PRESCRIBING INFORMATION

INCLUDING PATIENT MEDICATION INFORMATION

^{N}COPHYLAC® DROPS

Normethadone HCl and p-Hydroxyephedrine HCl Drops

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

Antitussive

Valeant Canada LP
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

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^{N}COPHYLAC® DROPS

Normethadone Hydrochlroride 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® DROPS 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® DROPS has not been studied in the pediatric population. Therefore the use of COPHYLAC® DROPS is not recommended in patients under 6 years of age.

CONTRAINDICATIONS

- 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 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 pregnant or during labour and delivery.
- Women who are breastfeeding

WARNINGS AND PRECAUTIONS

SERIOUS WARNINGS AND PRECAUTIONS

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.

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 cautioned not to consume alcohol while taking COPHYLAC® DROPS as it may increase the chance of experiencing serious adverse events, including death.

Abuse and Misuse

Like all opioids, **COPHYLAC® DROPS** is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, **COPHYLAC® DROPS** should be prescribed and handled with caution.

Opioids, such as **COPHYLAC® DROPS**, should be used with particular care in patients with a history of alcohol and illicit/prescription drug abuse.

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® DROPS 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.

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® DROPS only after weighing the potential therapeutic benefit against the hazards involved.

Neonatal Opioid Withdrawal Syndrome (NOWS)
Use of COPHYLAC® DROPS 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® DROPS with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, come and death. Because of these risks, avoid use of opioids 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® DROPS 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).**

Psychomotor Impairment

COPHYLAC® DROPS 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® DROPS 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.

In young children the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants. Benefit to risk ratio should be carefully considered especially in children with respiratory embarrassment, e.g. croup. Estimation of dosage relative to the child's age and weight is of great importance**.**

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

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® DROPS crosses the placental barrier and should not be administered to pregnant women unless in the judgment of the physician, potential benefits outweigh the risks.

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

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

Pediatrics (< 18 years of age): The safety and efficacy of COPHYLAC® DROPS has not been studied in the pediatric population. Therefore the use of COPHYLAC® DROPS is not recommended in patients under 6 years of age.

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® DROPS 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.

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® DROPS should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

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

DOSAGE AND ADMINISTRATION

Dosing Considerations

COPHYLAC® DROPS 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: For Adults and children over 14 years, the recommended dosage is 15 drops twice daily

Children: For children between 6 to 14 years of age the recommended dosage is 5 to 10 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® DROPS should be initiated at a low dose and slowly titrated to effect (see **WARNINGS AND PRECAUTIONS**).

Disposal

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

COPHYLAC® DROPS should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired COPHYLAC® DROPS should be properly disposed of as soon as it is no longer needed to prevent accidental exposure to others, including children or pets.

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.

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

DOSAGE FORMS, COMPOSITION AND PACKAGING

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

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

COPHYLAC® DROPS 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® DROPS is dispensed in bottles of 15 mL.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

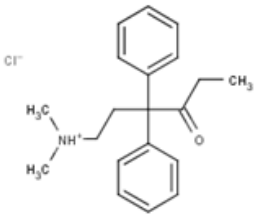
Drug Substance

Proper name:
Normethadone Hydrochloride

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

Molecular formula and molecular mass:
$C_{20}H_{25}NO \cdot HCl$, *331.88 g/mol*

Structural formula:

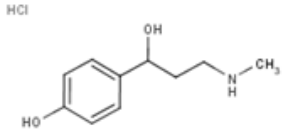


Proper name:
p-Hydroxyephedrine Hydrochloride

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

Molecular formula and molecular mass:
$C_{10}H_{15}NO_2 \cdot HCl$, 217.69 g/mol

Structural formula:



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

COPHYLAC® DROPS
Normethadone Hydrochloride and p-Hydroxyephedrine Hydrochloride Drops

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

What is COPHYLAC® DROPS used for?

Serious Warnings and Precautions

Taking COPHYLAC® DROPS 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.

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

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

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

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

Do not use COPHYLAC® DROPS if you:
- are allergic to normethadone HCl or p-hydroxyephedrine HCl or to any of the other ingredients in COPHYLAC® DROPS
- 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
- 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)
- are pregnant or planning to become pregnant or you are in labour
- are breastfeeding

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

- have a history of illicit or prescription drug or alcohol abuse
- have severe kidney disease
- have severe liver disease
- have low blood pressure
- have or had depression
- suffer from chronic or severe constipation
- have problems with your thyroid, adrenal or prostate gland
- have, or had in the past hallucinations or other severe mental problems
- are pregnant or planning to become pregnant
- are breastfeeding

Other warnings you should know about:
Accidentally taking COPHYLAC® DROPS can result in a fatal overdose. This is especially true if a child accidently takes it.

As with all opioids, taking normethadone HCl and p-hydroxyephedrine HCl drops may cause you to become dependent on it. Do not take more than the dose prescribed to you by your doctor.

If you took COPHYLAC® DROPS 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.

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

- drowsiness
- dizziness or
- lightheadedness

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

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

The following may interact with COPHYLAC® DROPS:

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking COPHYLAC® DROPS. It can lead to:
    - drowsiness
    - unusually slow or weak breathing
    - serious side effects or
    - a fatal overdose
- 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® DROPS 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

How to take COPHYLAC® DROPS:

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

Usual Dose:

Adults: For Adults and children over 14 years, the recommended dosage is 15 drops twice daily
Children: For children between 6 to 14 years of age the recommended dosage is 5 to 10 drops twice daily.

Overdose:

If you think you have taken too much COPHYLAC® DROPS, 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.

What are possible side effects from using COPHYLAC® DROPS?

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

Side effects may include:

- Drowsiness
- Insomnia
- Dizziness
- Fainting
- Nausea, vomiting, or a poor appetite
- Dry mouth
- Headache
- Problems with vision
- Weakness, uncoordinated muscle movement
- Itching
- Sweating
- Constipation

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.	✓		

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
We encourage you to report serious or unexpected side effects to Health Canada. The information is used to check for new safety concerns about health products. As a consumer, your report contributes to the safe use of health products for everyone.
3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

    Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

Storage:

COPHYLAC® DROPS should be stored at room temperature between 15 °C and 30 °C. Keep unused or expired COPHYLAC® DROPS in a secure place to prevent theft, misuse or accidental exposure to children and pets.
Keep COPHYLAC® DROPS out of sight and reach of children and pets.

Disposal:

COPHYLAC® DROPS 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® DROPS:

- 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; or by calling 1-800-361-4261.

This leaflet was prepared by Valeant Canada LP.

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