how they will react to the medication [see **PRECAUTIONS**].

Constipation
Advise patients of the potential for severe constipation, including management instructions and when to seek medical attention [see **ADVERSE REACTIONS, CLINICAL PHARMACOLOGY**].

Laboratory Tests
Although oxycodone may cross-react with some drug urine tests, no available studies were found which determined the duration of detectability of oxycodone in urine drug screens. However, based on pharmacokinetic data, the approximate duration of detectability for a single dose of oxycodone is roughly estimated to be one to two days following drug exposure.

Urine testing for opiates may be performed to determine illicit drug use and for medical reasons such as evaluation of patients with altered states of consciousness or monitoring efficacy of drug rehabilitation efforts. The preliminary identification of opiates in urine involves the use of an immunoassay screening and thin-layer chromatography (TLC). Gas chromatography/mass spectrometry (GC/MS) may be utilized as a third-stage identification step in the medical investigational sequence for opiate testing after immunoassay and TLC. The identities of 6-keto opiates (e.g., oxycodone) can further be differentiated by the analysis of their methoximetrimethylsilyl (MO-TMS) derivative.

Drug Interactions
Inhibitors of CYP3A4 and CYP2D6
The concomitant use of oxycodone hydrochloride and acetaminophen oral solution and CYP3A4 inhibitors, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g. ketoconazole), and protease inhibitors (e.g., ritonavir), can increase the plasma concentration of oxycodone, resulting in increased or prolonged opioid effects. These effects could be more pronounced with concomitant use of oxycodone hydrochloride and acetaminophen oral solution and CYP3A4 and CYP2D6 inhibitors, particularly when an inhibitor is added after a stable dose of oxycodone hydrochloride and acetaminophen oral solution is achieved [see **WARNINGS**].

After stopping a CYP3A4 inhibitor, as the effects of the inhibitor decline, the oxycodone plasma concentration will decrease [see **CLINICAL PHARMACOLOGY**], resulting in decreased opioid efficacy or a withdrawal syndrome in patients who had developed physical dependence to oxycodone hydrochloride and acetaminophen oral solution.

If concomitant use is necessary, consider dosage reduction of oxycodone hydrochloride and acetaminophen oral solution until stable drug effects are achieved. Monitor patients for respiratory depression and sedation at frequent intervals. If a CYP3A4 inhibitor is discontinued, consider increasing the oxycodone hydrochloride and acetaminophen oral solution dosage until stable drug effects are achieved. Monitor for signs of opioid withdrawal.

Inducers of CYP3A4
The concomitant use of oxycodone hydrochloride and acetaminophen oral solution and CYP3A4 inducers, such as rifampin, carbamazepine, and phenytoin, can decrease the plasma concentration of oxycodone [see **CLINICAL PHARMACOLOGY**], resulting in decreased efficacy or onset of a withdrawal syndrome in patients who have developed physical dependence to oxycodone hydrochloride and acetaminophen oral solution [see **WARNINGS**].

After stopping a CYP3A4 inducer, as the effects of the inducer decline, the oxycodone plasma concentration will increase [see **CLINICAL PHARMACOLOGY**], which could increase or prolong both the therapeutic effects and adverse reactions, and may cause serious respiratory depression.

If concomitant use is necessary, consider increasing the oxycodone hydrochloride and acetaminophen oral solution dosage until stable drug effects are achieved. Monitor for signs of opioid withdrawal. If a CYP3A4 inducer is discontinued, consider oxycodone hydrochloride and acetaminophen oral solution dosage reduction and monitor for signs of respiratory depression.

Benzodiazepines and Other CNS Depressants
Due to additive pharmacologic effect, the concomitant use of benzodiazepines and other CNS depressants such as benzodiazepines and other sedative hypnotics, anxiolytics, and tranquilizers, muscle relaxants, general anesthetics, antipsychotics, and other opioids, including alcohol, can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death.

Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation [see **WARNINGS**].

Serotonergic Drugs
The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system, such as selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), tryptans, 5-HT3 receptor antagonists, drugs that affect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), certain muscle relaxants (i.e., cyclobenzaprine, metaxalone), and monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue), has resulted in serotonin syndrome [see **PRECAUTIONS; Information for Patients/Caregivers**].

If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue oxycodone hydrochloride and acetaminophen oral solution if serotonin syndrome is suspected.

Monoamine Oxidase Inhibitors (MAOIs)
The concomitant use of opioids and MAOIs, such as phenelzine, tranylcypromine, linezolid, may manifest as serotonin syndrome or opioid toxicity (e.g., respiratory depression, coma) [see **WARNINGS**].

The use of oxycodone hydrochloride and acetaminophen oral solution is not recommended for patients taking MAOIs or within 14 days of stopping such treatment.

If urgent use of an opioid is necessary, use test doses and frequent titration of small doses to treat pain while closely monitoring blood pressure and signs and symptoms of CNS and respiratory depression.

Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics
The concomitant use of opioids with other opioid analgesics, such as butorphanol, nalbuphine, pentazocine, may reduce the analgesic effect of oxycodone hydrochloride and acetaminophen oral solution and/or precipitate withdrawal symptoms.

Advise patient to avoid concomitant use of these drugs.

Muscle Relaxants
Oxycodone hydrochloride and acetaminophen oral solution may enhance the neuromuscular-blocking action of skeletal muscle relaxants and produce an increase in the degree of respiratory depression.

If concomitant use is warranted, monitor patients for signs of respiratory depression that may be greater than otherwise expected and decrease the dosage of oxycodone hydrochloride and acetaminophen oral solution and/or the muscle relaxant as necessary.

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

If concomitant use is warranted, monitor patients for signs of diminished diuresis and/or effects on blood pressure and increase the dosage of the diuretic as needed.

Anticholinergic Drugs
The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.

If concomitant use is warranted, monitor patients for signs of urinary retention or reduced gastric motility when oxycodone hydrochloride and acetaminophen oral solution is used concomitantly with anticholinergic drugs.

Alcohol, ethyl
Hepatotoxicity has occurred in chronic alcoholics following various dose levels (moderate to excessive) of acetaminophen.

Oral Contraceptives
Increase in glucuronidation resulting in increased plasma clearance and a decreased half-life of acetaminophen.

Charcoal (activated)
Reduces acetaminophen absorption when administered as soon as possible after overdose.

Beta Blockers (Propranolol)
Propranolol appears to inhibit the enzyme systems responsible for the glucuronidation and oxidation of acetaminophen. Therefore, the pharmacologic effects of acetaminophen may be increased.

Loop Diuretics
The effects of the loop diuretic may be decreased because acetaminophen may decrease renal prostaglandin excretion and decrease plasma renin activity.

Lamotrigine
Serum lamotrigine concentrations may be reduced, producing a decrease in therapeutic effects.

Probenecid
Probenecid may increase the therapeutic effectiveness of acetaminophen slightly.

Zidovudine
The pharmacologic effects of zidovudine may be decreased because of enhanced non-hepatic or renal clearance of zidovudine

Drug/Laboratory Test Interactions
Depending on the sensitivity/specificity and the test methodology, the individual components of oxycodone hydrochloride and acetaminophen oral solution may cross-react with assays used in the preliminary detection of cocaine (primary urinary metabolite, benzoylecgonine) or marijuana (cannabinoids) in human urine. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. The preferred confirmatory method is gas chromatography/mass spectrometry (GC/MS). Moreover, clinical considerations and professional judgment should be applied to any drug-of-abuse test result, particularly when preliminary positive results are used.

Acetaminophen may interfere with home blood glucose measurement systems; decreases of >20% in mean glucose values may be noted. This effect appears to be drug, concentration and system dependent.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis
Long-term studies to evaluate the carcinogenic potential of the combination of oxycodone hydrochloride and acetaminophen have not been conducted.

Long-term studies in mice and rats have been completed by the National Toxicology Program to evaluate the carcinogenic potential of acetaminophen. In 2-year feeding studies, F344/N rats and B6C3F1 mice were fed a diet containing acetaminophen up to 6000 ppm. Female rats demonstrated equivocal evidence of carcinogenic activity based on increased incidences of mononuclear cell leukemia at 0.8 times the maximum human daily dose (MHDD) of 4 grams/day, based on a body surface area comparison. In contrast, there was no evidence of carcinogenic activity in male rats that received up to 0.7 times or mice at up to 1.2-1.4 times the MHDD, based on a body surface area comparison.

Mutagenesis
The combination of oxycodone hydrochloride and acetaminophen has not been evaluated for mutagenicity. Oxycodone alone was negative in a bacterial reverse mutation assay (Ames), an *in vitro* chromosome aberration assay with human lymphocytes without metabolic activation and an *in vivo* mouse micronucleus assay. Oxycodone was clastogenic in the human lymphocyte chromosomal assay in the presence of metabolic activation and in the mouse lymphoma assay with or without metabolic activation.

In the published literature, acetaminophen has been reported to be clastogenic when administered at 1500 mg/kg/day to the rat model (3.6-times the MHDD, based on a body surface area comparison). In contrast, no clastogenicity was noted at a dose of 750 mg/kg/day (1.8-times the MHDD, based on a body surface area comparison), suggesting a threshold effect.

Impairment of Fertility
In studies conducted by the National Toxicology Program, fertility assessments with acetaminophen have been completed in Swiss CD-1 mice via a continuous breeding study. There were no effects on fertility parameters in mice consuming up to 1.7 times the MHDD of acetaminophen, based on a body surface area comparison. Although there was no effect on sperm motility or sperm density in the epididymis, there was a significant increase in the percentage of abnormal sperm in mice consuming 1.78 times the MHDD (based on a body surface comparison) and there was a reduction in the number of mating pairs producing a fifth litter at this dose, suggesting the potential for cumulative toxicity with chronic administration of acetaminophen near the upper limit of daily dosing.

Published studies in rodents report that oral acetaminophen treatment of male animals at doses that are 1.2 times the MHDD and greater (based on a body surface comparison) result in decreased testicular weights, reduced spermatogenesis, reduced fertility, and reduced implantation sites in females given the same doses. These effects appear to increase with the duration of treatment. The clinical significance of these findings is not known.

Infertility
Chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible [see **ADVERSE REACTIONS**].

Pregnancy
Teratogenic Effects
Pregnancy Category C
Animal reproductive studies have not been conducted with oxycodone hydrochloride and acetaminophen oral solution. It is also not known whether oxycodone hydrochloride and acetaminophen oral solution can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Oxycodone hydrochloride and acetaminophen oral solution should not be given to a pregnant woman unless in the judgment of the physician, the potential benefits outweigh the possible hazards.

Nonteratogenic Effects
Fetal/Neonatal Adverse Reactions
Prolonged use of opioid analgesics during pregnancy for medical or nonmedical purposes can result in physical dependence in the neonate and neonatal opioid withdrawal syndrome shortly after birth.

Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn. Observe newborns for symptoms of neonatal opioid withdrawal syndrome and manage accordingly [see **WARNINGS**].

Labor or Delivery
Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist, such as naloxone, must be available for reversal of opioid-induced respiratory depression in the neonate. Oxycodone hydrochloride and acetaminophen oral solution is not recommended for use in pregnant women during or immediately prior to labor, when other analgesic techniques are more appropriate. Opioid analgesics, including oxycodone hydrochloride and acetaminophen oral solution, can prolong labor through actions which temporarily reduce the strength, duration, and frequency of uterine contractions. However, this effect is not consistent and may be offset by an increased rate of cervical dilation, which tends to shorten labor. Monitor neonates exposed to opioid analgesics during labor for signs of excess sedation and respiratory depression.

Nursing Mothers
Ordinarily, nursing should not be undertaken while a patient is receiving oxycodone hydrochloride and acetaminophen oral solution because of the possibility of sedation and/or respiratory depression in the infant. Oxycodone is excreted in breast milk in low concentrations, and there have been rare reports of somnolence and lethargy in babies of nursing mothers taking an oxycodone/acetaminophen product. Acetaminophen is also excreted in breast milk in low concentrations.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for oxycodone hydrochloride and acetaminophen oral solution and any potential adverse effects on the breastfed infant from oxycodone hydrochloride and acetaminophen oral solution or from the underlying maternal condition.

Infants exposed to oxycodone hydrochloride and acetaminophen oral solution through breast milk should be monitored for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped.

Pediatric Use
Safety and effectiveness of oxycodone hydrochloride and acetaminophen oral solution in pediatric patients have not been established.

Geriatric Use
Elderly patients (aged 65 years or older) may have increased sensitivity to oxycodone hydrochloride and acetaminophen oral solution. In general, use caution when selecting a dosage for an elderly patient, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

Respiratory depression is the chief risk for elderly patients treated with opioids, and has occurred after large initial doses were administered to patients who were not opioid-tolerant or when opioids were co-administered with other agents that depress respiration. Titrate the dosage of oxycodone hydrochloride and acetaminophen oral solution slowly in geriatric patients and monitor closely for signs of central nervous system and respiratory depression [see **WARNINGS**].

These drugs are known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Hepatic Impairment
In a pharmacokinetic study of oxycodone in patients with end-stage liver disease, oxycodone plasma clearance decreased and the elimination half-life increased.

Because oxycodone is extensively metabolized in the liver, its clearance may decrease in patients with hepatic impairment. Initiate therapy in these patients with a lower than usual dosage of oxycodone hydrochloride and acetaminophen oral solution and titrate carefully. Monitor closely for adverse events such as respiratory depression, sedation, and hypotension [see **CLINICAL PHARMACOLOGY**].

Renal Impairment
In a study of patients with end stage renal impairment, mean elimination half-life was prolonged in uremic patients due to increased volume of distribution and reduced clearance. Oxycodone should be used with caution in patients with renal impairment.

Because oxycodone is known to be substantially excreted by the kidney, its clearance may decrease in patients with renal impairment. Initiate therapy with a lower than usual dosage of oxycodone hydrochloride and acetaminophen solution and titrate carefully. Monitor closely for adverse events such as respiratory depression, sedation, and hypotension [see **CLINICAL PHARMACOLOGY**].

ADVERSE REACTIONS
The following adverse reactions have been identified during post approval use of oxycodone hydrochloride and acetaminophen oral solution. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Serious adverse reactions that may be associated with oxycodone hydrochloride and acetaminophen oral solution use include respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, and shock [see **OVERDOSAGE**].

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

Hypersensitivity reactions may include: Skin eruptions, urticarial, erythematous skin reactions. Hematologic reactions may include: thrombocytopenia, neutropenia, pancytopenia, hemolytic anemia. Rare cases of agranulocytosis have likewise been associated with acetaminophen use. In high doses, the most serious adverse effect is a dose-dependent, potentially fatal hepatic necrosis. Renal tubular necrosis and hypoglycemic coma also may occur.

Other adverse reactions obtained from postmarketing experiences with oxycodone and acetaminophen are listed by organ system and in decreasing order of severity and/or frequency as follows:

Body as a Whole: Anaphylactoid reaction, allergic reaction, malaise, asthenia, fatigue, chest pain, fever, hypothermia, thirst, headache, increased sweating, accidental overdose, non-accidental overdose

Cardiovascular: Hypotension, hypertension, tachycardia, orthostatic hypotension, bradycardia, palpitations, dysrhythmias

Central and Peripheral Nervous System: Stupor, tremor, paraesthesia, hypoaesthesia, lethargy, seizures, anxiety, mental impairment, agitation, cerebral edema, confusion, dizziness

Fluid and Electrolyte: Dehydration, hyperkalemia, metabolic acidosis, respiratory alkalosis

Gastrointestinal: Dyspepsia, taste disturbances, abdominal pain, abdominal distention, sweating increased, diarrhea, dry mouth, flatulence, gastrointestinal disorder, nausea, vomiting, pancreatitis, intestinal obstruction, ileus

Hepatic: Transient elevations of hepatic enzymes, increase in bilirubin, hepatitis, hepatic failure, jaundice, hepatotoxicity, hepatic disorder

Hearing and Vestibular: Hearing loss, tinnitus

Hematologic: Thrombocytopenia

Hypersensitivity: Acute anaphylaxis, angioedema, asthma, bronchospasm, laryngeal edema, urticaria, anaphylactoid reaction

Metabolic and Nutritional: Hypoglycemia, hyperglycemia, acidosis, alkalosis

Musculoskeletal: Myalgia, rhabdomyolysis

Ocular: Miosis, visual disturbances, red eye

Psychiatric: Drug dependence, drug abuse, insomnia, confusion, anxiety, agitation, depressed level of consciousness, nervousness, hallucination, somnolence, depression, suicide

Respiratory System: Bronchospasm, dyspnea, hyperpnea, pulmonary edema, tachypnea, aspiration, hypoventilation, laryngeal edema

Skin and Appendages: Erythema, urticaria, rash, flushing

Urogenital: Interstitial nephritis, papillary necrosis, proteinuria, renal insufficiency and failure, urinary retention

- Serotonin syndrome: Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of opioids with serotonergic drugs.
- Adrenal insufficiency: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.
- Anaphylaxis: Anaphylaxis has been reported with ingredients contained in oxycodone hydrochloride and acetaminophen oral solution.
- Androgen deficiency: Cases of androgen deficiency have occurred with chronic use of opioids [see **CLINICAL PHARMACOLOGY**].

DRUG ABUSE AND DEPENDENCE

Controlled Substance
Oxycodone hydrochloride and acetaminophen oral solution contains oxycodone, a Schedule II controlled substance.

Abuse
Oxycodone hydrochloride and acetaminophen oral solution contains oxycodone, a substance with a high potential for abuse similar to other opioids including fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxymorphone, and tapentadol. Oxycodone hydrochloride and acetaminophen oral solution can be abused and is subject to misuse, addiction, and criminal diversion [see **WARNINGS**].

All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

Prescription drug abuse is the intentional non-therapeutic use of a prescription drug, even once, for its rewarding psychological or physiological effects.

Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and includes: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

"Drug-seeking" behavior is very common in persons with substance use disorders. 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 health care provider(s). "Doctor shopping" (visiting multiple prescribers to obtain additional prescriptions) is common among drug abusers and people suffering from untreated addiction. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Health care providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction.

Oxycodone hydrochloride and acetaminophen oral solution, like other opioids, can be diverted for non-medical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests, as required by state and federal law, is strongly advised.

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.

Risks Specific to Abuse of Oxycodone Hydrochloride and Acetaminophen Oral Solution
Oxycodone hydrochloride and acetaminophen oral solution is for oral use only. Abuse of oxycodone hydrochloride and acetaminophen oral solution poses a risk of overdose and death. The risk is increased with concurrent abuse of oxycodone hydrochloride and acetaminophen oral solution with alcohol and other central nervous system depressants.

Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death.

Parenteral drug abuse is commonly associated with transmission of infectious diseases such as hepatitis and HIV.

Dependence
Both tolerance and physical dependence can develop during chronic opioid therapy. 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). Tolerance may occur to both the desired and undesired effects of drugs, and may develop at different rates for different effects.

Physical dependence is a physiological state in which the body adapts to the drug after a period of regular exposure, resulting in withdrawal symptoms after abrupt discontinuation or a significant dosage reduction of a drug. Withdrawal also may be precipitated through the administration of drugs with opioid antagonist activity (e.g., naloxone, nalmefene), mixed agonist/antagonist analgesics (e.g., pentazocine, butorphanol, nalbuphine), or partial agonists (e.g.,buprenorphine). Physical dependence may not occur to a clinically significant degree until after several days to weeks of continued opioid usage.

Do not abruptly discontinue oxycodone hydrochloride and acetaminophen oral solution in a patient physically dependent on opioids. Rapid tapering of oxycodone hydrochloride and acetaminophen oral solution in a patient physically dependent on opioids may lead to serious withdrawal symptoms, uncontrolled pain, and suicide. Rapid discontinuation has also been associated with attempts to find other sources of opioid analgesics, which may be confused with drug-seeking for abuse.

When discontinuing oxycodone hydrochloride and acetaminophen oral solution, gradually taper the dosage using a patient-specific plan that considers the following: the dose of oxycodone hydrochloride and acetaminophen oral solution the patient has been taking, the duration of treatment, and the physical and psychological attributes of the patient. To improve the likelihood of a successful taper and minimize withdrawal symptoms, it is important that the opioid tapering schedule is agreed upon by the patient. In patients taking opioids for a long duration at high doses, ensure that a multimodal approach to pain management, including mental health support (if needed), is in place prior to initiating an opioid analgesic taper [see **DOSAGE AND ADMINISTRATION, WARNINGS**].

Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal signs [see **PRECAUTIONS; Pregnancy**].

OVERDOSAGE
Following an acute overdosage, toxicity may result from the oxycodone or the acetaminophen.

Clinical Presentation
Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and, in some cases, pulmonary edema, bradycardia, hypotension, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations.

Acetaminophen
Dose-dependent potentially fatal hepatic necrosis is the most serious adverse effect of acetaminophen overdosage. Renal tubular necrosis, hypoglycemic coma, and coagulation defects may also occur.

Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Treatment of Overdose
Oxycodone
In case of overdose, priorities are the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed. Employ other supportive measures (including oxygen and vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life-support techniques.

The opioid antagonists, naloxone or nalmefene, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression secondary to oxycodone overdose, administer an opioid antagonist. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose.

Because the duration of opioid reversal is expected to be less than the duration of action of oxycodone in oxycodone hydrochloride and acetaminophen oral solution, carefully monitor the patient until spontaneous respiration is reliably reestablished. If the response to an opioid antagonist is suboptimal or only brief in nature, administer additional antagonist as directed by the product's prescribing information.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be initiated with care and by titration with smaller than usual doses of the antagonist.

Acetaminophen
Gastric decontamination with activated charcoal should be administered just prior to N-acetylcysteine (NAC) to decrease systemic absorption if acetaminophen ingestion is known or suspected to have occurred within a few hours of presentation. Serum acetaminophen levels should be obtained immediately if the patient presents 4 hours or more after ingestion to assess potential risk of hepatotoxicity; acetaminophen levels drawn less than 4 hours post-ingestion may be misleading. To obtain the best possible outcome, NAC should be administered as soon as possible where impending or evolving liver injury is suspected. Intravenous NAC may be administered when circumstances preclude oral administration.

Vigorous supportive therapy is required in severe intoxication. Procedures to limit the continuing absorption of the drug must be readily performed since the hepatic injury is dose dependent and occurs early in the course of intoxication.

DOSAGE AND ADMINISTRATION

Important Dosage and Administration Instructions
Ensure accuracy when prescribing, dispensing, and administering oxycodone hydrochloride and acetaminophen oral solution to avoid dosing errors due to confusion between mg and mL, and with other oxycodone hydrochloride and acetaminophen solutions of different concentrations, which could result in accidental overdose and death. Ensure the proper dose is communicated and dispensed. When writing prescriptions, include both the total dose in mg and the total dose in volume.

Always use a calibrated measuring device when administering oxycodone hydrochloride and acetaminophen oral solution to ensure the dose is measured and administered accurately. Health care providers should recommend a calibrated measuring device that can measure and deliver the prescribed dose accurately, and instruct caregivers to use extreme caution in measuring the dosage.

Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals [see **WARNINGS**].

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 [see **WARNINGS**].

Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy and following dosage increases with oxycodone hydrochloride and acetaminophen oral solution and adjust the dosage accordingly [see **WARNINGS**].

Initial Dosage
Initiating Treatment with Oxycodone Hydrochloride and Acetaminophen Oral Solution
The usual adult dosage is 5 mL (one teaspoonful) every 6 hours as needed for pain. The total daily dose of acetaminophen should not exceed 4 grams. (Maximum daily dose is 6 teaspoonfuls or 30 mL.)

It is of utmost importance that the dose of oxycodone hydrochloride and acetaminophen oral solution be administered accurately. A household teaspoon or tablespoon is not an adequate measuring device, especially when one-half or three-fourths of a teaspoonful is to be measured. Given the variability of the household spoon measure and the possibility of mistakenly using a tablespoon instead of a teaspoon, which could lead to overdosage, it is strongly recommended that caregivers obtain and use a calibrated measuring device. Health care providers should recommend a calibrated measuring device that can measure and deliver the prescribed dose accurately, and instruct caregivers to use extreme caution in measuring the dosage.

Conversion from Oxycodone Hydrochloride and Acetaminophen to Extended-Release Oxycodone
The relative bioavailability of oxycodone hydrochloride and acetaminophen oral solution compared to extended-release oxycodone is unknown, so conversion to extended-release oxycodone must be accompanied by close observation for signs of excessive sedation and respiratory depression.

Titration and Maintenance of Therapy
Individually titrate oxycodone hydrochloride and acetaminophen oral solution to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving oxycodone hydrochloride and acetaminophen oral solution to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as monitoring for the development of addiction, abuse, or misuse [see **WARNINGS**]. 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.

If the level of pain increases after dosage stabilization, attempt to identify the source of increased pain before increasing the oxycodone hydrochloride and acetaminophen oral solution dosage. If unacceptable opioid-related adverse reactions are observed, consider reducing the dosage. Adjust the dosage to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

Safe Reduction or Discontinuation of Oxycodone Hydrochloride and Acetaminophen Oral Solution
Do not abruptly discontinue oxycodone hydrochloride and acetaminophen oral solution in patients who may be physically dependent on opioids. Rapid discontinuation of opioid analgesics in patients who are physically dependent on opioids has resulted in serious withdrawal symptoms, uncontrolled pain, and suicide. Rapid discontinuation has also been associated with attempts to find other sources of opioid analgesics, which may be confused with drug-seeking for abuse. Patients may also attempt to treat their pain or withdrawal symptoms with illicit opioids, such as heroin, and other substances.

When a decision has been made to decrease the dose or discontinue therapy in an opioid-dependent patient taking oxycodone hydrochloride and acetaminophen oral solution, there are a variety of factors that should be considered, including the dose of oxycodone hydrochloride and acetaminophen oral solution the patient has been taking, the duration of treatment, the type of pain being treated, and the physical and psychological attributes of the patient. It is important to ensure ongoing care of the patient and to agree on an appropriate tapering schedule and follow-up plan so that patient and provider goals and expectations are clear and realistic. When opioid analgesics are being discontinued due to a suspected substance use disorder, evaluate and treat the patient, or refer for evaluation and treatment of the substance use disorder. Treatment should include evidence-based approaches, such as medication assisted treatment of opioid use disorder. Complex patients with co-morbid pain and substance use disorders may benefit from referral to a specialist.

There are no standard opioid tapering schedules that are suitable for all patients. Good clinical practice dictates a patient-specific plan to taper the dose of the opioid gradually. For patients on oxycodone hydrochloride and acetaminophen oral solution who are physically opioid-dependent, initiate the taper by a small enough increment (e.g., no greater than 10% to 25% of the total daily dose) to avoid withdrawal symptoms, and proceed with dose-lowering at an interval of every 2 to 4 weeks. Patients who have been taking opioids for briefer periods of time may tolerate a more rapid taper.

It may be necessary to provide the patient with lower dosage strengths to accomplish a successful taper. Reassess the patient frequently to manage pain and withdrawal symptoms, should they emerge. Common withdrawal symptoms include restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other signs and 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. If withdrawal symptoms arise, it may be necessary to pause the taper for a period of time or raise the dose of the opioid analgesic to the previous dose, and then proceed with a slower taper. In addition, monitor patients for any changes in mood, emergence of suicidal thoughts, or use of other substances.

When managing patients taking opioid analgesics, particularly those who have been treated for a long duration and/or with high doses for chronic pain, ensure that a multimodal approach to pain management, including mental health support (if needed), is in place prior to initiating an opioid analgesic taper. A multimodal approach to pain management may optimize the treatment of chronic pain, as well as assist with the successful tapering of the opioid analgesic [see **WARNINGS; Withdrawal, DRUG ABUSE AND DEPENDENCE**].

HOW SUPPLIED
Oxycodone hydrochloride and acetaminophen oral solution, each 5 mL (teaspoonful) of which contains oxycodone hydrochloride 10 mg and acetaminophen 300 mg, is supplied as a red, tropical fruit punch flavored liquid in 120 mL bottles, NDC 72887-648-12.

Storage
Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Dispense in a tight, light-resistant container with a child-resistant closure.

Store oxycodone hydrochloride and acetaminophen oral solution securely and dispose of properly [see **PRECAUTIONS; Information for Patients/Caregivers**].

Distributed by:
FH2 Pharma LLC
Delray Beach, FL 33444

Product Information

Flat Size: 12.25" x 21"
Folded Size: 1.25" x 1.25"
Number of Panels: 170 Panel
Paper Weight: 26# Opaque Offset
Ink: Food Grade Black