

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

<sup>N</sup>**DALMACOL**

Hydrocodone Bitartrate,  
Etafedrine Hydrochloride, Doxylamine Succinate,  
Sodium Citrate and Alcohol Syrup

Hydrocodone bitartrate hemipentahydrate 0.33 mg/mL,  
etafedrine hydrochloride 3.33 mg/mL,  
doxylamine succinate 1.2 mg/mL,  
sodium citrate dihydrate 40 mg/mL  
and alcohol anhydrous 0.05 mL/mL

ANTITUSSIVE / ANTIHISTAMINIC / DECONGESTANT

**LABORATOIRE RIVA Inc.**  
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# <sup>N</sup>**DALMACOL**

Antitussive / Antihistaminic / Decongestant

## **PART I: HEALTH PROFESSIONAL INFORMATION**

### **SUMMARY PRODUCT INFORMATION**

<b>Route of Administration</b>	<b>Dosage Form / Strength</b>	<b>Non medicinal Ingredients</b>
Oral	Syrup  Hydrocodone Bitartrate Hemipentahydrate 0.33 mg/mL, Etafedrine Hydrochloride 3.33 mg/mL, Doxylamine Succinate 1.2 mg/mL, Sodium Citrate Dihydrate 40 mg/mL and Alcohol Anhydrous 0.05 mL/mL	Amaranth, Peach Flavour, Caramel Color, Citric Acid, Fruity Flavour, Glycerin, Menthol, Methylparaben, Propylparaben, Raspberry Flavour, Sorbitol, Sucrose, Thyme Oil, Purified Water, Yellow FD & C #6

### **INDICATIONS AND CLINICAL USE**

#### **Adults**

**DALMACOL** is indicated for the treatment of adults with 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)**

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

## CONTRAINDICATIONS

- Children younger than 6 years of age.
- Patients who are hypersensitive to the active substances, including hydrocodone bitartrate 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**)

## 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, DALMACOL (which includes hydrocodone bitartrate) 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**

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

### **Accidental Exposure**

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

### **Neonatal Opioid Withdrawal Syndrome**

Prolonged maternal use of DALMACOL 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 DALMACOL 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 DALMACOL and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

### **General**

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

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

**Patients should be instructed not to give DALMACOL (which includes hydrocodone bitartrate) to anyone other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death. DALMACOL should be stored securely to avoid theft or misuse.**

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

### **Abuse and Misuse**

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

DALMACOL 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 DALMACOL; extreme caution and awareness is warranted to mitigate the risk.

### **Cardiovascular**

Hydrocodone bitartrate administration may result in hypotension and dizziness.

### **Dependence/Tolerance**

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

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

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

Patients on prolonged therapy could experience withdrawal symptoms following abrupt discontinuation of therapy or upon administration of an opioid antagonist. Some of the symptoms that may be associated with abrupt withdrawal of an opioid include body aches, diarrhea, gooseflesh, loss of appetite, nausea, nervousness or restlessness, anxiety, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in

sweating, palpitations, unexplained fever, weakness and yawning (see **ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage**).

## **Endocrine**

### **Adrenal Insufficiency**

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

### **Gastrointestinal Effects**

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

### **Neonatal Opioid Withdrawal Syndrome (NOWS)**

Use of **DALMACOL** 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 **DALMACOL** 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 **DALMACOL** is used with benzodiazepines, alcohol, or other CNS depressants.

**DALMACOL** 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**).

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

**Serotonin Syndrome:** **DALMACOL** could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs (e.g. anti-depressants, migraine medications). Treatment with the serotonergic drug should be discontinued if such events (characterized by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. **DALMACOL** 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.

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

### **Psychomotor Impairment**

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

### **Respiratory**

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression from opioid use, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid



antagonists, depending on the patient's clinical status. **DALMACOL** 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 **DALMACOL**, 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 **DALMACOL** and following dose increases.

Hydrocodone bitartrate, included in **DALMACOL** is not recommended for use in any patient in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, lung infections, multiple trauma or extensive surgical procedures.

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

**Hydrocodone, included in DALMACOL, is not indicated for patients under 18 years of age.**

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

**Use in Patients with Chronic Pulmonary Disease:** Monitor patients with significant chronic obstructive pulmonary disease or cor pulmonale, and patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression for respiratory depression, particularly when initiating therapy and titrating with **DALMACOL**, as in these patients, even usual therapeutic doses of **DALMACOL** may decrease respiratory drive to the point of apnea. The use of **DALMACOL** 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**).

### **Special Populations**

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

**Pregnant Women:** Studies in humans have not been conducted. **DALMACOL** 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, can be life-threatening (see **WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome (NOWS)**).

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, **DALMACOL** 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 **DALMACOL** is used in this population.

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

**DALMACOL** 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

Seldom occurrences of adverse effects of **DALMACOL** are drowsiness, dizziness, nausea, nervousness, palpitation or increased blood pressure.

**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

### Overview

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

### Drug-Drug Interactions

**Monoamine Oxidase Inhibitors:** **DALMACOL** is contraindicated in patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy) (see **CONTRAINDICATIONS**).

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

**Inhibitors of CYP3A4 and CYP2D6:** The concomitant use of **DALMACOL** and CYP3A4 inhibitors, such as macrolide antibiotics (e.g., erythromycin), azole-antifungal agents (e.g. ketoconazole), or protease inhibitors (e.g., ritonavir), can increase the plasma concentration of hydrocodone, resulting in increased or prolonged opioid effects. These effects could be more pronounced with concomitant use of **DALMACOL** and CYP2D6 and CYP3A4 inhibitors, particularly when an inhibitor is added after a stable dose of **DALMACOL** is achieved.

Avoid the use of **DALMACOL** while taking a CYP3A4 or CYP2D6 inhibitor. If concomitant use is necessary, monitor patients for respiratory depression and sedation at frequent intervals.

### **Drug-Lifestyle Interactions**

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

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

## **DOSAGE AND ADMINISTRATION**

### **Pediatrics (<18 years of age):**

**DALMACOL is not indicated for use in patients younger than 18 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of hydrocodone to hydromorphone and because of the benefits of symptomatic treatment of cough do not outweigh the risks for use of hydrocodone in these patients.**

**DALMACOL** is contraindicated in children younger than 6 years of age.

### ***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 **DALMACOL** is 30 mL (10 morphine milligram equivalent (MME)). Each patient should be assessed for their risk prior to prescribing **DALMACOL**, 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 **DALMACOL**.*

### **Dosing Considerations**

**DALMACOL** may be taken with or without food, with a glass of water.

### **Recommended Dose and Dosage Adjustment**

Adults: 5 mL every 3 to 5 hours but not more than 30 mL in any 24-hour period.

### **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. **DALMACOL** 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 **DALMACOL**. 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**

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

**DALMACOL should never be disposed of in household trash.** Disposal via a pharmacy take back program is recommended. Unused or expired **DALMACOL** 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.
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**Symptoms:** Slow pulse, flushed face, feeling of lightness in head, temporary anuria, nausea and vomiting, gastric pain, convulsive motions, tremor, respiratory paralysis, extreme general vasodilation.

**Treatment:** Naloxone HCl

## **STORAGE AND STABILITY**

Store at room temperature (15°C - 30°C)

## **DOSAGE FORMS, COMPOSITION AND PACKAGING**

**DALMACOL** is a red limpid syrup.

### **Composition:**

**DALMACOL** contains following medicinal ingredients: hydrocodone bitartrate, etafedrine hydrochloride, doxylamine succinate, sodium citrate dihydrate and alcohol anhydrous.

**DALMACOL** contains following non medicinal ingredients: amaranth, peach flavour, caramel color, citric acid, fruity flavour, glycerin, menthol, methylparaben, propylparaben, raspberry flavour, sorbitol, sucrose, thyme oil, purified water, yellow FD & C #6.

### **Packaging:**

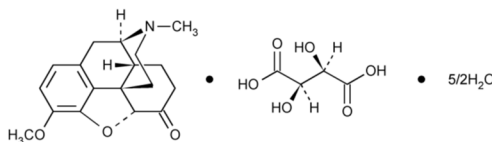
**DALMACOL** is available in 500 mL and 2 L bottles.

## PART II: SCIENTIFIC INFORMATION

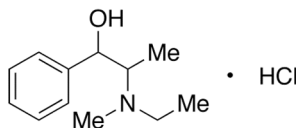
### PHARMACEUTICAL INFORMATION

#### Drug Substance

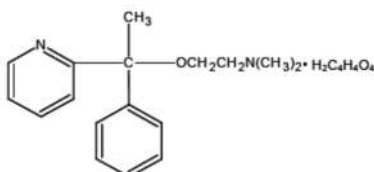
Proper name: Hydrocodone Bitartrate Hemipentahydrate  
Chemical name: Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-, (5a)-, [R-(R\*,R\*)]-2,3-dihydroxybutanedioate (1 : 1), hydrate (2 : 5). 4,5a-Epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1 : 1) hydrate (2 : 5)  
Molecular formula:  $C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2.5H_2O$   
CAS #: 34195-34-1; 6190-38-1  
Molecular weight: 494.49  
Structural formula:



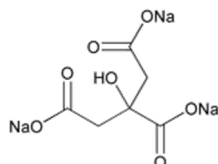
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Chemical name: 1. (1R,2S)-2-[Ethyl (methyl)amino]-1-phenylpropan-1-ol Hydrochloride.  
2. (1R,2S)-2-Ethylmethylamino-1-phenyl-1-propanol Hydrochloride  
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CAS #: 5591-29-7  
Molecular weight: 229.75  
Structural formula:



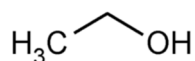
Proper name: Doxylamine Succinate  
 Chemical name: Ethanamine, N,N-dimethyl-2-[1-phenyl-1-(2-pyridinyl)ethoxy]-, butanedioate (1:1) 2-[a-[2-(dimethylamino)ethoxy]-a-methylbenzyl] pyridine succinate (1:1)  
 Molecular formula:  $C_{17}H_{22}N_2O \cdot C_4H_6O_4$   
 CAS #: 562-10-7  
 Molecular weight: 388.46  
 Structural formula:



Proper name: Sodium Citrate Dihydrate  
 Chemical name: 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, trisodium salt; Trisodium citrate (dihydrate)  
 Molecular formula:  $C_6H_5Na_3O_7 \cdot 2H_2O$   
 CAS #: 6132-04-3  
 Molecular weight: 294.10  
 Structural formula:



Proper name: Alcohol Anhydrous  
 Chemical name: Ethyl alcohol  
 Molecular formula:  $C_2H_6O$   
 CAS #: 64-17-5  
 Molecular weight: 46.07  
 Structural formula:





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

**PATIENT MEDICATION INFORMATION**

**<sup>N</sup>DALMACOL**

**Hydrocodone Bitartrate,  
Etfedrine Hydrochloride, Doxylamine Succinate,  
Sodium Citrate and Alcohol Syrup**

Read this carefully before you start taking **DALMACOL** 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 **DALMACOL**.

**Serious Warnings and Precautions**

- **Even if you take DALMACOL 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 DALMACOL. 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 DALMACOL. They could die from taking it. If a person has not been prescribed DALMACOL, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took DALMACOL 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 DALMACOL 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 DALMACOL used for?**

**DALMACOL** is used for the temporary relief of cough, in adults, associated with:

- allergies, or
- the common cold

**DALMACOL** 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 DALMACOL work?**

Hydrocodone bitartrate acts on the brain to suppress cough.

### **What are the ingredients in DALMACOL?**

Medicinal ingredients: hydrocodone bitartrate hemipentahydrate, etafedrine hydrochloride, doxylamine succinate, sodium citrate dihydrate and alcohol anhydrous.

Non-medicinal ingredients: amaranth, peach flavour, caramel color, citric acid, fruity flavour, glycerin, menthol, methylparaben, propylparaben, raspberry flavour, sorbitol, sucrose, thyme oil, purified water, yellow FD & C #6.

### **DALMACOL comes in the following dosage forms:**

Red syrup.

### **Do not use DALMACOL if you:**

- your doctor did not prescribe it for you
- are allergic to hydrocodone bitartrate, etafedrine hydrochloride, doxylamine succinate, sodium citrate, alcohol or to any of the other ingredients in **DALMACOL**
- 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. If you breastfeed and take **DALMACOL**, seek immediate medical care for your baby if they are overly drowsy, sedate, 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 **DALMACOL**.

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

**Other warnings you should know about:**

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

Stop taking DALMACOL 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. As with all opioids, taking hydrocodone bitartrate may cause you to become dependent on it. Do not take more than the dose prescribed to you by your doctor.**

**Breathing problems: DALMACOL 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 problem
- recent multiple traumas or extensive surgical procedures

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

If you are pregnant and are taking **DALMACOL**, 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 **DALMACOL**. 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 **DALMACOL**. **DALMACOL** 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 **DALMACOL**.

**Serotonin Syndrome:** Hydrocodone bitartrate, one of the ingredients of **DALMACOL** 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 **DALMACOL** 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 DALMACOL:**

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking **DALMACOL**. 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 **DALMACOL**
- 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 **DALMACOL** with monoamine oxidase inhibitors (MAOI) or if you have taken MAOI's in the last 14 days.
- drugs used to treat serious mental or emotional disorders (such as schizophrenia)
- antihistamines (drugs used to treat allergies)
- anti-emetics (drugs used to prevent vomiting)
- drugs used to treat muscle spasms and back pain
- warfarin (such as coumadin) and other anticoagulants (used to prevent or treat blood clots)
- anti-retroviral drugs (use to treat viral infections)
- anti-fungal drugs (used to treat fungal infections)
- antibiotic drugs (used to treat bacterial infections)
- some heart medication (such as beta blockers)
- tranquilizers, sedatives, sedating antihistamines, other depressants
- drugs used to treat migraines (e.g. triptans)
- grapefruit juice
- St. John's Wort

### **How to take DALMACOL:**

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

### **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 **DALMACOL**. Be sure to use **DALMACOL** only for the condition for which it was prescribed.

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

Adults: 5 mL every 3 to 5 hours but not more than 30 mL in any 24-hour period.

### **Stopping your Medication:**

If you have been taking **DALMACOL** 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 **DALMACOL**. 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 **DALMACOL**.

### **Refilling your Prescription for DALMACOL:**

A new written prescription is required from your doctor each time you need more **DALMACOL**. 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 **DALMACOL**, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Signs of overdose may include:

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

**Missed Dose:**

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

**What are possible side effects from using DALMACOL?**

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

Side effects may include:

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

<b>Serious side effects and what to do about them</b>			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>RARE:</b>			
<b>Overdose:</b> hallucinations, confusion, inability to walk normally, slow or weak breathing, extreme sleepiness, sedation, or dizziness, floppy muscles/low muscle tone, cold and clammy skin			✓
<b>Respiratory Depression:</b> Slow, shallow or weak breathing			✓
<b>Allergic Reaction:</b> rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
<b>Bowel Blockage (impaction):</b> abdominal pain, severe constipation, nausea			✓
<b>Withdrawal:</b> nausea, vomiting, diarrhea, anxiety, shivering, cold and clammy skin, body aches, loss of appetite, sweating.		✓	
<b>Fast, Slow or Irregular Heartbeat:</b> heart palpitations		✓	
<b>Low Blood Pressure:</b> dizziness, fainting, light-headedness	✓		
<b>Serotonin Syndrome:</b> 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 DALMACOL in a secure place to prevent theft, misuse or accidental exposure.**
- **Keep DALMACOL 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 DALMACOL, get emergency help right away.**
- **Store at room temperature (15°C - 30°C).**

**Disposal:**

**DALMACOL 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 DALMACOL:**

- 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>); the manufacturer's website [www.labriva.com](http://www.labriva.com), or by calling 1-800-363-7988.

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