PRESCRIBING INFORMATION

[N] pdp-HYDROCODONE
(Hydrocodone Bitartrate Syrup)
1 mg/1 mL

Antitussive

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Hydrocodone Bitartrate Syrup
1 mg/1 mL

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Non-medicinal Ingredients
Oral	1 mg/1 mL Syrup	Artificial Cherry Flavor, Caramel DS, FD&C Red No. 2, Hydrochloric Acid, Methylparaben, Propylparaben, Purified Water, Sorbitol Solution 70% and Sucrose.

INDICATIONS AND CLINICAL USE

Adults

pdp-HYDROCODONE (hydrocodone bitartrate) is indicated for the control of exhausting, non-productive cough.

Geriatrics (> 65 years of age)

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, concomitant disease or other drug therapy.

Pediatrics (< 18 years of age)

pdp-HYDROCODONE is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients (see also CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics; and DOSAGE AND ADMINISTRATION).

CONTRAINDICATIONS

- Children younger than 6 years of age.

- Patients who are hypersensitive to the active substance pdp-HYDROCODONE or other opioid analgesics or to any ingredient in the formulation. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the Product Monograph.

- In patients with known or suspected mechanical gastrointestinal obstruction (e.g., bowel obstruction or strictures) or any diseases/conditions that affect bowel transit (e.g., ileus of any type).

- Patients with suspected surgical abdomen (e.g., acute appendicitis or pancreatitis).

- Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus.

- Patients with acute respiratory depression, elevated carbon dioxide levels in the blood and cor pulmonale.

- Patients with acute alcoholism, delirium tremens, and convulsive disorders.

- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure, and head injury.

- Patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy).

WARNINGS AND PRECAUTIONS

SERIOUS WARNINGS AND PRECAUTIONS

Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with controlled release opioid formulations, pdp-HYDROCODONE should only be used in patients for whom alternative non-opioid treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate cough management (see DOSAGE AND ADMINISTRATION).

Addiction, Abuse, and Misuse
pdp-HYDROCODONE poses risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Each patient's risk should be assessed prior to prescribing pdp-HYDROCODONE, and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS). pdp-HYDROCODONE should be stored securely to avoid theft or misuse.

Life-threatening Respiratory Depression: OVERDOSE
Serious, life-threatening, or fatal respiratory depression may occur with use of pdp-HYDROCODONE. Infants exposed in-utero or through breast milk are at risk of life-threatening respiratory depression upon delivery or when nursed. Patients should be monitored for respiratory depression, especially during initiation of pdp-HYDROCODONE or following a dose increase. Further, instruct patients of the hazards related to taking opioids including fatal overdose.

Accidental Exposure
Accidental exposure to pdp-HYDROCODONE, especially by children, can result in a fatal overdose of hydrocodone bitartrate (see DOSAGE AND ADMINISTRATION, Disposal, for instructions on proper disposal).

Neonatal Opioid Withdrawal Syndrome
Prolonged maternal use of pdp-HYDROCODONE during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening (see WARNINGS AND PRECAUTIONS).

Interaction with Alcohol
The co-ingestion of alcohol with pdp-HYDROCODONE should be avoided as it may result in dangerous additive effects, causing serious injury or death (see WARNINGS AND PRECAUTIONS and DRUG INTERACTIONS)

Risks from Concomitant Use With Benzodiazepines Or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death (see

WARNINGS AND PRECAUTIONS, Neurologic and DRUG INTERACTIONS).

- **Reserve concomitant prescribing of pdp-HYDROCODONE 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.**

General

Before prescribing medication to suppress or modify cough, it is important to ascertain that the underlying cause of the cough is identified, that modification of the cough does not increase the risk of clinical or physiological complications, and that appropriate therapy for the primary disease is provided.

Accidental ingestion, especially by children can result in a fatal overdose of hydrocodone bitartrate (see DOSAGE AND ADMINISTRATION, disposal, for instructions on proper disposal).

Patients should be instructed not to give pdp-HYDROCODONE to anyone other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death. pdp-HYDROCODONE should be stored securely to avoid theft or misuse.

Patients should be cautioned not to consume alcohol while taking pdp-HYDROCODONE as it may increase the chance of experiencing serious adverse events, including death.

Administer with caution to patients hypersensitive to sympathomimetic preparations, patients with hyperthyroidism, diabetes mellitus and glaucoma

Abuse and Misuse

Like all opioids, pdp-HYDROCODONE is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, pdp-HYDROCODONE should be prescribed and handled with caution.

Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse and abuse.

Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse and abuse.

Use in Drug and Alcohol Addiction

pdp-HYDROCODONE is an opioid with no approved use in the management of addictive disorders. Its proper usage in individuals with drug or alcohol dependence, either active or in remission is for the management of cough requiring opioids. Patients with a history of addiction to drugs or alcohol may be at higher risk of becoming addicted to pdp-HYDROCODONE; extreme caution and awareness is warranted to mitigate the risk.

Cardiovascular

pdp-HYDROCODONE administration may result in hypotension and dizziness.

Dependence/Tolerance

As with other opioids, tolerance and physical dependence may develop upon repeated administration of pdp-HYDROCODONE and there is a potential for development of psychological dependence.

Physical dependence and tolerance reflect the neuroadaptation of the opioid receptors to chronic exposure to an opioid, and are separate and distinct from abuse and addiction. Tolerance, as well as physical dependence, may develop upon repeated administration of opioids, and are not by themselves evidence of an addictive disorder or abuse.

Continuous dosage over extended periods of time may cause a hydrocodone bitartrate dependent state.

Patients on prolonged therapy could experience withdrawal symptoms following abrupt discontinuation of therapy or upon administration of an opioid antagonist. Some of the symptoms that may be associated with abrupt withdrawal of an opioid include body aches, diarrhea, gooseflesh, loss of appetite, nausea, nervousness or restlessness, anxiety, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning (see ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage).

Endocrine

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.

Gastrointestinal Effects
pdp-HYDROCODONE and other morphine-like opioids have been shown to decrease bowel motility. Patients with chronic constipation should be given the drug only after weighing the potential therapeutic benefit against the hazards involved. Hydrocodone bitartrate may obscure the diagnosis or clinical course of patients with acute abdominal conditions (see CONTRAINDICATIONS).

Neonatal Opioid Withdrawal Syndrome (NOWS)
Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening.

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.

pdp-HYDROCODONE is not recommended to be used in pregnant women unless, in the judgement of the physician, the potential benefits outweigh the risks. If pdp-HYDROCODONE was used during pregnancy, special attention to NOWS is warranted.

Neurologic

Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol)
Hydrocodone bitartrate should be used with caution and in a reduced dosage during concomitant administration of other opioid analgesics, general anesthetics, phenothiazines and other tranquilizers, sedative-hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, benzodiazepines, centrally-active anti-emetics and other CNS depressants. Respiratory depression, hypotension and profound sedation, coma or death may result. When such combination therapy is contemplated, a substantial reduction in the dose of one or both agents should be considered, and patients should be carefully monitored.

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 opioid cough medications and benzodiazepines, other CNS depressants, or alcohol.

Advise both patients and caregivers about the risks of respiratory depression and sedation when pdp-HYDROCODONE 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 (see DRUG INTERACTIONS).

pdp-HYDROCODONE should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects, including death (see CONTRAINDICATIONS and ADVERSE REACTIONS, Sedation, and DRUG INTERACTIONS).

Head Injury
The respiratory depressant effects of hydrocodone bitartrate, and the capacity to elevate cerebrospinal fluid pressure, may be greatly increased in the presence of an already elevated intracranial pressure produced by trauma. Also, hydrocodone bitartrate may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, hydrocodone bitartrate must be used with extreme caution and only if it is judged essential (see CONTRAINDICATIONS).

Use in Patients with Convulsive or Seizure Disorders
The hydrocodone bitartrate in pdp-HYDROCODONE may aggravate convulsions in patients with convulsive disorders, and may induce or aggravate seizures in some clinical settings. Therefore, pdp-HYDROCODONE should not be used in these patients (see CONTRAINDICATIONS).

Serotonin syndrome
pdp-HYDROCODONE could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs (e.g. anti-depressants, migraine medications). Treatment with the serotonergic drug should be discontinued if such events (characterized by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. pdp-HYDROCODONE should not be used in combination with MAO inhibitors or serotonin-precursors (such as L-tryptophan, oxitriptan) and should be used with caution in combination with other serotonergic drugs (triptans, certain tricyclic antidepressants, lithium, tramadol, St. John's Wort) due to the risk of serotonergic syndrome (see DRUG INTERACTIONS).

Psychomotor Impairment

pdp-HYDROCODONE may impair the mental and/or physical abilities needed for certain potentially hazardous activities such as driving a car or operating machinery. Patients should be cautioned accordingly. Patients should also be cautioned about the combined effects of hydrocodone bitartrate with other CNS depressants, including other opioids, phenothiazine, sedative/hypnotics and alcohol.

Respiratory

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression from opioid use, 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. pdp-HYDROCODONE should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia (see **CONTRAINDICATIONS**).

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of pdp-HYDROCODONE, the risk is greatest during the initiation of therapy or following a dose increase. Patients should be closely monitored for respiratory depression when initiating therapy with pdp-HYDROCODONE and following dose increases.

Hydrocodone, including pdp-HYDROCODONE, is not recommended for use in any patient in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, lung infections, multiple trauma or extensive surgical procedures

Life-threatening respiratory depression is more likely to occur in the elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients.

Hydrocodone, including pdp-HYDROCODONE, is not indicated for patients under 18 years of age. Hydrocodone is contraindicated in patients below the age of 6 years In young children,

the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants. The use of hydrocodone bitartrate in children less than 6 years of age has been associated with fatal respiratory depression. A 5-year-old child treated for cough died after a few hours of exposure to hydrocodone bitartrate; the child was a CYP2D6 poor metabolizer and was concomitantly exposed to clarithromycin, a CYP3A4 inhibitor and valproic acid, a broad-spectrum inhibitor of the uridine diphosphate glucuronosyltransferases (UGTs), resulting in blood hydrocodone levels associated with fatality. Such a scenario of hydrocodone overdose can be equally plausible in CYP2D6 intermediate, extensive, and ultra rapid metabolizers, especially in the presence of other drug interactions and physical vulnerabilities for children up to 18 years of age and adults. Exercise caution when administering pdp-HYDROCODONE because of the potential for respiratory depression. If respiratory depression occurs, discontinue and use naloxone hydrochloride when indicated to antagonize the effect and other supportive measures as necessary.

Use in Patients with Chronic Pulmonary Disease
Monitor patients with significant chronic obstructive pulmonary disease or cor pulmonale, and patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression for respiratory depression, particularly when initiating therapy and titrating with pdp-HYDROCODONE, as in these patients, even usual therapeutic doses of pdp-HYDROCODONE may decrease respiratory drive to the point of apnea. In these patients, use of alternative non-opioid analgesics should be considered, if possible. The use of pdp-HYDROCODONE is contraindicated in Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see CONTRAINDICATIONS).

Sexual Function/Reproduction

Long-term use of opioids may be associated with decreased sex hormone levels and symptoms such as low libido, erectile dysfunction, or infertility (see ADVERSE REACTIONS, Post-Market Adverse Drug Reactions).

Special Populations

Special Risk Groups
Hydrocodone bitartrate should be administered with caution to patients with a history of alcohol and drug abuse and in a reduced dosage to debilitated patients, and in patients with severely impaired pulmonary function, Addison's disease, hypothyroidism, myxedema, toxic psychosis, prostatic hypertrophy or urethral stricture.

Pregnant Women
Studies in humans have not been conducted. pdp-HYDROCODONE crosses the placental barrier and is not recommended to be administered to pregnant women unless, in the judgement of the physician, potential benefits outweigh the risks.

Pregnant women using opioids should not discontinue their medication abruptly as this can cause pregnancy complication such as miscarriage or still-birth. Tapering should be slow and under medical supervision to avoid serious adverse events to the fetus.

Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening (see WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome).

Labour, Delivery and Nursing Women
Since opioids can cross the placental barrier and are excreted in breast milk, pdp-HYDROCODONE is not recommended to be used in nursing women and during labour and delivery unless, in the judgement of the physician, the potential benefits outweigh the risks. Life-threatening respiratory depression can occur in the infant if opioids are administered to the mother. Naloxone, a drug that counters the effects of opioids, should be readily available if pdp-HYDROCODONE is used in this population.

Pediatrics (< 18 years of age)
pdp-HYDROCODONE is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients (see INDICATIONS AND CLINICAL USE, CONTRAINDICATIONS, and DOSAGE AND ADMINISTRATION).

pdp-HYDROCODONE is contraindicated in children younger than 6 years of age. In young children, the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants.

Geriatrics (> 65 years of age)
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range and titrate slowly, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS

Respiratory System
Hydrocodone produces dose-related respiratory depression by acting directly on brain stem respiratory centres.

Cardiovascular System
Hypertension, postural hypotension and palpitations.

Genitourinary System
Ureteral spasm, spasm of vesical sphincters and urinary retention has been reported with opiates.

Central Nervous System

Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, dizziness, psychic dependence, mood changes and blurred vision.

Gastrointestinal System
Nausea and vomiting occur more frequently in ambulatory than in recumbent patients. Constipation may also occur.

Drug Abuse and Dependence
Special care should be exercised in prescribing hydrocodone for emotionally unstable patients and for those with a history of drug misuse. Such patients should be closely supervised when long-term therapy is contemplated.

Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, hydrocodone bitartrate syrup should always be prescribed and administered with caution. Physical dependence is the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome.

Patients physically dependent on opioids will develop an abstinence syndrome upon abrupt discontinuation of the opioid or following administration of a narcotic antagonist. The character and severity of the withdrawal symptoms are related to the degree of physical dependence. Manifestations of opioid withdrawal are similar to, but milder than that of morphine and include: lacrimation, rhinorrhea, yawning, sweating, restlessness, dilated pupils, anorexia, gooseflesh, irritability, and tremor. In more severe forms, nausea, vomiting, intestinal spasm and diarrhea, increased heart rate and blood pressure, chills, and pains in bones and muscles of the back and extremities may occur. Peak effects will usually be apparent at 48 to 72 hours.

Treatment of withdrawal is usually managed by providing sufficient quantities of an opioid to suppress severe withdrawal symptoms and then gradually reducing the dose of opioid over a period of several days.

DRUG INTERACTIONS

Do not use with a monoamine oxidase inhibitor (MAOI) or for 2 weeks after stopping the MAOI drug (see CONTRAINDICATIONS).

Interaction with Benzodiazepines and Other Central Nervous System (CNS) Depressants (including alcohol)
Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants (e.g. other opioids, sedatives/hypnotics, antidepressants, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, phenothiazines, neuroleptics, antihistamines, antiemetics, and alcohol) and beta-blockers, increases the risk of respiratory depression, profound sedation, coma, and death and should be avoided (see WARNINGS AND PRECAUTIONS, Neurologic, Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol) and Psychomotor Impairment). pdp-HYDROCODONE should not be consumed with

alcohol as it may increase the chance of experiencing dangerous side effects.

Serotonergic Agents
Coadministration of hydrocodone bitartrate with a serotonergic agent, such as a Selective Serotonin Re-Uptake Inhibitor or a Serotonin Norepinephrine Re-Uptake Inhibitor, may increase the risk of serotonin syndrome, a potentially life-threatening condition (see WARNINGS AND PRECAUTIONS, Neurologic).

Inhibitors of CYP3A4 and CYP2D6:
The concomitant use of pdp-HYDROCODONE and CYP3A4 inhibitors, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g. ketoconazole), or protease inhibitors (e.g., ritonavir), can increase the plasma concentration of hydrocodone, resulting in increased or prolonged opioid effects. These effects could be more pronounced with concomitant use of pdp-HYDROCODONE and CYP2D6 and CYP3A4 inhibitors, particularly when an inhibitor is added after a stable dose of pdp-HYDROCODONE is achieved.
Avoid the use of pdp-HYDROCODONE while taking a CYP3A4 or CYP2D6 inhibitor. If concomitant use is necessary, monitor patients for respiratory depression and sedation at frequent intervals.

Drug-Lifestyle Interactions

The concomitant use of alcohol should be avoided (see WARNINGS AND PRECAUTIONS, General).

Patients should be cautioned not to operate vehicles or hazardous machinery until their response to the drug has been determined.

DOSAGE AND ADMINISTRATION

Increasing Risk with Higher Doses
All doses of opioids carry an inherent risk of fatal or non-fatal adverse events. This risk is increased with higher doses. Each patient should be assessed for their risk prior to prescribing pdp-HYDROCODONE, as the likelihood of experiencing serious adverse events can depend upon the type of opioid and duration of treatment, as well as the patient's own level of tolerance. In addition, the coughing should be assessed routinely to confirm the most appropriate dose and the need for further use of pdp-HYDROCODONE.

Pediatrics (< 18 years of age):
pdp-HYDROCODONE is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients.

pdp-HYDROCODONE is contraindicated in children younger than 6 years of age.

Recommended Dose and Dosage Adjustment

Adults
5 mg (5 mL (one teaspoonful) of syrup) not less than 4 hours apart, after meals and at bedtime with food or a glass of milk, not to exceed 30 mg (30 mL (six teaspoonfuls) of syrup) in a 24-hour period. Maximum single dose 15 mg (15 mL (three teaspoonfuls) of syrup).

Geriatrics
Respiratory depression has occurred in the elderly following administration of large initial doses of opioids to patients who were not opioid-tolerant or when opioids were co-administered with other agents that can depress respiration pdp-HYDROCODONE should be initiated at a low dose and slowly titrated to effect (see WARNINGS AND PRECAUTIONS).

Adjustment or Reduction of Dosage
Physical dependence with or without psychological dependence tends to occur with chronic administration of opioids, including pdp-HYDROCODONE. Withdrawal (abstinence) symptoms may occur following abrupt discontinuation of therapy. These symptoms may include body aches, diarrhea, goosebumps, loss of appetite, nausea, nervousness or restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning.

Missed Dose

If the patient forgets to take one or more doses, they should take their next dose at the next scheduled time and in the normal amount.

Disposal

pdp-HYDROCODONE should be kept in a safe place, out of the sight and reach of children before, during and after use. pdp-HYDROCODONE should not be used in front of children, since they may copy these actions.

pdp-HYDROCODONE should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired pdp-HYDROCODONE should be properly disposed of as soon as it is no longer needed to prevent accidental exposure to others, including children or pets. If temporary storage is required before disposal, a sealed child-proof container, such as a biohazard waste container or a lockable medication box could be obtained from a pharmacy.

OVERDOSAGE

For management of a suspected drug overdose, call your regional Poison Control Centre.

Symptoms

Serious overdosage with hydrocodone may be 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, clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur.

Treatment

Primary attention should be given to the re-establishment of adequate respiratory exchange by providing a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone HCl is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including hydrocodone. An appropriate dose of naloxone HCl should be administered preferably by the IV route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of hydrocodone 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. The instructions contained in the package insert should be carefully observed. Oxygen, IV fluids, vasopressors, and other supportive measures should be employed as indicated. Gastric emptying may be useful in removing unabsorbed drug. Activated charcoal may be of benefit.

STORAGE AND STABILITY

Keep out of reach of children.

Keep tightly closed.

Store at 15 to 30°C. Dispense syrup in a tight, light resistant container.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Each 1 mL of red-cherry-flavored syrup contains: Hydrocodone Bitartrate 1 mg.

Nonmedicinal ingredients: Artificial Cherry Flavor, Caramel DS, FD&C Red No. 2, Hydrochloric Acid, Methylparaben, Propylparaben, Purified Water, Sorbitol Solution 70% and Sucrose.

ACTION AND CLINICAL PHARMACOLOGY

Clinical trials have proven hydrocodone bitartrate to be an effective antitussive agent which is pharmacologically 2 to 8 times as potent as codeine. At equi-effective doses, its sedative action is greater than that of codeine. The precise mechanisms of action of hydrocodone and other opiates are not known; however, hydrocodone is believed to act by directly depressing the cough centre. In excessive doses, hydrocodone, like other opium derivatives, can depress respiration. The effects of therapeutic doses of hydrocodone on the cardiovascular system are insignificant. The constipating effects of hydrocodone are much weaker than those of morphine and no stronger than those of codeine. Hydrocodone can produce miosis, euphoria, physical and psychological dependence. At therapeutic antitussive doses, it does exert analgesic effects. Following a 10-mg oral dose of hydrocodone administered to 5 male human subjects, the mean peak serum concentration was 23.6 ± 5.2 ng/mL. Maximum serum levels were achieved at approximately 1.3 ± 0.3 hours and the half-life was determined to be approximately 3.8 ± 0.3 hours. Hydrocodone exhibits a complex pattern of metabolism including O-demethylation, N-demethylation and 6-keto reduction to the corresponding 6-α- and 6-β-hydroxymetabolites.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

[N]pdp-HYDROCODONE
Hydrocodone Bitartrate Syrup

Read this carefully before you start taking **pdp-HYDROCODONE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **pdp-HYDROCODONE**.

Serious Warnings and Precautions

- **Even if you take pdp-HYDROCODONE as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death.**
- **You may get life-threatening breathing problems while taking pdp-HYDROCODONE. This is less likely to happen if you take it as prescribed by your doctor. Babies are at risk of life-threatening breathing problems if their mothers take opioids while pregnant or nursing.**
- **You should never give anyone your pdp-HYDROCODONE. They could die from taking it. If a person has not been prescribed pdp-HYDROCODONE, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took pdp-HYDROCODONE while you were pregnant, whether for short or long periods of time or in small or large doses, your baby can suffer life-threatening withdrawal symptoms after birth. This can occur in the days after birth and for up to 4 weeks after delivery. If your baby has any of the following symptoms:**
  - **has changes in their breathing (such as weak, difficult or fast breathing)**
  - **is unusually difficult to comfort**
  - **has tremors (shakiness)**
  - **has increased stools, sneezing, yawning, vomiting, or fever**

  Seek immediate medical help for your baby.
- **Taking pdp-HYDROCODONE 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.**

What is pdp-HYDROCODONE used for?
pdp-HYDROCODONE is used for the temporary relief, in adults, of coughs, runny nose, stuffy nose associated with:

- Allergies, or
- The common cold

pdp-HYDROCODONE is not for use in patients younger than 18 years of age. In patients this age, the risks of life-threatening breathing problems outweigh the benefits of treating the cough with hydrocodone.

How does pdp-HYDROCODONE work?
Hydrocodone bitartrate acts on the brain to supress cough.

Hydrocodone belongs to the family of cough medicines (cough suppressants).

What are the ingredients in pdp-HYDROCODONE?
Medicinal ingredients: Hydrocodone Bitartrate
Non-medicinal ingredients: Artificial Cherry Flavor, Caramel DS, FD&C Red No. 2, Hydrochloric Acid, Methylparaben, Propylparaben, Purified Water, Sorbitol Solution 70% and Sucrose.

pdp-HYDROCODONE comes in the following dosage forms:
Bottle of 100 mL and 500 mL

Do not use pdp-HYDROCODONE if you:
- your doctor did not prescribe it for you
- are allergic to hydrocodone bitartrate or any of the other ingredients in pdp-HYDROCODONE
- have severe asthma, trouble breathing, or other breathing problems
- have bowel blockage or narrowing of the stomach or intestines
- have severe pain in your abdomen
- have a head injury
- are at risk for having seizures
- you have a brain tumor
- suffer from alcoholism
- are taking or have taken within the past 2 weeks a Monoamine Oxidase inhibitor (MAOi) (such as phenelzine sulphate, tranylcypromine sulphate, moclobemide or selegiline)
- you are going to have, or recently had, a planned surgery
-

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take pdp-HYDROCODONE. Talk about any health conditions or problems you may have, including if you:

- have a history of illicit or prescription drug or alcohol abuse
- have severe kidney, liver or lung disease
- have low blood pressure
- have diabetes
- have heart or thyroid problem

- have glaucoma
- have past or current depression
- suffer from chronic or severe constipation
- have persistent or chronic cough (as occurs with smoking), high blood pressure,
- have problems with your adrenal or prostate gland
- have, or had in the past hallucinations or other severe mental problemsor under a physician`s care

Other warnings you should know about:

Some people metabolize hydrocodone at a much faster rate than the general population. This may lead to accidental overdose especially in patients younger than 18 years of age. Stop taking pdp-HYDROCODONE and seek immediate medical help if you start feeling confused have shallow breathing, or extreme sleepiness. If you know that you metabolize hydrocodone at a much faster rate, tell your doctor BEFORE starting this medication.

Stop taking pdp-HYDROCODONE and consult your healthcare professional if:

- you get higher fever, rash or persistent headache along with the cough.
- your symptoms or cough worsen.

These could be signs of a serious condition.

Opioid dependence and addiction
There are important differences between physical dependence and addiction. It is important that you talk to your doctor if you have any questions or concerns about abuse, addiction or physical dependence. As with all opioids, taking Hydrocodone bitartrate **may cause you to become dependent on it. Do not take more than the dose prescribed to you by your doctor.**

Pregnancy, nursing, labour and delivery
Do not use pdp-HYDROCODONE while pregnant, nursing, during labour or delivery. Opioids can be transferred to your baby through breast milk, or while still in the womb. pdp-HYDROCODONE can then cause life-threatening breathing problems in your unborn baby or nursing infant.

If you are pregnant and are taking pdp-HYDROCODONE, it is important that you don't stop taking your medication all of a sudden. If you do, it can cause a miscarriage or a still-birth. Your doctor will monitor and guide you on how to slowly stop taking pdp-HYDROCODONE. This may help avoid serious harm to your unborn baby.

Driving and using machines:
Before you do tasks, which may require special attention, you should wait until you know how you react to pdp-HYDROCODONE. pdp-HYDROCODONE can cause:

- drowsiness
- dizziness or
- light-headedness

This can usually occur after you take your first dose and when your dose is increased.

Disorder of the adrenal gland:
You may develop a disorder of the adrenal gland called adrenal insufficiency. This means that your adrenal gland is not making enough of certain hormones. You may experience symptoms such as:

- nausea, vomiting
- feeling tired, weak or dizzy

- decreased appetite

You may be more likely to have problems with your adrenal gland if you have been taking opioids for longer than one month. Your doctor may do tests, give you another medication, and slowly take you off pdp-HYDROCODONE.

Serotonin Syndrome:
Hydrocodone bitartrate, one of the ingredients of pdp-HYDROCODONE can cause Serotonin Syndrome, a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop Serotonin Syndrome if you take pdp-HYDROCODONE with certain antidepressants or migraine medications.

Serotonin Syndrome symptoms include:
- fever, sweating, shivering, diarrhea, nausea, vomiting;
- muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of coordination;
- fast heartbeat, changes in blood pressure;
- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

Sexual Function/Reproduction:
Long term use of opioids may lead to a decrease in sex hormone levels. It may also lead to low libido (desire to have sex), erectile dysfunction or being infertile.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with pdp-HYDROCODONE:
- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking pdp-HYDROCODONE. It can lead to:
    - drowsiness
    - unusually slow or weak breathing
    - serious side effects or
    - a fatal overdose
- other sedative drugs which may enhance the drowsiness caused by pdp-HYDROCODONE
- opioid analgesics (drugs used to treat pain)
- general anesthetics (drugs used during surgery)
- benzodiazepines (drugs used to help you sleep or that help reduce anxiety)
- antidepressants (for depression and mood disorders). **Do not** take pdp-HYDROCODONE with MAO inhibitors (MAOi) or if you have taken MAOi's in the last 14 days.
- drugs used to treat serious mental or emotional disorders (such as schizophrenia)
- antihistamines (drugs used to treat allergies)
- anti-emetics (drugs used to prevent vomiting)
- drugs used to treat muscle spasms and back pain

- warfarin (such as coumadin) and other anticoagulants (used to prevent or treat blood clots)
- some anti-retroviral drugs (used to treat viral infections)
- some anti-fungal drugs (used to treat fungal infections)
- some antibiotic drugs (used to treat bacterial infections)
- some heart medication (such as beta blockers)
- tranquilizers, sedatives, sedating antihistamines, other depressants

- drugs used to treat migraines (e.g. triptans)
- grapefruit juice
- St. John's Wort

How to take pdp-HYDROCODONE**:**

- Your doctor will prescribe the lowest dose that works to control your symptoms.
- Higher doses can lead to more side effects and a greater chance of overdose.
- pdp-HYDROCODONE may be taken with or without food, with a glass of water.

Usual Dose:
Adults
5 mg (5 mL (one teaspoonful) of syrup) not less than 4 hours apart, after meals and at bedtime with food or a glass of milk, not to exceed 30 mg (30 mL (six teaspoonfuls) of syrup) in a 24-hour period. Maximum single dose 15 mg (15 mL (three teaspoonfuls) of syrup).

Stopping your Medication
If you have been taking pdp-HYDROCODONE for more than a few days, you should not stop taking it all of a sudden. Your doctor will monitor and guide you on how to slowly stop taking BRAND NAME. You should do it slowly to avoid uncomfortable symptoms such as having:

- body aches
- diarrhea
- goosebumps
- loss of appetite
- nausea
- feeling nervous or restless
- runny nose
- sneezing
- tremors or shivering
- stomach cramps
- rapid heart rate (tachycardia)
- having trouble sleeping
- an unusual increase in sweating
- heart palpitations
- an unexplained fever
- weakness
- yawning

By reducing or stopping your opioid treatment, your body will become less used to opioids. If you start treatment again, you will need to start at the lowest dose. You may overdose if you restart at the last dose you took before you slowly stopped taking pdp-HYDROCODONE.

Refilling your Prescription for pdp-HYDROCODONE:
A new written prescription is required from your doctor each time you need more pdp-HYDROCODONE.
Only obtain prescriptions for this medicine from the doctor in charge of your treatment. Do not seek prescriptions from other doctors unless you switch to another doctor for your illness.

Overdose:

If you think you have taken too much pdp-HYDROCODONE, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Signs of overdose may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness

Missed Dose:
Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take your medicine and skip the missed dose. Do not take two doses at the same time.

What are possible side effects from using pdp-HYDROCODONE?
These are not all the possible side effects you may feel when taking pdp-HYDROCODONE. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Drowsiness
- Insomnia
- Dizziness
- Fainting
- Nausea, vomiting, or a poor appetite
- Dry mouth
- Headache
- Problems with vision
- Weakness, uncoordinated muscle movement
- Itching
- Sweating
- Constipation
- Low sex drive, impotence (erectile dysfunction), infertility

Serious side effects and what to do about them				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
RARE	**Overdose:** hallucinations, confusion, inability to walk normally, slow or weak breathing, extreme sleepiness, sedation, or dizziness, floppy muscles/low muscle tone, cold and clammy skin			√
	Respiratory Depression: slow, shallow or weak breathing			√
	Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			√
	Bowel Blockage (impaction): abdominal pain, severe constipation, nausea			√
	Fast, Slow or Irregular Heartbeat: heart palpitations		√	
	Low Blood Pressure: dizziness, fainting, light-headedness	√		
	Serotonin Syndrome: agitation or restlessness, loss of muscle control or muscle twitching, tremor, diarrhea			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- **Keep unused or expired pdp-HYDROCODONE in a secure place to prevent theft, misuse or accidental exposure.**
- **Keep tightly closed**
- **Keep pdp-HYDROCODONE under lock, out of sight and reach of children and pets.**
- **Never take medicine in front of small children as they will want to copy you. Accidental ingestion by a child is dangerous and may result in death. If a child accidentally takes pdp-HYDROCODONE, get emergency help right away.**
- Store at 15 to 30°C. Dispense syrup in a tight, light resistant container.

Disposal:

pdp-HYDROCODONE should never be thrown into household trash, where children and pets may find it. It should be returned to a pharmacy for proper disposal.

If you want more information about pdp-HYDROCODONE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling the manufacturer at 1-888-550-6060.

This leaflet was prepared by

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