

Donatuss DC Syrup

Rx Only

DESCRIPTION

Each 5 mL (one teaspoonful) for oral administration contains:

Dihydrocodeine Bitartrate 7.5 mg

(WARNING-May be habit forming)

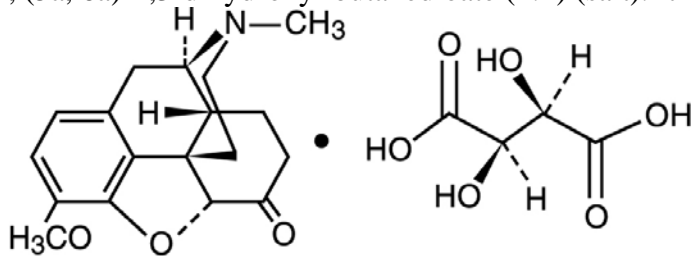
Phenylephrine Hydrochloride 7.5 mg

Guaifenesin 50 mg

This product contains the following inactive ingredients: Bitter Mask, FD&C Blue #1, FD&C Red #40, Grape Flavor, Propylene Glycol, Purified Water, Sodium Saccharin, Sucrose.

This product contains ingredients of the following therapeutic classes: Antitussive, Decongestant and Expectorant.

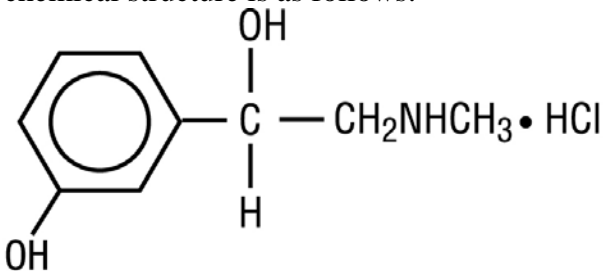
Dihydrocodeine Bitartrate is an antitussive with the chemical name (Morphinan-6-ol,4,5-epoxy-3- methoxy-17-methyl-, (5a, 6a)-2,3-dihydroxy- butanedioate (1:1) (salt). It has the following structural formula:



$C_{18}H_{23}NO_3 \cdot C_4H_6O_6$

M.W. 451.47

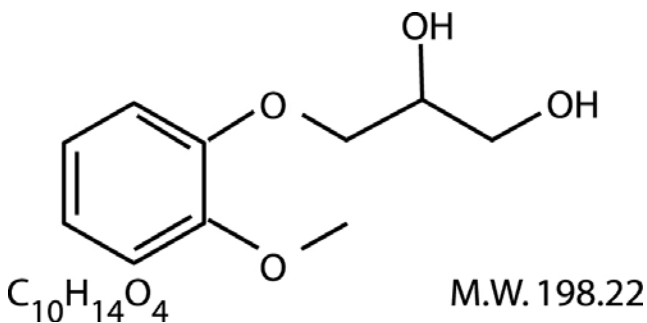
Phenylephrine hydrochloride is an orally effective nasal decongestant. Chemically it is Benzenemethanol, 3-hydroxy-a-[(methylamino)methyl]-, hydrochloride (R)-(-)-m-Hydroxy-a- [(methylamino)methyl] benzyl alcohol hydrochloride. Its chemical structure is as follows:



$C_9H_{13}NO_2 \cdot HCl$

M.W. 203.67

Guaifenesin is an expectorant with the chemical name 1,2-Propanediol,3-(2-methoxyphenoxy)-, (±)-. It has the following structural formula:



$C_{10}H_{14}O_4$

M.W. 198.22

CLINICAL PHARMACOLOGY

Dihydrocodeine is a semisynthetic narcotic analgesic/antitussive related to codeine, with multiple actions qualitatively similar to those of codeine: the most prominent of these involve the central nervous system and organs with smooth muscle components.

Phenylephrine hydrochloride affects its vasoconstrictor activity by releasing noradrenaline from sympathetic nerve endings, and from direct stimulation of α -adrenoreceptors in blood vessels.

Guaifenesin is an expectorant, which increases respiratory tract fluid secretions and helps to loosen phlegm and bronchial secretions. By reducing the viscosity of secretions, guaifenesin increases the efficiency of the cough reflex and of ciliary action in removing accumulated secretions from the trachea and bronchi.

INDICATIONS AND USAGE

This product is indicated for the temporary relief of nasal congestion and dry, non-productive cough associated with upper respiratory tract infections and allergies.

CONTRAINDICATIONS

This combination product is contraindicated in patients with hypersensitivity to dihydrocodeine, codeine, or any of the active or inactive components listed above, or in any situation where opioids are contraindicated including significant respiratory depression (in unmonitored settings or in the absence of resuscitation equipment), acute or severe bronchial asthma or hypercapnia, and paralytic ileus. Sympathomimetic agents are contraindicated in patients with severe hypertension, severe coronary artery disease, patients with narrow angle glaucoma, bronchial asthma, urinary retention, peptic ulcer, and during an asthmatic attack. This product is contraindicated in women who are pregnant.

WARNINGS

General: Considerable caution should be exercised in patients with hypertension, diabetes mellitus, ischemic heart disease, hyperthyroidism, increased intraocular pressure, and prostatic hypertrophy. The elderly (60 years and older) are more likely to exhibit adverse reactions.

Usage In Ambulatory Patients: Dihydrocodeine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.

Respiratory Depression: Respiratory depression is the most dangerous acute reaction produced by opioid agonist preparations, although it is rarely severe with usual doses. Opioids decrease the respiratory tidal volume, minute ventilation, and sensitivity to carbon dioxide. Respiratory depression occurs most frequently in elderly or debilitated patients, usually after large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration. This combination product should be used with caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale and in patients with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or respiratory depression.

Hypertensive Effect: Dihydrocodeine, like all opioid analgesics, may cause hypotension in patients whose ability to maintain blood pressure has been compromised by a depleted blood volume or who received concurrent therapy with drugs such as phenothiazine or other agents which compromise vasomotor tone. This product may produce orthostatic hypotension in ambulatory patients. This combination product should be administered with caution to patients with circulatory shock since vasodilation produced by the drug may further reduce cardiac output and blood pressure.

Dependence: Dihydrocodeine can produce drug dependence of the codeine type and has the potential of being abused. This product should be prescribed and administered with the appropriate degree of caution (See Drug Abuse and Dependence section).

PRECAUTIONS

General: This combination product should be used with caution in elderly or debilitated patients or those with any of the following conditions: adrenocortical insufficiency (e.g., Addison's disease); asthma; central nervous system depression or coma; chronic obstructive pulmonary disease; decreased respiratory reserve (including emphysema, severe obesity, cor pulmonale, or kyphoscoliosis); delirium tremens; diabetes, head injury; hypotension; hypertension; increased intracranial pressure; myxedema or hypothyroidism; prostatic hypertrophy or urethral structure; and toxic psychosis. The benefits and risks of opioids in patients taking monoamine oxidase inhibitors and in those with a history of drug abuse should be carefully considered. This combination product may aggravate convulsions in patients with convulsive disorders, and like all opioids, may induce or aggravate seizures in some clinical settings.

Drug Interactions:

General: Sympathomimetic amines may reduce the antihypertensive effects of methyldopa, mecamylamine, reserpine, and veratrum alkaloids.

Other CNS Depressants: Patients receiving other opioid analgesics, sedatives or hypnotics, muscle relaxants, general anesthetics, centrally acting anti-emetics, phenothiazines or other tranquilizers, or alcohol concomitantly with this product may exhibit additive depressant effects on the central nervous system. When such combination therapy is contemplated, the dose of one or both agents should be reduced. Concomitant use of dihydrocodeine with alcohol and other CNS depressants may have an additive effect.

Monoamine Oxidase Inhibitors: Dihydrocodeine, like all opioids, interact with monoamine oxidase inhibitors causing central nervous system excitation and hypertension. MAO inhibitors and beta-adrenergic blockers increase the affects of sympathomimetics.

Information for Patients:

Patients receiving this product should be given the following information:

- This product may inhibit mental or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.
- Report any adverse experiences occurring during therapy.
- Do not adjust the dose of this product without consulting the prescribing professional.
- Do not combine this product with alcohol or other central nervous system depressants.
- Women of childbearing potential who become, or are planning to become pregnant should be advised to consult their physician regarding the effects of opioids and other drug use during pregnancy on themselves and their unborn child.

Patients should be advised that this product is a potential drug of abuse. They should protect it from theft, and it should never be given to anyone other than the individual for whom it was prescribed.

Pregnancy: Teratogenic Effects -Pregnancy Category

C: Animal reproduction studies have not been conducted with this product. It is also not known whether this combination product can cause fetal harm when administered to pregnant women or can affect reproduction capacity in males and females. This combination product should be given to a pregnant woman only if clearly needed, especially during the first trimester.

Nonteratogenic Effects:

Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. The intensity of the syndrome does not always correlate with the duration of the maternal opioid use or dose. There is no consensus on the best method of managing withdrawal. Chlorpromazine 0.7-1.0 mg/kg q6h, phenobarbital 2 mg/kg q6h, and paregoric 2-4 drops/kg q4h, have been used to treat withdrawal symptoms in infants. The duration of therapy is 4 to 28 days, with dosages decreased as tolerated.

Labor and Delivery: This product is not recommended for use by women during and immediately before labor and delivery because oral opioids may cause respiratory depression in the newborn.

Nursing Mothers: Due to the possible passage of the ingredients into breast milk, this product should not be given to nursing mothers.

Pediatric Use: This product is not recommended for use in children under six years of age. Children under two years may be more susceptible to respiratory arrest, coma, and death. Very young children may be more susceptible to the effects, especially the vasopressor effects of sympathomimetic amines. Appropriate studies on the relationship of age to the effects of guaifenesin have not been performed in the pediatric population. However, no pediatric specific problems have been documented to date.

Geriatric Use: This product should be given with caution to the elderly.

Hepatic Impairment: This product should be given with caution to patients with hepatic insufficiency. Since dihydrocodeine is metabolized by the liver the effects of this combination product should be monitored closely in such patients.

Renal Impairment: This product should be used with caution and at reduced dosage in the presence of impaired renal function.

Pancreatic/biliary Tract Disease: Opioids may cause spasms of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including pancreatitis.

ADVERSE REACTIONS

The most frequently observed adverse reactions with dihydrocodeine include light-headedness, dizziness, drowsiness, headache, fatigue, sedation, sweating, nausea, vomiting, constipation, pruritus, and skin reactions. With the exception of constipation, tolerance develops to most of these effects. Other reactions that have been observed with dihydrocodeine or opioids include respiratory depression, orthostatic hypotension, cough suppression, confusion, diarrhea, miosis, abdominal pain, dry mouth, indigestion, anorexia, spasm of biliary tract, and urinary retention. Physical and psychological dependence are possibilities. Hypersensitivity reactions (include anaphylactoid reactions), hallucinations, vivid dreams, granulomatous interstitial nephritis, severe narcosis and acute renal failure have been reported rarely during dihydrocodeine administration. Other reactions observed with the ingredients in this product include lassitude, nausea, giddiness, dryness of mouth, blurred vision, cardiac palpitations, flushing, increased irritability or excitement (especially in children).

DRUG ABUSE AND DEPENDENCE

This combination product is subject to the provisions of the Controlled Substances Act and has been placed in Schedule III. Dihydrocodeine can produce drug dependence of the codeine type and therefore has the potential of being abused. Psychological dependence, physical dependence, and tolerance may develop upon repeat administration of dihydrocodeine, and it should be prescribed and administered with the same degree of caution appropriate to the use of other opioid medications. Symptoms of dihydrocodeine withdrawal consist of irritability, restlessness, insomnia, diaphoresis, anxiety, and palpitations.

OVERDOSAGE

An overdose of this product is a potentially lethal poly-drug overdose situation, and consultation with a regional Poison Control Center is recommended. A listing of the Poison Control Centers can be found in a standard reference such as the Physician's Desk Reference.

Signs and Symptoms:

Symptoms of an overdose include pinpoint pupils, respiratory depression, extreme somnolence progressing to stupor, loss of consciousness or coma, skeletal muscle flaccidity, cold and clammy skin and other symptoms common with

narcotic overdose. Convulsions, cardiovascular collapse, and death may occur. A single case of acute rhabdomyolysis associated with an overdose of dihydrocodeine has been reported.

Recommended Treatment:

Immediate treatment of an overdose of this product includes support of cardiovascular function and measures to reduce further drug absorption. Vomiting should be induced with syrup of ipecac. If the patient is alert and has adequate laryngeal reflexes, oral activated charcoal should follow. The first dose should be accompanied by an appropriate cathartic. Gastric lavage may be necessary. Hypotension is usually hypovolemic and should be treated with fluids. Endotracheal intubation and artificial respiration may be necessary. The pure opioid antagonist naloxone or nalmexone is a specific antidote against respiratory depression that results from opioid overdose. Opioid antagonists should not be given in the absence of clinically significant respiratory or circulatory depression secondary to opioid overdose. They should be administered cautiously to persons who are known, or suspected to be, physically dependent on any opioid agonist including dihydrocodeine. In such cases, an abrupt or complete reversal of opioid effects may precipitate an acute abstinence syndrome. The prescribing information for the specific opioid antagonist should be consulted for details of their proper use.

DOSAGE AND ADMINISTRATION

Adults and children over 12 years:

1 to 2 teaspoonfuls (5 mL to 10 mL), every 4 to 6 hours, as needed.

Children 6 to under 12 years of age:

1/2 to 1 teaspoonful (2.5 mL to 5 mL), every 4 to 6 hours, as needed.

Not recommended for children under 6 years of age.

HOW SUPPLIED

Donatuss DC Syrup is supplied as a alcohol free,☐ gluten free syrup with a grape flavor in 16 fl oz☐ (473 mL) bottles, NDC 16477-136-16, and 15 mL professional samples, NDC 16477-136-15.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN. IN CASE OF ACCIDENTAL OVERDOSE, SEEK PROFESSIONAL ASSISTANCE OR CONTACT A POISON CONTROL CENTER IMMEDIATELY.

Store at controlled room temperature, 15°-30°C (59°-86°F).

Tamper evident by foil seal under cap. Do not use if foil seal is broken or missing.

Supplied in a tight, light-resistant container as defined in the USP/NF with a child-resistant closure.

Rx Only

Manufactured for:

Laser Pharmaceuticals, Inc.

Greenville, SC 29615

Manufactured by:

Great Southern Laboratories

Houston, TX 77099

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