PRESCRIBING INFORMATION

[N] CODEINE 15

Codeine Phosphate Tablets, USP
15 mg

[N] CODEINE 30

Codeine phosphate Tablets, USP
30 mg

Opioid Analgesic/Antitussive

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Table of contents

[N] CODEINE 15 and [N] CODEINE 30
Codeine Phosphate Tablets, USP
15 mg and 30 mg Tablets

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Tablets	Colloidal Silicon Dioxide, Lactose, Magnesium Stearate, Microcrystalline Cellulose and Sodium Croscarmellose.

INDICATIONS AND CLINICAL USE

Adults

CODEINE 15 and CODEINE 30 is indicated for the symptomatic treatment of mild to moderate pain of various causes and the control of exhausting, nonproductive cough which does not respond to non-opioid antitussives. **CODEINE 15 and CODEINE 30** is not indicated as an as-needed (prn) analgesic.

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 (see **ACTION AND CLINICAL PHARMACOLOGY**, **Special Populations and Conditions**, **Geriatrics**).

Pediatrics (< 12 years of age)

The safety and efficacy of CODEINE 15 and CODEINE 30 has not been studied in the pediatric population. Regardless of clinical setting, the use of codeine is contraindicated in patients below the age of 12 years due to increased safety concerns (see **CONTRAINDICATIONS** and **WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics**).

CONTRAINDICATIONS

- Patients who are hypersensitive to the active substance codeine phosphate 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 Prescribing Information.
- 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 mild pain that can be managed with other pain medications.
- 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).
- Women who are breast-feeding, pregnant or during labour and delivery.
- Pediatric patients <12 years of age
- Pediatric patients (<18 years of age) who have undergone tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome

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 risks of overdose and death with immediate release opioid formulations, CODEINE 15 and CODEINE 30 (codeine phosphate) should only be used in patients for whom alternative treatment options (e.g., non-opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate management of pain (see DOSAGE AND ADMINISTRATION).

Addiction, Abuse, and Misuse

CODEINE 15 and CODEINE 30 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 CODEINE 15 and CODEINE 30, and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS). CODEINE 15 and CODEINE 30 should be stored securely to avoid theft or misuse.

Life-threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of CODEINE 15 and CODEINE 30. Patients should be monitored for respiratory depression, especially during initiation of CODEINE 15 and CODEINE 30 or following a dose increase.

Tablets: **CODEINE 15 and CODEINE 30 must be swallowed whole. Cutting, breaking, crushing, chewing, or dissolving CODEINE 15 and CODEINE 30 can lead to dangerous adverse events including death (see WARNINGS AND PRECAUTIONS).**

SERIOUS WARNINGS AND PRECAUTIONS

Accidental Exposure

Accidental ingestion of even one dose of CODEINE 15 and CODEINE 30, especially by children, can result in a fatal overdose of Codeine phosphate (see DOSAGE AND ADMINISTRATION, Disposal, for instructions on proper disposal).

Neonatal Opioid Withdrawal Syndrome

Prolonged maternal use of CODEINE 15 and CODEINE 30 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 CODEINE 15 and CODEINE 30 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 central nervous system (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 CODEINE 15 and CODEINE 30 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

Patients should be instructed not to give CODEINE 15 and CODEINE 30 (codeine phosphate) tablets to anyone other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death. CODEINE 15 and CODEINE 30 should be stored securely to avoid theft or misuse.

CODEINE 15 and CODEINE 30 should only be prescribed by persons knowledgeable in the continuous administration of potent opioids, in the management of patients receiving potent opioids for the treatment of pain, and in the detection and management of respiratory depression, including the use of opioid antagonists.

Patients should be cautioned not to consume alcohol while taking **CODEINE 15 and CODEINE 30** as it may increase the chance of experiencing serious adverse events, including death.

Hyperalgesia that will not respond to a further dose increase of codeine phosphate can occur at particularly high doses. A codeine phosphate dose reduction or change in opioid may be required.

Abuse and Misuse

Like all opioids, **CODEINE 15 and CODEINE 30** is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, **CODEINE 15 and CODEINE 30** 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.

Opioids, such as **CODEINE 15 and CODEINE 30**, should be used with particular care in patients with a history of alcohol and illicit/prescription drug abuse. However, concerns about abuse, addiction, and diversion should not prevent the proper management of pain.

CODEINE 15 and CODEINE 30 is intended for oral use only. The tablets should be swallowed whole, and not chewed or crushed. Abuse of oral dosage forms can be expected to result in serious adverse events, including death.

Cardiovascular

Codeine phosphate administration may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of drugs such as phenothiazines and other tranquilizers, sedative/hypnotics, tricyclic antidepressants or general anesthetics. These patients should be monitored for signs of hypotension after initiating or titrating the dose of CODEINE 15 and CODEINE 30.

The use of **CODEINE 15 and CODEINE 30** in patients with circulatory shock should be avoided as it may cause vasodilation that can further reduce cardiac output and blood pressure.

Dependence/Tolerance

As with other opioids, tolerance and physical dependence may develop upon repeated administration of **CODEINE 15 and CODEINE 30** 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.

Patients on prolonged therapy should be tapered gradually from the drug if it is no longer required for pain control. Withdrawal symptoms may occur 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 analgesic 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).**

Use in Drug and Alcohol Addiction

CODEINE 15 and CODEINE 30 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 pain requiring opioid analgesia.

Gastrointestinal Effects

Codeine phosphate and other morphine-like opioids have been shown to decrease bowel motility. Codeine phosphate 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.

Use of **CODEINE 15 and CODEINE 30** is contraindicated in pregnant women (see **CONTRAINDICATIONS**).

Neurologic

Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol): CODEINE 15 and CODEINE 30 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. 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 **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 **CODEINE 15 and CODEINE 30** 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**).

CODEINE 15 and CODEINE 30 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**).

Severe pain antagonizes the subjective and respiratory depressant actions of opioid analgesics. Should pain suddenly subside, these effects may rapidly become manifest.

Serotonin Syndrome: Codeine phosphate tablets 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 serotoninergic 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. CODEINE 15 and CODEINE 30 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**).

Head Injury: The respiratory depressant effects of codeine phosphate, 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, codeine phosphate may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, codeine phosphate must be used with extreme caution and only if it is judged essential (see **CONTRAINDICATIONS).**

Peri-Operative Considerations

CODEINE 15 and CODEINE 30 is not indicated for pre-emptive analgesia (administration pre-operatively for the management of post-operative pain).

In the case of planned chordotomy or other pain-relieving operations, patients should not be treated with CODEINE 15 and CODEINE 30 for at least 24 hours before the operation and CODEINE 15 and CODEINE 30 should not be used in the immediate post-operative period.

Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. Thereafter, if **CODEINE 15 and CODEINE 30** is to be continued after the patient recovers from the post-operative period, a new dosage should be administered in accordance with the changed need for pain relief. The risk of withdrawal in opioid-tolerant patients should be addressed as clinically indicated.

The administration of analgesics in the peri-operative period should be managed by healthcare providers with adequate training and experience (e.g., by an anesthesiologist).

Codeine phosphate and other morphine-like opioids have been shown to decrease bowel motility. Ileus is a common post-operative complication, especially after intra-abdominal surgery with opioid analgesia. Caution should be taken to monitor for decreased bowel motility in post-operative patients receiving opioids. Standard supportive therapy should be implemented.

CODEINE 15 and CODEINE 30 should not be used in the early post-operative period (12 to 24 hours post-surgery) unless the patient is ambulatory and gastrointestinal function is normal.

Psychomotor Impairment

CODEINE 15 and CODEINE 30 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 Codeine phosphate with other CNS depressants, including other opioids, phenothiazine, sedative/hypnotics and alcohol.

Respiratory

Respiratory Depression: 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. Codeine phosphate 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 CODEINE 15 and CODEINE 30, 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 CODEINE 15 and CODEINE 30 and following dose increases.

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.

To reduce the risk of respiratory depression, proper dosing and titration of CODEINE 15 and CODEINE 30 are essential. Overestimating the CODEINE 15 and CODEINE 30 dose when converting patients from another opioid product can result in a fatal overdose with the first dose. In these patients, the use of non-opioid analgesics should be considered, if feasible (see **WARNINGS AND PRECAUTIONS**, **Special Populations**, **Special Risk Groups**, and **DOSAGE AND ADMINISTRATION**).

Respiratory depression and death have occurred in children who received codeine in the postoperative period following tonsillectomy and/or adenoidectomy and had evidence of being ultra-rapid metabolizers of codeine (i.e., multiple copies of the gene for cytochrome P450

isoenzyme 2D6 or high morphine concentrations). Children with obstructive sleep apnea who are treated with codeine for post-tonsillectomy and/or adenoidectomy pain may be particularly sensitive to the respiratory depressant effects of codeine that has been rapidly metabolized to morphine. Codeine-containing products are contraindicated for post-operative pain management in all pediatric patients undergoing tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome (see **CONTRAINDICATIONS**).

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 preexisting respiratory depression for respiratory depression, particularly when initiating therapy and titrating with CODEINE 15 and CODEINE 30, as in these patients, even usual therapeutic doses of CODEINE 15 and CODEINE 30 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 CODEINE 15 and CODEINE 30 is contraindicated in patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see **CONTRAINDICATIONS**).

Sensitivity/Resistance

Pruritus, urticaria, other skin rashes, edema, diaphoresis, wheal and flare over the vein with i.v. injection. Because of close structural similarities, patients exhibiting systemic allergy to morphine (e.g., generalized rash, shortness of breath) should not receive codeine, diamorphine, hydromorphone, oxycodone or oxymorphone.

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.

Special Populations

Special Risk Groups: Codeine phosphate 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. CODEINE 15 and CODEINE 30 crosses the placental barrier and should not be administered to pregnant women unless in the judgment of the physician, potential benefits outweigh the risks

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

Labour, Delivery and Nursing Women: Since opioids can cross the placental barrier and are excreted in breast milk, CODEINE 15 and CODEINE 30 should not be used unless, in the judgement of the physician, the potential benefits outweigh the risks. Respiratory depression can occur in the infant if opioids are administered during labour. Naloxone, a drug that counters the effects of opiates, should be readily available.

Pediatrics (< 12 years of age): The safety and efficacy of CODEINE 15 and CODEINE 30 have not been studied in the pediatric population. Regardless of clinical setting, the use of codeine is contraindicated in patients below the age of 12 years due to increased safety concerns (see **CONTRAINDICATIONS** and **WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics**).

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** and **ACTION AND CLINICAL PHARMACOLOGY**, **Special Populations and Conditions**, **Geriatrics**).

Patients with Hepatic and/or Renal Impairment:

Codeine should be given with caution and the initial dose should be reduced in certain patients such as the debilitated and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture (see **DOSAGE AND ADMINISTRATION**.

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-Marketing Experience**)

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse effects of codeine phosphate tablets are similar to those of other opioid analgesics, and represent an extension of pharmacological effects of the drug class. The major hazards of opioids include respiratory and central nervous system depression and to a lesser degree, circulatory depression, respiratory arrest, shock and cardiac arrest.

The most frequently observed adverse effects of codeine phosphate are: Sedation, nausea and vomiting, constipation and sweating. These effects seem to be more prominent in ambulatory patients and in those not experiencing severe pain. In such individuals, lower doses are advisable. Some adverse reactions may be alleviated if the patient lies down.

Sedation: Sedation is a common side effect of opioid analgesics, especially in opioid naïve individuals. Sedation may also occur partly because patients often recuperate from prolonged fatigue after the relief of persistent pain. Most patients develop tolerance to the sedative effects of opioids within three to five days and, if the sedation is not severe, will not require any treatment except reassurance. If excessive sedation persists beyond a few days, the dose of the opioid should be reduced and alternate causes investigated. Some of these are: concurrent CNS depressant medication, hepatic or renal dysfunction, brain metastases, hypercalcemia and respiratory failure. If it is necessary to reduce the dose, it can be carefully increased again after three or four days if it is obvious that the pain is not being well controlled. Dizziness and unsteadiness may be caused by postural hypotension, particularly in elderly or debilitated patients, and may be alleviated if the patient lies down.

Nausea and Vomiting: Nausea is a common side effect on initiation of therapy with opioid analgesics and is thought to occur by activation of the chemoreceptor trigger zone, stimulation of the vestibular apparatus and through delayed gastric emptying. The prevalence of nausea declines following continued treatment with opioid analgesics. When instituting therapy with an opioid for chronic pain, the routine prescription of an antiemetic should be considered. In the cancer patient, investigation of nausea should include such causes as constipation, bowel obstruction, uremia, hypercalcemia, hepatomegaly, tumor invasion of celiac plexus and concurrent use of drugs with emetogenic properties. Persistent nausea which does not respond to dosage reduction may be caused by opioid-induced gastric stasis and may be accompanied by other symptoms including anorexia, early satiety, vomiting and abdominal fullness. These symptoms respond to chronic treatment with gastrointestinal prokinetic agents.

Constipation: Practically all patients become constipated while taking opioids on a persistent basis. In some patients, particularly the elderly or bedridden, fecal impaction may result. It is essential to caution the patients in this regard and to institute an appropriate regimen of bowel management at the start of prolonged opioid therapy. Stimulant laxatives, stool softeners, and other appropriate measures should be used as required. As fecal impaction may present as overflow diarrhea, the presence of constipation should be excluded in patients on opioid therapy prior to initiating treatment for diarrhea.

The following adverse effects occur less frequently with opioid analgesics and include those reported in codeine phosphate clinical trials, whether related or not to codeine phosphate.

Cardiovascular: Supraventricular tachycardia, bradycardia, palpitations, faintness, syncope, postural hypotension and hypertension, and phlebitis following i.v. injection.

Gastrointestinal: Dry mouth, nausea, vomiting, constipation, biliary tract spasm, laryngospasme, anorexia, diarrhea, cramps, dyspepsia, taste alterations.

General and CNS: Drowsiness, sedation, euphoria, dysphoria, weakness, headache, agitation, seizures, uncoordinated muscle movements, alterations of mood, dreams, hallucinations and disorientation, visual disturbances, insomnia, miosis, toxic psychoses.

Genitourinary: Urinary retention or hesitance, antidiuretic effect, reduced libido and/or potency.

Respiratory:

Codeine, including CODEINE 15 and CODEINE 30 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.

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 physiologic complications, and that appropriate therapy for the primary disease is provided.

Use with extreme caution in patients having an acute asthmatic attack, patients with chronic obstructive pulmonary disease or cor pulmonale, patients having a substantially decreased respiratory reserve and patients with preexisting respiratory depression, hypoxia or hypercapnia. Usual therapeutic doses may decrease respiratory drive while simultaneously, increasing airway resistance to the point of apnea. In patients with asthma or pulmonary emphysema, codeine may, due to its drying action on the respiratory mucosa, increase viscosity of bronchial secretions and suppress the cough reflex.

Use with caution in sedated or debilitated patients, in patients who have undergone thoracotomies or laparotomies, since suppression of the cough reflex may lead to retention of secretions postoperatively in these patients.

The respiratory depressant effects of codeine and its capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury or intracranial lesions or pre-existing increase in intracranial pressure. Opioids produce adverse reactions which may obscure the clinical course of a patient with head injuries. In such patients, codeine must be used with extreme caution and only if its use is deemed essential.

Use with caution in patients with seizures as they may be exacerbated or induced by opioids. Use with caution in patients with cardiac arrhythmias due to the cholinergic effects of the drug.
Codeine should be given with caution and the initial dose should be reduced in certain patients such as the debilitated and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture.

Hypersensitivity:

Pruritus, urticaria, other skin rashes, edema, diaphoresis, wheal and flare over the vein with i.v. injection. Because of close structural similarities, patients exhibiting systemic allergy to morphine (e.g., generalized rash, shortness of breath) should not receive codeine, diamorphine, hydromorphone, oxycodone or oxymorphone.

Nausea and Vomiting:

Occur frequently after single doses of narcotics or as an early unwanted effect of regular opioid analgesic therapy.

Withdrawal Syndrome:

Physical dependence with or without psychological dependence tends to occur with chronic administration. An abstinence syndrome may be precipitated when an opioid analgesic is abruptly discontinued or opioid antagonists are administered. The following withdrawal symptoms may be observed after abrupt discontinuation of an opioid analgesic: body aches, diarrhea, gooseflesh, loss of appetite, nervousness or restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, nausea, sleep disturbances, unusual increase in sweating and yawning, weakness, tachycardia and unexplained fever. With appropriate medical use and gradual withdrawal from opioid analgesics, these symptoms are usually mild.

Other:

Abnormal liver function test results (propoxyphene flushing/warmth).

Post-Marketing Experience:

Androgen deficiency: Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical 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. Patients presenting with symptoms of androgen deficiency should undergo laboratory evaluation.

DRUG INTERACTIONS

Serious Drug Interactions

Neuromuscular Blocking Agents:

Opioid analgesics may enhance the effects of neuromuscular blocking agents resulting in increased respiratory depression.

Overview

Interaction with Central Nervous System (CNS) Depressants:

Interaction with Benzodiazepines and Other Central Nervous System (CNS)

Depressants: 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. 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 AND PRECAUTIONS, Neurologic, Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol) and Psychomotor Impairment**). CODEINE 15 and CODEINE 30 should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

Coadministration of codeine phosphate 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).

Drug-Drug Interactions

Anticholinergics:

Concomitant use of drugs with antimuscarinic activity may increase the risk of severe constipation and/or urinary retention.

Cimetidine:

Concurrent administration of cimetidine may lead to increased effect or toxicity of opioid analgesics.

CNS Agents:

Concomitant administration of other CNS drugs such as sedatives, hypnotics, phenothiazines, anesthetics and alcohol may increase the sedative and depressant effects of opioid analgesics. If the concomitant use of these drugs is considered necessary, their doses should be reduced accordingly.

MAO Inhibitors:

Serious adverse reactions have been reported in patients who receive MAO inhibitors with pethidine. Other opioid analgesics should be used with extreme caution, if at all, in patients taking MAO inhibitors (including selegiline) or within 14 days of such therapy.

Opioid Antagonists:

Naltrexone and agonist-antagonist opioid analgesics (i.e., pentazocine, nalbuphine, butorphanol) should not be administered to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic. In these patients, mixed agonist-antagonists may reduce the analgesic effect or may precipitate withdrawal symptoms.

Other Opioids:

The use of more than one opioid agonist at a time is usually inappropriate; additive CNS depressant, respiratory depressant and hypotensive effects may occur if 2 or more agonists are used concurrently. Potentiation of effects may occur with a previously administered long-acting opioid analgesic.

Tricyclic Antidepressants:

Tricyclic antidepressants may enhance opioid-induced respiratory depression.

Warfarin:

Opioid agonists may potentiate the anticoagulant effects of coumarin anticoagulants.

Drug Laboratory Test Interactions:

Opioid analgesics may interfere with certain diagnostic procedures, by increasing plasma amylase and lipase concentrations and by increasing CSF pressure. Gastric emptying is delayed by these drugs so gastric emptying studies will not be valid.

Drug-Lifestyle Interactions

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

DOSAGE AND ADMINISTRATION

CODEINE 15 and CODEINE 30 should only be used in patients for whom alternative treatment options are ineffective or not tolerated (e.g., non-opioid analgesics).

CODEINE 15 and CODEINE 30 Tablets must be swallowed whole. Cutting, breaking, crushing, chewing, or dissolving CODEINE 15 and CODEINE 30 can lead to dangerous adverse events including death (see WARNINGS AND PRECAUTIONS).

Dosing Considerations

CODEINE 15 and CODEINE 30 (codeine phosphate tablets) should be used with caution within 12 hours pre-operatively and within the first 12-24 hours post-operatively (see **WARNINGS AND PRECAUTIONS, Peri-operative Considerations**).

CODEINE 15 and CODEINE 30 is not indicated for rectal administration.

CODEINE 15 and CODEINE 30 may be taken with or without food with a glass of water.

The dose initiation should follow a conservative approach in certain patients such as the debilitated and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture.

The recommended adult starting dose in these patients should be at 1/3 to 1/2 the usual starting dose followed by careful dose titration to adequate pain control according to their clinical situation.

Recommended Dose and Dosage Adjustment

Codeine, including CODEINE 15 and CODEINE 30, should be prescribed at the lowest effective dose for the shortest period of time. Dosing should be as needed every 4 to 6 hours and not on scheduled intervals.

15 and 30 mg tablets:

Analgesia:

Oral Administration; adults and children 12 years of age or older: 15 to 60 mg every 4 to 6 hours as necessary.

Antitussive:

Oral: Adults and children 12 years of age or older: 15 to 30 mg every 6 to 8 hours as necessary to a maximum of 120 mg daily.

Children under 12 years of age: Safety and efficacy of codeine in children has not been established and its use in this age group is contraindicated due to increased safety concerns (see **CONTRAINDICATIONS**).

Doses should be adjusted in renal failure: For creatinine clearance of 10 to 50 mL/min, decrease the dose by 25% and titrate. If creatinine clearance is less than 10 mL/min, decrease the dose by 50% and titrate.

Patients Not Receiving Opioids at the Time of Initiation of Codeine Treatment:

The usual initial adult dose of **CODEINE 15 and CODEINE 30** for patients who have not previously received opioid analgesics is 15 to 30 mg, orally, every 4 to 6 hours as necessary.

Patients Currently Receiving Opioids:

For patients who are currently receiving other opioids, please refer to the following table to determine the approximate analgesic equivalences of various opioid analgesics.

OPIOID ANALGESICS: APPROXIMATE ANALGESIC EQUIVALENCES [1]

Drug	Equivalent Dose (mg) [2] (compared to morphine 10 mg IM)		Duration of Action (hours)
	Parenteral	**Oral**	
Strong Opioid Agonists:			
Morphine	10	60 [3]	3-4
Oxycodone	15	30 [4]	2-4
Hydromorphone	1.5	7.5	2-4
Anileridine	25	75	2-3
Levorphanol	2	4	4-8
Meperidine [6]	75	300	1-3
Oxymorphone	1.5	5 (rectal)	3-4
Methadone [5]	-	-	-
Heroin	5-8	10-15	3-4
Weak Opioid Agonists:			
Codeine	120	200	3-4
Propoxyphene	50	100	2-4
Mixed Agonist-Antagonists [7]:			
Pentazocine [6]	60	180	3-4
Nalbuphine	10	-	3-6
Butorphanol	2	-	3-4

Footnotes:

[1] References:

- Expert Advisory Committee on the Management of Severe Chronic Pain in Cancer Patients, Health and Welfare Canada. Cancer pain: A monograph on the management of cancer pain. Ministry of Supplies and Services Canada, 1987. Cat. No. H42-2/5-1984E.
- Foley KM. The treatment of cancer pain. N Engl J Med 1985;313(2):84-95.
- Aronoff GM, Evans WO. Pharmacological management of chronic pain: A review. In: Aronoff GM, editor. Evaluation and treatment of chronic pain. 2nd ed. Baltimore (MD): Williams and Wilkins; 1992. p. 359-68.
- Cherny NI, Portenoy RK. Practical issues in the management of cancer pain. In: Wall PD, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 1437- 67.

[2] **Most of the data were derived from single-dose, acute pain studies and should be considered an approximation for selection of doses when treating chronic pain. As analgesic conversion factors are approximate and patient response may vary, dosing should be individualized according to relief of pain and side effects. Because of incomplete cross-tolerance, dose reductions of 25% to 50% of the equianalgesic dose may be appropriate in some patients when converting from one opioid to another, particularly at high doses. [†]Upward titration may be required to reach appropriate maintenance doses.**

[†] Levy MH. Pharmacologic treatment of cancer pain. N Engl J Med 1996;335:1124-1132.

[3] **For acute pain, the oral or rectal dose of morphine is six times the injectable dose. However, for chronic dosing, clinical experience indicates that this ratio is 2-3:1 (i.e., 20- 30 mg of oral or rectal morphine is equivalent to 10 mg of parenteral morphine).**

[4] Based on single entity oral oxycodone in acute pain.

[5] Extremely variable equianalgesic dose. Patients should undergo individualized titration starting at an equivalent to 1/10 of the morphine dose.

[6] Not recommended for the management of chronic pain.

[7] Mixed agonist-antagonists can precipitate withdrawal in patients on pure opioid agonists.

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. CODEINE 15 and CODEINE 30 should be initiated at a low dose and slowly titrated to effect (see **WARNINGS AND PRECAUTIONS** and **ACTION AND CLINICAL PHARMACOLOGY**).

Use with Non-Opioid Medications:

If a non-opioid analgesic is being provided, it may be continued. If the non-opioid is discontinued, consideration should be given to increasing the opioid dose to compensate for the non-opioid analgesic. **CODEINE 15 and CODEINE 30** can be safely used concomitantly with usual doses of other non-opioid analgesics.

Dose Titration:

Dose titration is the key to success with opioid analgesic therapy. **Proper optimization of doses scaled to the relief of the individual's pain should aim at administration of the lowest dose which will achieve the overall treatment goal of satisfactory pain relief with acceptable side effects.**

Dosage adjustments should be based on the patient's clinical response.

Adjustment or Reduction of Dosage:

Physical dependence with or without psychological dependence tends to occur with chronic administration of opioids, including codeine phosphate tablets. Withdrawal (abstinence) symptoms may occur following abrupt discontinuation of therapy. These symptoms may include body aches, diarrhea, gooseflesh, 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.

Patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control. In patients who are appropriately treated with opioid analgesics and who undergo gradual withdrawal for the drug, these symptoms are usually mild (see **WARNINGS AND PRECAUTIONS**).

Disposal

CODEINE 15 and CODEINE 30 should be kept in a safe place, out of the sight and reach of

children before, during and after use. CODEINE 15 and CODEINE 30 should not be used in front of children, since they may copy these actions.

CODEINE 15 and CODEINE 30 should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired CODEINE 15 and CODEINE 30 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.

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.

OVERDOSAGE

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

Symptoms:

euphoria, dysphoria visual disturbances, hypotension and coma or death from respiratory depression.

Treatment:

Symptomatic and supportive therapy. Maintain ventilation and administer oxygen as needed. The opioid antagonist naloxone should be administered. If the patient is conscious and has not lost the gag reflex, empty the stomach by inducing emesis with ipecac syrup. If the patient is extremely drowsy, unconscious, convulsing or has no gag reflex, perform gastric lavage. Follow with activate charcoal (50 to 100 g in adults) and a cathartic.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Codeine exerts its effect on opiate receptors, primarily in the CNS and smooth muscle. Its effects include: analgesia, respiratory depression, suppression of the cough reflex, decreased gastrointestinal motility. CNS changes and stimulation of the chemoreceptor trigger zone which causes nausea and vomiting.

Pharmacokinetics:

Codeine is well absorbed orally and from parenteral sites. Onset of analgesic action occurs in 10 to 30 minutes after parenteral administration or in up to 45 minutes following an oral dose. Peak effect is reached in 30 to 60 minutes after an i.m. or s.c. dose or 1 to 2 hours after oral dosing. Analgesia lasts 4 to 6 hours. Codeine's antitussive effect peaks within 1 to 2 hours and lasts up to 4 hours. Its plasma half-life is approximately 3 to 4 hours but may be as long as 19 hours in anephric patients. Codeine is approximately 7% bound to plasma protein; its volume of

distribution is 2.5 to 3.5 L/kg. It is primarily metabolized by the liver, and its metabolites, some active, are eliminated in the urine. Only a small fraction (0.01) is excreted unchanged.

See Annex 1 (opioid analgesics: approximate analgesic equivalence) for the opioid analgesic response equivalent to that from 10 mg of morphine.

Central Nervous System:

Codeine phosphate produces respiratory depression by direct action on brain stem respiratory centres. The respiratory depression involves both a reduction in the responsiveness of the brain stem centres to increases in CO_2 tension and to electrical stimulation.

Codeine phosphate depresses the cough reflex by direct effect on the cough centre in the medulla. Antitussive effects may occur with doses lower than those usually required for analgesia.

Codeine phosphate 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 origin may produce similar findings). Marked mydriasis rather than miosis may be seen with hypoxia in the setting of codeine phosphate overdose.

Gastrointestinal Tract and Other Smooth Muscle:

Codeine phosphate 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 gastric, biliary and pancreatic secretions, spasm of the sphincter of Oddi, and transient elevations in serum amylase.

Cardiovascular System:

Codeine phosphate may produce release of histamine with or without associated peripheral vasodilation. Manifestations of histamine release and/or peripheral vasodilatation may include pruritus, flushing, red eyes, hyperhidrosis and/or orthostatic hypotension.

Endocrine System:

Opioids may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical signs and symptoms may be manifest from these hormonal changes.

Immune System:

In vitro and animal studies indicate that opioids have a variety of effects on immune functions, depending on the context in which they are used. The clinical significance of these findings is unknown.

Special Populations and Conditions

Pediatrics:

The use of codeine is contraindicated in patients below the age of 12 years due to increased safety

concerns (see **CONTRAINDICATIONS** and **WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics**).

Geriatrics:

Elderly patients may be more susceptible to adverse effects, especially respiratory depression and constipation. Caution is advised; the initial dose should be reduced and effects monitored. Elimination and metabolism may be slowed; lower doses or longer dosing intervals may be required.

STORAGE AND STABILITY

Store between 15-30 °C.

SPECIAL HANDLING INSTRUCTIONS

Not applicable.

DOSAGE FORMS, COMPOSITION AND PACKAGING

CODEINE 15: each white tablet contains 15 mg of codeine phosphate. Also contains as non-medicinal ingredients: Colloidal Silicon Dioxide, Lactose, Magnesium Stearate, Microcrystalline Cellulose and Sodium Croscarmellose. Available in bottles of 100 tablets.

CODEINE 30: each white tablet contains 30 mg of codeine phosphate. Also contains as non-medicinal ingredients: Colloidal Silicon Dioxide, Lactose, Magnesium Stearate, Microcrystalline Cellulose and Sodium Croscarmellose. Available in bottles of 100 and 500 tablets.

Store between 15-30 °C.

PART II: SCIENTIFIC INFORMATION

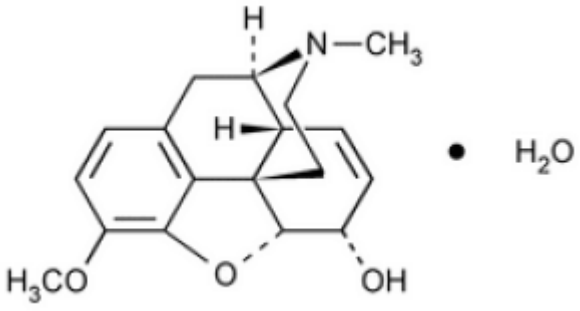
PHARMACEUTICAL INFORMATION

Proper name: **Codeine phosphate**

Chemical name: Morphinan-6-ol,7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-, (5α, 6α)-, phosphate (1:1) (salt).

Molecular formula: $C_{18}H_{24}NO_7P$
C54.41%, H6.09%, N3.53%, O28.18%, P7.79%

Structural formula**:**



Molecular weight: 397.37

Physical state: Hemihydrate, fine, white, needle-shaped crystals; a crystalline powder; odourless, affected by light.

Solubility: Freely soluble in water, very soluble in hot water, slightly soluble in alcohol, more soluble in boiling alcohol.

ANNEX 1

OPIOID ANALGESICS: APPROXIMATE ANALGESIC EQUIVALENCES [1]

Drug	Equivalent Dose (mg) [2] (compared to morphine 10 mg IM)		Duration of Action (hours)
Strong Opioid Agonists:			
Morphine (single dose)	10	60	3-4
(chronic dose)	10	20-30 [3]	3-4
Hydromorphine	1.5-1	6-7.5	2-4
Anileridine	25	75	2-3
Levophanol	2	4	4-8
Meperidine [1]	75	300	1-3
Oxymorphone	1.5	5(rectal)	3-4
Methadone [2]	-	-	-
Heroin	5-8	10-15	3-4
Weak Opioid Agonists:		-	-
Codeine	120	200	3-4
Oxycodone	5-10	10-15	2-4
Propoxyphene	50	100	2-4
Mixed Agonist Antagonists [3]			
Pentazocine [1]	60	180	3-4
Nalbuphine	10	-	3-6
Butorphanol	2	-	3-4

Most of these data were derived from single-dose, acute pain studies and should be considered
2 an approximation for selection of doses when treating chronic pain.
For acute pain, the oral dose of morphine is six times the injectable dose. However, for chronic dosing, this ration becomes 2 or 3: 1, possibly due to the accumulation of active
3 metabolites.
These drugs are not recommended for the management of chronic pain.

REFERENCES

1. Cancer Pain: A monograph on the Management of Cancer Pain, Health and WelfareCanada 1984.

2. Foley, K.M. New Engl. J. Med. 313: 84-95, 1985. Aronoff, G.M. and Evans, W.O., In: Evaluation and Treatment of chronic Pain 2nd Ed., G.M. Aronoff (Ed.), Williams and Wilkins, Baltimore, pp. 359-368 1992.

3. Cheerny, N.I. and Portenoy, R.K., In:Textbook of Pain, 3rd Ed., P.D. Wall and R. Melzack (Eds.), Churchill Livingstone, London, pp. 1437-1467, 1994.

4. TEVA-CODEINE Prescribing Information, Teva Canada Limited, Submission Control No. 205236 Dated October 17, 2017.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

^{N}CODEINE 15 and ^{N}CODEINE 30
Codeine phosphate Tablets, USP

Read this carefully before you start taking **CODEINE 15 and CODEINE 30** 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 **CODEINE 15 and CODEINE 30**.

Serious Warnings and Precautions

- **Even if you take CODEINE 15 and CODEINE 30 as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death.**
- **When you take CODEINE 15 and CODEINE 30 it must be swallowed whole. Do not cut, break, crush, chew, dissolve the tablet. This can be dangerous and can lead to death or seriously harm you.**
- **You may get life-threatening breathing problems while taking CODEINE 15 and CODEINE 30. This is less likely to happen if you take it as prescribed by your doctor.**
- **You should never give anyone your CODEINE 15 and CODEINE 30. They could die from taking it. If a person has not been prescribed CODEINE 15 and CODEINE 30, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took CODEINE 15 and CODEINE 30 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 CODEINE 15 and CODEINE 30 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 CODEINE 15 and CODEINE 30 used for?

CODEINE 15 and CODEINE 30 is used for adults and children 12 years and older to relieve:
- mild to moderate pain
- non-productive cough that does not respond to other cough medicines

Your pain may increase or decrease from time to time and your doctor may need to change the amount of codeine you take daily (daily dosage).

How does CODEINE 15 and CODEINE 30 work?

Codeine belongs to a class of drugs which is commonly referred to as opiates, opioids or narcotics, and also includes fentanyl, hydromorphone, morphine and oxycodone.

CODEINE 15 and CODEINE 30 is a painkiller belonging to the class of drugs known as opioids. It relieves pain by acting on specific nerve cells of the spinal cord and brain.

CODEINE 15 and CODEINE 30 is indicated for the symptomatic treatment of mild to moderate pain of various causes and the control of exhausting, nonproductive cough which does not respond to non- opioid antitussives.

What are the ingredients in CODEINE 15 and CODEINE 30?

Medicinal ingredients: Codeine phosphate

Non-medicinal ingredients: Colloidal Silicon Dioxide, Lactose, Magnesium Stearate, Microcrystalline Cellulose and Sodium Croscarmellose.

CODEINE 15 and CODEINE 30 comes in the following dosage forms:

Tablet: 15mg and 30 mg

Do not use CODEINE 15 and CODEINE 30 if:

- your doctor did not prescribe it for you;
- your pain is mild;
- you are allergic to codeine phosphate or any of the other ingredients in CODEINE 15 and CODEINE 30
- you can control your pain by the occasional use of other pain medications. This includes those available without a prescription
- you have severe asthma, trouble breathing, or other breathing problems
- you have any heart problems
- you have bowel blockage or narrowing of the stomach or intestines
- you have severe pain in your abdomen
- you have a head injury
- you are at risk for seizures
- you suffer from alcoholism
- you have a condition where the small bowel does not work properly (paralytic ileus) or you have severe pain in your abdomen, or are at risk of blocked intestines;

- you had surgery less than 24 hours ago;
- you 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 a planned surgery
- you are pregnant or planning to become pregnant or you are in labour
- you are breastfeeding
- you are less than 12 years old
- you are less than 18 years old and are having (or have recently had) your tonsils or adenoids removed because of frequent interruption of breathing during sleep

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CODEINE 15 and CODEINE 30. 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 disease
- have severe liver disease
- have low blood pressure
- have or had depression
- suffer from chronic or severe constipation
- have problems with your thyroid, adrenal or prostate gland
- have, or had in the past hallucinations or other severe mental problems
- are pregnant or planning to become pregnant
- are breastfeeding
- are suffer from migraines

Other warnings you should know about:

Driving and using machines: Before you do tasks which may require special attention, you should wait until you know how you react to CODEINE 15 and CODEINE 30. CODEINE 15 and CODEINE 30 can cause:

- drowsiness
- dizziness or
- lightheadedness

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

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 CODEINE 15 and CODEINE 30:

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking CODEINE 15 and CODEINE 30. It can lead to:
    - drowsiness
    - unusually slow or weak breathing

    - serious side effects or
    - a fatal overdose
- other 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 CODEINE 15 and CODEINE 30 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 for the prevention of vomiting)
- drugs used to treat muscle spasms and back pain
- drugs used to treat migraines (e.g. triptans)
- warfarin (such as coumadin) and other anticoagulants (used for prevention or treatment of blood clots)
- anti-retroviral drugs (used to treat viral infections)
- anti-fungal drugs (used to treat fungal infections)
- antibiotic drugs (used to treat bacterial infections)
- some heart medication (such as beta blockers)
- grapefruit juice

How to take CODEINE 15 and CODEINE 30:

CODEINE 15 and CODEINE 30 tablets must be swallowed whole and should not be chewed, dissolved or crushed, since this can cause the release of too much codeine that can seriously harm you. The 30 mg strength has a score line to facilitate halving, if directed by your doctor. The half tablets should also be swallowed intact.

You should not consume alcohol while taking CODEINE 15 and CODEINE 30, as it may increase the chance of experiencing dangerous side effects.

Keep CODEINE 15 and CODEINE 30 out of sight and reach of children. You should not give CODEINE 15 and CODEINE 30 to anyone as inappropriate use may have severe medical consequences, including death.

Usual Adult Starting Dose:

Your dose is tailored/personalized just for you. Be sure to follow your doctor's dosing instructions exactly. Do not increase or decrease your dose without consulting your doctor.

Review your pain regularly with your doctor to determine if you still need CODEINE 15 and CODEINE 30. Be sure to use CODEINE 15 and CODEINE 30 only for the condition for which it was prescribed.

If your pain increases or you develop any side effect as a result of taking CODEINE 15 and CODEINE 30, tell your doctor immediately.

CODEINE 15 and CODEINE 30 is not recommended for rectal administration.

Usual dose (Adults and children 12 years of age or older):

Pain:

Tablets: 15 to 60 mg every 4 to 6 hours if necessary.

Cough:

Tablets: 15 to 30 mg every 6 to 8 hours if necessary to a maximum of 120 mg daily.

Your doctor should prescribe CODEINE 15 and CODEINE 30 at the lowest effective dose for the shortest period of time. Take CODEINE 15 and CODEINE 30 every 4-6 hours as needed.

Stopping your Medication

If you have been taking CODEINE 15 and CODEINE 30 for more than a few days you should not stop taking it all of a sudden. You should check with your doctor for directions on how to slowly stop taking it. You should do it slowly to avoid uncomfortable symptoms such as having:

- body aches
- diarrhea
- gooseflesh
- 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
- an unexplained fever
- weakness
- yawning

Refilling your Prescription for CODEINE 15 and CODEINE 30:

A new written prescription is required from your doctor each time you need more CODEINE 15 and CODEINE 30. Therefore, it is important that you contact your doctor before your current supply runs out.

Overdose:

If you think you have taken too much CODEINE 15 and CODEINE 30, 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:

If you miss one dose, take it as soon as possible. However, if it is almost time for your next dose, then skip the missed dose. Do not take two doses at once. If you miss several doses in succession, talk to your doctor before restarting your medication.

What are possible side effects from using CODEINE 15 and CODEINE 30?

These are not all the possible side effects you may feel when taking CODEINE 15 and CODEINE 30. 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

Talk with your doctor or pharmacist about ways to prevent constipation when you start using CODEINE 15 and CODEINE 30.

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			✓
Withdrawal: nausea, vomiting, diarrhea, anxiety, shivering, cold and clammy skin, body aches, loss of appetite, sweating.		✓	
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.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:

Store at room temperature 15 – 30°C.

Keep unused or expired CODEINE 15 and CODEINE 30 in a secure place to prevent theft, misuse or accidental exposure.

Keep CODEINE 15 and CODEINE 30 out of sight and reach of children and pets.

Disposal:

CODEINE 15 and CODEINE 30 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 CODEINE 15 and CODEINE 30:

- 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 or by contacting Laboratoire Riva Inc. at: 1-800-363-7988.

This leaflet was prepared by:

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