PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

# [N] LINCTUS CODEINE BLANC
## Codeine phosphate 2 mg/mL (Oral Solution)

**Opioid Antitussive**

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## PART I: HEALTH PROFESSIONAL INFORMATION

## 1 INDICATIONS

LINCTUS CODEINE BLANC is indicated for the control of exhausting, nonproductive cough which does not respond to non-opioids.

**Pediatrics (<18 years of age):** LINCTUS CODEINE BLANC 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 codeine to morphine and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of codeine in these patients (see also **CONTRAINDICATIONS and DOSAGE AND ADMINISTRATION**).

### 1.1 Geriatrics

**Geriatrics >65 years of age:** Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness. 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)**.

## 2 CONTRAINDICATIONS

LINCTUS CODEINE BLANC is contraindicated in:

- 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 **DOSAGE FORMS, COMPOSITION AND PACKAGING**.
- 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, diabetes, heart or thyroid disease or glaucoma.
- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure, and head injury.
- CYP2D6 ultra-rapid metabolizers who convert codeine into its active metabolite more rapidly and completely than other people (see WARNINGS AND PRECAUTIONS, Risk of Death in Ultra-Rapid Metabolizers of Codeine; SYMPTOMS AND TREATMENT OF OVERDOSAGE, Codeine)
- Patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy).
- Women who are breast-feeding, pregnant or during labour and delivery (see **SERIOUS WARNINGS AND PRECAUTIONS**, and **WARNINGS AND PRECAUTIONS).**

- Pediatric patients < 12 years of age
- Pediatric patients (<18 years of age) who have undergone tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome

## 3 SERIOUS WARNINGS AND PRECAUTIONS BOX

**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, LINCTUS CODEINE BLANC 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 cough management (see DOSAGE AND ADMINISTRATION).**

**Addiction, Abuse, and Misuse**
**LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC, and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS). LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC. 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 LINCTUS CODEINE BLANC or following a dose increase. Further, instruct patients of the hazards related to taking opioids including fatal overdose.**

**Accidental Exposure**
**Accidental ingestion of even one dose of LINCTUS CODEINE BLANC, 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 LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC 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.**

## 4 DOSAGE AND ADMINISTRATION

**Pediatrics (under 18 years)**
LINCTUS CODEINE BLANC 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 codeine to morphine and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of codeine in these patients.

LINCTUS CODEINE BLANC should only be used in patients for whom alternative treatment options (e.g. non-opioid antitussive) are ineffective or not tolerated or would be otherwise inadequate to provide appropriate management of cough (see 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. The maximum recommended daily dose of LINCTUS CODEINE BLANC is 120 mg (18 morphine milligram equivalent). Each patient should be assessed for their risk prior to prescribing LINCTUS CODEINE BLANC, as the likelihood of experiencing serious adverse events can depend upon the type of opioid, 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 LINCTUS CODEINE BLANC.**

### 4.1 Dosing Considerations

- LINCTUS CODEINE BLANC may be taken with or without food with a glass of water.

### 4.2 Recommended Dose and Dosage Adjustment

Codeine, including LINCTUS CODEINE BLANC, should be prescribed at the lowest effective dose for the shortest period of time.

**Adults (18 years and older) :** 5 to 10 mL every 4 to 6 hours as necessary.

**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. LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC. 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.

### 4.3 Administration

LINCTUS CODEINE BLANC must be taken orally.

### 4.4 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.

### 4.5 Disposal

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

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

## 5 OVERDOSAGE

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|---|
| For management of a suspected drug overdose, contact your regional poison control center. |

### 5.1 Symptoms:

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

### 5.2 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

## 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

**Table – Dosage Forms, Strengths, Composition and Packaging.**

| Route of Administration | Dosage Form / Strength | Non-medicinal Ingredients |
|---|---|---|
| Oral | Solution /<br>Codeine Phosphate 2 mg/mL | Purified water, glycerin, alcohol, methylparaben, propylparaben. |

## 7 WARNINGS AND PRECAUTIONS

### 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.

Codeine, including LINCTUS CODEINE BLANC 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.

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

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

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

Patients should be counselled to stop use and consult a physician if symptoms or cough worsen or persist for more than 7 days, or if high fever, rash or persistent headache is present, as these could be signs of a serious condition.

Patients should be counselled to discontinue codeine products and to seek urgent medical help at the earliest sign of codeine toxicity including symptoms such as confusion, shallow breathing, or extreme sleepiness which may be life threatening.

**Abuse and Misuse**

Like all opioids, LINCTUS CODEINE BLANC is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC, should be used with particular care in patients with a history of alcohol and illicit/prescription drug abuse

LINCTUS CODEINE BLANC is intended for oral use only.

**Cardiovascular**

Codeine administration may result in hypotension and dizziness. Use with caution in patients with cardiac arrhythmias due to the cholinergic effects of the drug.

**Driving and Operating Machinery**

Due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery. LINCTUS CODEINE BLANC 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.

**Dependence/Tolerance**

As with other opioids, tolerance and physical dependence may develop upon repeated administration of LINCTUS CODEINE BLANC 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.

**Use in Drug and Alcohol Addiction**

LINCTUS CODEINE BLANC 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~~ cough requiring opioid analgesia. Patients with a history of addiction to drugs or alcohol may be at higher risk of becoming addicted to LINCTUS CODEINE BLANC; extreme caution and awareness is warranted to mitigate the risk.

**Endocrine and Metabolism**

**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**
Codeine and other morphine-like opioids have been shown to decrease bowel motility. Codeine may obscure the diagnosis or clinical course of patients with acute abdominal conditions. Codeine should not be used in patients with diarrhea associated with pseudomembranous colitis. Use with caution in patients with acute ulcerative colitis or other severe inflammatory bowel disease due to the risk of toxic megacolon.

**Constipation:** LINCTUS CODEINE BLANC causes a reduction in gastrointestinal motility associated with an increase smooth muscle tone. Constipation is a frequently reported side effect of part of an opioid treatment. Patients should be advised of steps to prevent constipation and consider the prophylactic use of laxatives. Particular caution advised in patients with chronic constipation.

**Gastrointestinal transit:** Clinical conditions or medical products that cause sudden shortening and marked gastrointestinal transit time may lead to decreased absorption of Codeine phosphate in LINCTUS CODEINE BLANC and may cause withdrawal symptoms in patients with physical dependence on opioids.

**Acute abdominal disorders:** Opioid administration may overshadow the diagnosis or the clinical course of acute abdominal conditions. Therefore, it is important to make sure that the patient does not show bowel obstruction, or even Ileus, before initiating treatment.

**Neonatal Opioid Withdrawal Syndrome (NOWS)**
Use of LINCTUS CODEINE BLANC is contraindicated in pregnant women (see **CONTRAINDICATIONS**).

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.

**Neurologic**
**Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol):**
Concomitant use of opioids, including LINCTUS CODEINE BLANC, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Because of these risks, avoid use of opioid cough medications in

patients taking benzodiazepines, other CNS depressants, or alcohol (see DRUG INTERACTIONS).

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with 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 LINCTUS CODEINE BLANC is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs).

**Serotonin Syndrome:** LINCTUS CODEINE BLANC 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. LINCTUS CODEINE BLANC 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**
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.

**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 LINCTUS CODEINE BLANC, 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 LINCTUS CODEINE BLANC 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.

**Risk Factors for Life-Threatening Respiratory Depression in Children**
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). Codeine-containing products are contraindicated for all children younger than 12 years of age

- 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**).
- Avoid the use of codeine-containing products in adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of codeine unless the benefits outweigh the risks. Risk factors include conditions associated with hypoventilation, such as postoperative status, obstructive sleep apnea, obesity, severe pulmonary disease, neuromuscular disease, and concomitant use of other medications that cause respiratory depression.

**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 LINCTUS CODEINE BLANC, as in these patients, even usual therapeutic doses of LINCTUS CODEINE BLANC may decrease respiratory drive to the point of apnea. The use of LINCTUS CODEINE BLANC is contraindicated in Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see **CONTRAINDICATIONS**).

**Risk of Death in Ultra-Rapid Metabolizers of Codeine**
Some individuals may be ultra-rapid metabolizers due to a specific CYP2D6*2x2 genotype. These individuals convert codeine into its active metabolite, morphine, more rapidly and completely than other people. This rapid conversion results in higher than expected serum morphine levels. Even at labelled dosage regimens, individuals who are ultra-rapid metabolizers may have life-threatening or fatal respiratory depression or experience overdose symptoms such as extreme sleepiness, confusion, or shallow breathing. . (See also Labour, Delivery and Nursing Women in **Special Populations**).

The prevalence of this CYP2D6 phenotype varies widely and has been estimated at 0.5 to 1% in Chinese and Japanese, 0.5 to 1% in Hispanics, 1 to 10% in Caucasians, 3% in African Americans, and 16 to 28% in North Africans, Ethiopians, and Arabs. Data are not available for other ethnic groups. When physicians prescribe codeine-containing drugs, they should choose the lowest effective dose for the shortest period of time and inform their patients about these risks and the signs of morphine overdose (see DOSAGE AND ADMINISTRATION, Dosing Considerations).

**Risk of Interactions with Drugs Affecting Cytochrome P450 Isoenzymes**
The effects of concomitant use or discontinuation of cytochrome P450 3A4 inducers, 3A4 inhibitors, or 2D6 inhibitors with codeine are complex. Use of cytochrome P450 3A4 inducers, 3A4 inhibitors, or 2D6 inhibitors with Robitussin® AC requires careful consideration of the Page 10 of 27 effects on the parent drug, codeine, and the active metabolite, morphine. (See DRUG INTERACTIONS).

**Sexual Health**
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**).

## 7.1 Special Populations

### 7.1.1 Pregnant Women

**Pregnant Women:** Studies in human have not been conducted. LINCTUS CODEINE BLANC crosses the placental barrier and is contraindicated in pregnant women and during labour and delivery. Women of childbearing potential who become or are planning to become pregnant should be advised to consult a physician prior to initiating or continuing therapy with LINCTUS CODEINE BLANC

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**).

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.

**Labour and Delivery:** 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 LINCTUS CODEINE BLANC is used in this population (See WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome).

### 7.1.2 Breast-feeding

Since opioids can cross the placental barrier and are excreted in breast milk, LINCTUS CODEINE BLANC is contraindicated in nursing women and during labour and delivery. 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 LINCTUS CODEINE BLANC is used in this population.

Codeine is secreted into human milk. In women with normal codeine metabolism (normal CYP2D6 activity), the amount of codeine secreted into human milk is low and dose-dependent. **However, some women are ultra-rapid metabolisers of codeine (see CONTRAINDICATIONS, Ultra-Rapid Metabolisers of Codeine; and WARNINGS AND**

**PRECAUTIONS, Risk of Death in Ultra-rapid Metabolizers of Codeine). These women achieve higher-than-expected serum levels of codeine's active metabolite, morphine, leading to higher-than-expected levels of morphine in breast milk and potentially dangerously high serum morphine levels in their breast-fed infants. Therefore, maternal use of codeine can potentially lead to serious adverse reactions, including death in nursing infants.**

Since there is a risk of infant exposure to codeine and morphine through breast milk, LINCTUS CODEINE BLANC is contraindicated in breast-feeding. Prescribers should closely monitor mother-infant pairs and notify treating pediatricians about any use of codeine during breast-feeding.

### 7.1.3 Pediatrics

LINCTUS CODEINE BLANC 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 codeine to morphine and because the benefits of symptomatic treatment of cough do not outweigh the risks for use of codeine in these patients (see **INDICATIONS, CONTRAINDICATIONS**, and **DOSAGE AND ADMINISTRATION**)

### 7.1.4 Geriatrics

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**).

### 7.1.5 Special Risk Groups

Codeine phosphate should be administered with caution to patients with a history of alcohol and drug abuse, or history of seizures, and in a reduced dosage to debilitated patients, and those with severe impairment of hepatic or renal function, and to patients with severely impaired pulmonary function, Addison's disease, hypothyroidism, myxedema, toxic psychosis, prostatic hypertrophy or urethral stricture.

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

Adverse effects of LINCTUS CODEINE BLANC are similar to those of other opioid antitussives 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.

Adverse reactions due to codeine phosphate may include drowsiness, nausea, vomiting and

constipation. Infrequent adverse effects include palpitation, dry mouth, skin rash, pruritus and, rarely, hyperhidrosis and agitation have been reported. Respiratory depression is seen in higher dosage, and there is a potential for tolerance, psychological dependence or physical dependence to occur.

**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.

The following adverse effects occur less frequently with opioid products and include those reported in LINCTUS CODEINE BLANC 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, laryngospasm, 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.

**Nausea and Vomiting:** Occur frequently after single doses of narcotics or as an early unwanted effect of regular opioid analgesic therapy.

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

### 8.2 Post-Market Adverse Reactions

**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.

## 9 DRUG INTERACTIONS

### 9.1 Serious Drug Interactions Box

**Serious Drug Interactions**

***Neuromuscular Blocking Agents:***
*Opioid analgesics may enhance the effects of neuromuscular blocking agents resulting in increased respiratory depression.*

## 9.2 Overview

**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**). LINCTUS CODEINE BLANC should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

**Interaction with Serotonin**
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).

## 9.3 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.

**Interactions with Drugs Affecting Cytochrome P450 Isoenzymes**
The effects of concomitant use or discontinuation of CYP3A4 inducers, CYP3A4 inhibitors, or CYP2D6 inhibitors with codeine are complex, and requires careful consideration of the effects on the parent drug, codeine, and the active metabolite, morphine.

Avoid the use of LINCTUS CODEINE BLANC while taking CYP3A4 inducers, CYP3A4 inhibitors, or CYP2D6 inhibitors. If concomitant use is necessary, monitor patients for respiratory depression and sedation at frequent intervals or for signs of opioid withdrawal.

**CYP3A4 inhibitors:** The concomitant use of LINCTUS CODEINE BLANC 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 codeine and its subsequent metabolism by CYP2D6, resulting in greater morphine levels, which could increase or prolong opioid effects. The discontinuation of a concomitantly used CYP3A4 inhibitor might results in a reduced efficacy of LINCTUS CODEINE BLANC

**CYP2D6 inhibitors:** The concomitant use of LINCTUS CODEINE BLANC and CYP2D6 inhibitors (e.g., amiodarone, quinidine) may result in a decrease in active metabolite morphine plasma concentration, leading to decreased efficacy or symptoms of opioid withdrawal. The discontinuation of a concomitantly used CYP2D6 inhibitor may lead to an increased metabolism to morphine, which could increase or prolong adverse reactions and may cause potentially fatal respiratory depression.

**CYP3A4 inducers**: The concomitant use of LINCTUS CODEINE BLANC and CYP3A4 inducers, such as rifampin, carbamazepine, and phenytoin, may result in a decreased plasma concentration of codeine and its active metabolite morphine, leading to decreased efficacy or symptoms of opioid withdrawal. The discontinuation of a concomitantly used CYP3A4 inducer can increase the plasma concentration of codeine and its active metabolite morphine which could increase or prolong adverse reactions and may cause potentially fatal respiratory depression.

### 9.4 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.

### 9.5 Drug-Lifestyle Interactions

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

## 10 ACTION AND CLINICAL PHARMACOLOGY

### 10.1 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.

**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 CO2 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.

### 10.2 Pharmacodynamics

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.

### 10.3 Pharmacokinetics

**Special Populations and Conditions**

**Pediatrics (< 18 years of age):**
LINCTUS CODEINE BLANC 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 codeine to morphine and because the benefits of symptomatic treatment of cough = do not outweigh the risks for use of codeine in these patients (see **INDICATIONS, CONTRAINDICATIONS, and DOSAGE AND ADMINISTRATION**).

***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.

## 11 STORAGE, STABILITY AND DISPOSAL

Store between 15 - 30 C.

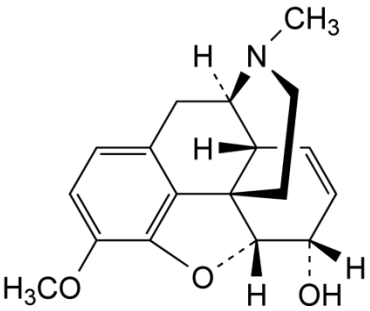
## 12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

## PART II: SCIENTIFIC INFORMATION

## 13 PHARMACEUTICAL INFORMATION

### Drug Substance

| | |
|---|---|
| Proper name: | Codeine phosphate |
| Chemical name: | 7,8-Didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate hemihydrate |
| Molecular formula: | $C_{18}H_{21}NO_3,H_3PO_4,½H_2O$ |
| Molecular mass: | 406.4 |
| Structural formula: |  , $H_3PO_4$ , $^1/_2\ H_2O$ <br> https://www.pharmacopoeia.com/bp-2018/monographs/codeine-phosphate.html?date=2018-01-01&text=codeine+phosphate |
| Physicochemical properties: | Hemihydrate, fine, white, needle-shaped crystals; a crystalline powder; odorless, affected by light. |
| Solubility: | Freely soluble in water, very soluble in hot water, slightly soluble in alcohol, more soluble in boiling alcohol. |

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE**

**PATIENT MEDICATION INFORMATION**

**[N] LINCTUS CODEINE BLANC**
**Codeine phosphate 2 mg/mL (Oral Solution)**
**Opioid antitussive**

Read this carefully before you start taking LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC.

**SERIOUS WARNINGS AND PRECAUTIONS**

- **Even if you take LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC. 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 LINCTUS CODEINE BLANC. They could die from taking it. If a person has not been prescribed LINCTUS CODEINE BLANC, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC used for?**
LINCTUS CODEINE BLANC used for control of exhausting, nonproductive cough which does not respond to non-opioid medication.

LINCTUS CODEINE BLANC 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 codeine.

**How does LINCTUS CODEINE BLANC work?**
Codeine phosphate is a medication belonging to the class of drugs known as opioids which includes codeine, fentanyl, morphine and oxycodone. Codeine acts on the brain to suppress cough.

**What are the ingredients in LINCTUS CODEINE BLANC?**

| | |
|---|---|
| Medicinal ingredients: | Codeine phosphate |
| Non-medicinal ingredients: | Purified water, glycerin, alcohol, methylparaben, propylparaben. |

**LINCTUS CODEINE BLANC comes in the following dosage forms:**
This product is a liquid solution for oral use.

**Do not use LINCTUS CODEINE BLANC if:**
- your doctor did not prescribe it for you
- are allergic to Codeine phosphate or to any of the other ingredients in LINCTUS CODEINE BLANC
- have severe asthma, trouble breathing, or other breathing problems
- have bowel blockage or narrowing of the stomach or intestines
- have a head injury
- are at risk for having seizures
- have diabetes
- have heart or thyroid problems
- have glaucoma
- 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)
- have been told by your doctor that you break down codeine rapidly. This can lead to codeine overdose even at the usual adult dose.
- are pregnant or planning to become pregnant or you are in labour
- are breastfeeding. The use of codeine-containing products while breast-feeding may harm your baby. If you breastfeed and take LINCTUS CODEINE BLANC, seek immediate medical care for your baby if they are overly drowsy, sedated, have difficulty breast-feeding, have breathing difficulties, and are floppy (have decreased muscle tone). This is very serious for the baby and can lead to death. Tell the baby's doctor that you are breastfeeding and took LINCTUS CODEINE BLANC

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take LINCTUS CODEINE BLANC. 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 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 problems
- or under a physician's care.

**Other warnings you should know about**

**Some people metabolize codeine at a much faster rate than the general population. This may lead to accidental overdose. Stop taking LINCTUS CODEINE BLANC and seek immediate medical help if you start feeling confused, have shallow breathing, or extreme sleepiness. If you know that you metabolize codeine at a much faster rate, tell your doctor BEFORE starting this medication.**

Stop taking LINCTUS CODEINE BLANC and consult with your healthcare professional if:
- you get a high fever, rash or persistent headache along with the cough.
- your symptoms or cough worsen or continue for more than 7 days.

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 codeine 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 LINCTUS CODEINE BLANC while pregnant, nursing, during labour or delivery. Opioids can be transferred to your baby through breast milk, or while still in the womb. LINCTUS CODEINE BLANC can then cause life-threatening breathing problems in your unborn bay or nursing infant.

If you are pregnant and are taking LINCTUS CODEINE BLANC, 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 LINCTUS CODEINE BLANC. 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 LINCTUS CODEINE BLANC. LINCTUS CODEINE BLANC can cause:
- drowsiness;
- dizziness or;
- lightheadedness.

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 LINCTUS CODEINE BLANC.

**Serotonin Syndrome:**
LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC with certain anti-depressants 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 LINCTUS CODEINE BLANC:**

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. Do not drink alcohol while you are taking LINCTUS CODEINE BLANC. 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 LINCTUS CODEINE BLANC;
- 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 LINCTUS CODEINE BLANC 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)

- antitussives (cough medicines)
- decongestants
- expectorants drugs used to treat muscle spasms and back pain
- 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 medications (such as beta blockers)
- tranquilizers, sedatives, sedating antihistamines, other depressantsgrapefruit juicedrugs used to treat migraines (e.g. triptans)St. John's Wort.

**How to take LINCTUS CODEINE BLANC:**
- Your doctor will prescribe the lowest dose that works to control your symptoms.
- It is recommended that you only take LINCTUS CODEINE BLANC for up to 7 days. If you need to take LINCTUS CODEINE BLANC for longer, your doctor will determine the best dose for you to lower the risk of side effects and overdose. Higher doses can lead to more side effects and a greater chance of overdose.
- LINCTUS CODEINE BLANC may be taken with or without food, with a glass of water.

**Usual Adult dose:**

**Adults (18 years and older):**
- 5 to 10 mL every 4 to 6 hours as necessary or as directed by your doctor.
- with a full glass of water.

**Stopping your Medication:**
If you have been taking LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC. 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 LINCTUS CODEINE BLANC.

**Refilling your Prescription for LINCTUS CODEINE BLANC:**
A new written prescription is required from your doctor each time you need more LINCTUS CODEINE BLANC. Therefore, it is important that you contact your doctor before your current supply runs out.

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 LINCTUS CODEINE BLANC, immediately 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 oral solution 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 a row, talk to your doctor before restarting your medication.

**What are possible side effects from using LINCTUS CODEINE BLANC?**

These are not all the possible side effects you may feel when taking LINCTUS CODEINE BLANC. If you experience any side effects not listed here, contact your healthcare professional.

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

Talk with your doctor or pharmacist about ways to prevent constipation when you start using LINCTUS CODEINE BLANC.

| 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 LINCTUS CODEINE BLANC in a secure place to prevent theft, misuse or accidental exposure.**
- **Keep LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC, get emergency help right away.**
- Store at room temperature (15˚- 30˚C). Keep in a dry place.

**Disposal:**
**LINCTUS CODEINE BLANC 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 LINCTUS CODEINE BLANC:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this consumer 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 contacting Laboratoire Atlas Inc. at: Phone (Toll free) : 1-844-284-7890; Fax: 524-254-3006; Email: info@laboratoireatlas.com

This leaflet was prepared by Laboratoire Atlas Inc.

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