PRESCRIBING INFORMATION
INCLUDING PATIENT MEDICATION INFORMATION

^{N}COPHYLAC®

Normethadone HCl and p-Hydroxyephedrine HCl Drops
Drops, Normethadone HCl 10 mg/mL (1%) and p-Hydroxyephedrine HCl 20 mg/mL (2%)

Antitussive

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

Date of Revision:
June 24th, 2020

Submission Control No: 230752

Table of Contents

^{N}COPHYLAC®

Normethadone Hydrochloride and p-Hydroxyephedrine Hydrochloride Drops

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Drops of normethadone HCl 10 mg/mL (1%) and p-hydroxyephedrine HCl 20 mg/mL (2%)	Citric Acid Anhydrous, Glycerine, Lemon Oil, Methylparaben, and Purified Water.

INDICATIONS AND CLINICAL USE

Adults

COPHYLAC® is indicated for the treatment of cough associated with inflamed mucosa, which does not respond to products of lesser potency.

Geriatrics (> 65 years of age)

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

Pediatrics (<18 years of age)

The safety and efficacy of COPHYLAC® has not been studied in the pediatric population. COPHYLAC® is not indicated for use in patients younger than 18 years of age because the risks related to opioids may outweigh the benefits of symptomatic treatment of cough in these patients (see **CONTRAINDICATION**, **WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics**; and **DOSAGE AND ADMINISTRATION**).

CONTRAINDICATIONS

COPHYLAC® is contraindicated in:

- Patients who are hypersensitive to the active substances normethadone hydrochloride (HCl) and p-hydroxyephedrine hydrochloride (HCl) or other opioid analgesics or to any ingredient

in the formulation. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the Product Monograph.
- In patients with known or suspected mechanical gastrointestinal obstruction (e.g., bowel obstruction or strictures) or any diseases/conditions that affect bowel transit (e.g., ileus of any type).
- Patients with suspected surgical abdomen (e.g., acute appendicitis or pancreatitis).
- Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus.
- Patients with acute respiratory depression, elevated carbon dioxide levels in the blood and cor pulmonale.
- Patients with acute alcoholism, delirium tremens, and convulsive disorders.
- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure, and head injury.
- Patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy).
- Women who are breast-feeding, and during pregnancy, or during labour and delivery (see **SERIOUS WARNINGS AND PRECAUTIONS**, and **WARNINGS AND PRECAUTIONS**).
- Children < 6 years of age (see WARNINGS AND PRECAUTIONS, Respiratory).

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, COPHYLAC® (normethadone) should only be used in patients for whom alternative non-opioid treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate cough management (see DOSAGE AND ADMINISTRATION).

Addiction, Abuse, and Misuse

COPHYLAC® 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 COPHYLAC® and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS, Abuse and Misuse). COPHYLAC® 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 COPHYLAC®. 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 COPHYLAC® or

following a dose increase. Further, instruct patients of the hazards related to taking opioids, including fatal overdose.

Accidental Exposure
Accidental exposure to COPHYLAC® , especially by children, can result in a fatal overdose of normethadone (see DOSAGE AND ADMINISTRATION, Disposal, for instructions on proper disposal).

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

Interaction with Alcohol
The co-ingestion of alcohol with COPHYLAC® 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). Avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol.

- **Reserve concomitant prescribing of COPHYLAC® and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

General

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

Accidental ingestion, especially by children can result in a fatal overdose of normethadone HCl and p-hydroxyephedrine HCl drops (see DOSAGE AND ADMINISTRATION, disposal, for instructions on proper disposal).

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

Abuse and Misuse

Like all opioids, COPHYLAC® is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, COPHYLAC® 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.

Use in Drug and Alcohol Addiction

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

Cardiovascular

Normethadone HCl and p-hydroxyephedrine HCl drops administration may result in hypotension and dizziness.

Dependence/Tolerance

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

Endocrine

Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms

and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

Gastrointestinal Effects

Normethadone HCl and p-hydroxyephedrine HCl drops and other morphine-like opioids have been shown to decrease bowel motility. Normethadone HCl and p-hydroxyephedrine HCl drops may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Patients with chronic constipation should be given COPHYLAC® only after weighing the potential therapeutic benefit against the hazards involved.

Neonatal Opioid Withdrawal Syndrome (NOWS)

Use of COPHYLAC® 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 COPHYLAC® 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 if COPHYLAC® is used with benzodiazepines, alcohol, or other CNS depressants.

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

Serotonin toxicity / Serotonin syndrome

Serotonin toxicity, also known as serotonin syndrome, is a potentially life-threatening condition and has been reported with opioids, particularly during combined use with other serotonergic drugs. (See DRUG INTERACTIONS).

Serotonin toxicity is characterised by neuromuscular excitation, autonomic stimulation (e.g. tachycardia, flushing) and altered mental state (e.g. anxiety, agitation, hypomania). In accordance with the Hunter Criteria, serotonin toxicity diagnosis is likely when, in the presence of at least one serotonergic agent, one of the following is observed:

- Spontaneous clonus
- Inducible clonus or ocular clonus with agitation or diaphoresis
- Tremor and hyperreflexia
- Hypertonia and body temperature >38°C and ocular clonus or inducible clonus.

If concomitant treatment with COPHYLAC® and other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. If serotonin toxicity is suspected, discontinuation of the serotonergic agents should be considered.

COPHYLAC® should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects, including death (see **CONTRAINDICATIONS** and **DRUG INTERACTIONS, Drug-Lifestyle Interactions**).

Psychomotor Impairment

COPHYLAC® 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 normethadone HCl and p-hydroxyephedrine HCl drops with other CNS depressants, including other opioids, phenothiazine, sedative/hypnotics and alcohol.

Respiratory

Normethadone HCl and p-hydroxyephedrine HCl drops, including COPHYLAC® is not recommended for use in any patient in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, lung infections, multiple trauma or extensive surgical procedures.

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

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. COPHYLAC® 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 COPHYLAC®, 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 COPHYLAC® and following dose increases.

Young Children
In young children the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants. COPHYLAC® is contraindicated in all children under 6 years of age.

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

Sexual Function/Reproduction

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

Special Populations

Special Risk Groups
Normethadone HCl and p-hydroxyephedrine HCl drops 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. COPHYLAC® crosses the placental barrier and is contraindicated in pregnant women.

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).**

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, Delivery and Nursing Women
Since opioids can cross the placental barrier and are excreted in breast milk, COPHYLAC® is contraindicated in nursing women and during labour and delivery. Life-threatening 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 if COPHYLAC® is used in this population.

Pediatrics (< 18 years of age)
COPHYLAC® is not indicated for use in patients younger than 18 years of age because the risks related to opioids may not outweigh the benefits of symptomatic treatment of cough in these patients (see **INDICATIONS, CONTRAINDICATIONS**, and **DOSAGE AND ADMINISTRATION**).

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

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

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The adverse effects of COPHYLAC® 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.

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

Interaction with Central Nervous System (CNS) Depressants

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

Interaction with Serotoninergic Agents
Coadministration of COPHYLAC® with a serotonergic agent (see examples below) may increase the risk of serotonin syndrome, a potentially life-threatening condition (see WARNINGS AND PRECAUTIONS). Examples of serotonergic agents include: Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5- HT3 receptor antagonists, St Johns Wort, lithium, drugs that affect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), certain muscle relaxants (e.g. cyclobenzaprine), serotonin-precursors (such as L-tryptophan, oxitriptan), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).

MAO Inhibitors

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

Interactions with Drugs Affecting Cytochrome P450 Isoenzyme CYP3A4

Avoid the use of COPHYLAC® while taking CYP3A4 inducers or CYP3A4 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 COPHYLAC® 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 normethadone, which could increase or prolong opioid effects. The discontinuation of a concomitantly used CYP3A4 inhibitor might therefore result in a reduced efficacy of COPHYLAC®

CYP3A4 inducers
The concomitant use of COPHYLAC® and CYP3A4 inducers, such as rifampin, carbamazepine, and phenytoin, may result in a decreased plasma concentration of normethadone, leading to decreased efficacy or symptoms of opioid withdrawal. The discontinuation of a concomitantly used CYP3A4 inducer can increase the plasma concentration of normethadone which could increase or prolong adverse reactions and may cause potentially fatal respiratory depression.

Drug-Lifestyle Interactions

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

DOSAGE AND ADMINISTRATION

COPHYLAC® is not indicated for use in patients younger than 18 years of age because the risks related to opioids may not outweigh the benefits of symptomatic treatment of cough in these patients.

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

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 COPHYLAC® is 30 drops for adults. Each patient should be assessed for their risk prior to prescribing COPHYLAC®, as the likelihood of experiencing serious adverse events can depend upon the type of opioid and duration of treatment, as well as the patient's own level of tolerance. In

addition, the coughing should be assessed routinely to confirm the most appropriate dose and the need for further use of COPHYLAC®.

Dosing Considerations

COPHYLAC® may be taken plain with sugar or in any beverage, preferably after breakfast and at bedtime. Drops are dispensed by inverting the drop dispensing bottle.

Recommended Dose and Dosage Adjustment

Adults

The recommended dosage is 15 drops twice daily

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. COPHYLAC® 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 COPHYLAC® 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.**Missed Dose**

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

Disposal

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

COPHYLAC® should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired COPHYLAC® 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 lockable medication box could be obtained from a pharmacy.

OVERDOSAGE

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

Symptoms

An overdose of 4 mL taken within 4 to 5 hours has produced transient nausea, cold sweat, and tachycardia in one reported case. Should 33% or more of one bottle be ingested, paralysis of the respiratory centre may result.

Treatment

Overdoses cases must be treated with naloxone HCl.

STORAGE AND STABILITY

COPHYLAC® bottles should be stored between 15°C and 30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

COPHYLAC® (normethadone HCl and p-hydroxyephedrine HCl drops) is available as sugar free solution for oral administration.

Composition
Each mL of COPHYLAC® sugar free solution contains normethadone HCl 10 mg (1%) and p-hydroxyephedrine HCl 20 mg (2%).

COPHYLAC® contains the following non-medicinal ingredients: Citric Acid Anhydrous, Glycerine, Lemon Oil, Methylparaben and Purified Water. Energy: 3.3 kJ (0.8 kcal).

Packaging
COPHYLAC® is dispensed in bottles of 15 mL.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

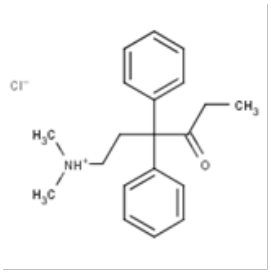
Proper name: Normethadone Hydrochloride

Chemical name: 6-dimethylamino-4,4-diphenyl-hexan-3-one

Molecular formula: $C_{20}H_{25}NO \cdot HCl$

Molecular mass: 331.88 g/mol

Structural formula:



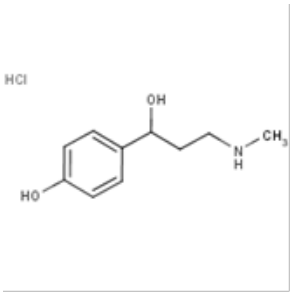
Proper name: p-Hydroxyephedrine Hydrochloride

Chemical name: 4-[1-Hydroxy-2-(methylamino)propyl] phenol hydrochloride

Molecular formula: $C_{10}H_{15}NO_2 \cdot HCl$

Molecular mass: 217.69 g/mol

Structural formula:



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

COPHYLAC®
Normethadone Hydrochloride and p-Hydroxyephedrine Hydrochloride Drops

Read this carefully before you start taking COPHYLAC® 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 COPHYLAC®.

Serious Warnings and Precautions

- **Even if you take COPHYLAC® 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 COPHYLAC®. 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 COPHYLAC®. If a person has not been prescribed COPHYLAC®, they could die from taking it. This is especially true for children.**
- **If you took COPHYLAC® 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 COPHYLAC® 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 COPHYLAC® used for?

COPHYLAC® is used for the temporary relief of cough associated with inflamed mucosa, which does not respond to products of lesser potency.

COPHYLAC® 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 treatment.

How does COPHYLAC® work?
Normethadone hydrochloride (HCl) and p-hydroxyephedrine hydrochloride (HCl) drops act on the brain to supress cough.

What are the ingredients in COPHYLAC®?
Medicinal ingredients: Normethadone HCl and p-hydroxyephedrine HCl.
Non-medicinal ingredients: Citric acid anhydrous, glycerine, lemon oil, methylparaben and purified water.

COPHYLAC® comes in the following dosage forms:
Sugar free solution (drops) containing 1% normethadone HCl and 2% p-hydroxyephedrine HCl.

Do not use COPHYLAC® if:
- Your doctor did not prescribe it for you
- You are allergic to normethadone HCl or p-hydroxyephedrine HCl or to any of the other ingredients in COPHYLAC®
- You have severe asthma, trouble breathing, or other breathing problems
- You have bowel blockage or narrowing of the stomach or intestines
- You have a head injury
- You are at risk for having seizures
- You have diabetes
- You have heart or thyroid problems
- You have glaucoma
- You have a brain tumor
- You suffer from alcoholism
- 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)
- are pregnant or planning to become pregnant or you are in labour
- are breastfeeding. The use of normethadone-containing products while breast-feeding may harm your baby. If you breastfeed and take COPHYLAC®, seek immediate medical care for your baby if they are overly drowsy, sedated, have difficulty breast-feeding, have breathing difficulties, or 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 COPHYLAC®

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take COPHYLAC®. 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 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:

Stop taking COPHYLAC® and seek immediate medical help if you start feeling confused, have shallow breathing, or extreme sleepiness.

Stop taking COPHYLAC® 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.

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 questions or concerns about abuse, addiction or physical dependence.

Breathing problems: COPHYLAC® is not recommended for anyone who has or is at risk for breathing problems such as:

- lung infections, or respiratory conditions
- neuromuscular disorders
- severe heart problems
- recent multiple traumas or extensive surgical procedures

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

If you are pregnant and are taking COPHYLAC®, 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 COPHYLAC®. 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 COPHYLAC®. COPHYLAC® 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 COPHYLAC®.

Serotonin Syndrome: Normethadone, the ingredient in COPHYLAC® 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 COPHYLAC® 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 COPHYLAC®:

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking COPHYLAC®. 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 COPHYLAC®
- 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 COPHYLAC® with MAO inhibitors (MAOi) or if you have taken MAOi's in the last 14 days.
- drugs used to treat serious mental or emotional disorders (such as schizophrenia)

- antihistamines (drugs used to treat allergies)
- anti-emetics (drugs used to prevent vomiting)
- drugs used to treat muscle spasms and back pain
- some heart medications (such as beta blockers)
- drugs used to treat migraines (e.g. triptans)
- St. John's Wort

How to take COPHYLAC®:
COPHYLAC® may be taken plain with sugar or in any beverage, preferably after breakfast and at bedtime.

- Your doctor will prescribe the lowest dose that works to control your symptoms.
- Higher doses can lead to more side effects and a greater chance of overdose.

Usual Dose:
Be sure to follow your doctor's dosing instructions exactly. Do not increase or decrease your dose without consulting your doctor.

Your doctor will prescribe the lowest dose that works to control your cough. Higher doses can lead to more side effects and a greater chance of overdose. Review your symptoms regularly with your doctor to determine if you still need COPHYLAC®. Be sure to use COPHYLAC® only for the condition for which it was prescribed.

If you develop any side effect as a result of taking COPHYLAC®, tell your doctor immediately.

Adults: The recommended dosage is 15 drops twice daily.

Stopping your Medication
If you have been taking COPHYLAC® 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 COPHYLAC®. 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 COPHYLAC®.

Refilling your Prescription for COPHYLAC®:
A new written prescription is required from your doctor each time you need more COPHYLAC®. 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.

Overdose:

If you think you have taken too much COPHYLAC®, 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 missed a dose of this medication, take it as soon as you remember. But if it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Go back to the regular dosing schedule. Do not take two doses at the same time. If you miss several doses in a row, talk to your doctor before restarting your medication.

What are possible side effects from using COPHYLAC®?
These are not all the possible side effects you may feel when taking COPHYLAC®. 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

- 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 COPHYLAC®

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: a reaction which may cause feelings of agitation or restlessness, flushing, muscle twitching, involuntary eye movements, heavy sweating, high body temperature (>38°C), or rigid muscles			✓

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 COPHYLAC® in a secure place to prevent theft, misuse or accidental exposure to children and pets.**
- **Keep COPHYLAC® 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 COPHYLAC®, get emergency help right away.**
- **Store at room temperature (15-30°C).**

Disposal:
COPHYLAC® 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 COPHYLAC®:

- 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 calling 1-800-361-4261.

This leaflet was prepared by Bausch Health, Canada Inc.

Last revised: June 24th, 2020