

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

^N**DIMETANE[®] EXPECTORANT DC**

Brompheniramine Maleate, Phenylephrine Hydrochloride, Guaifenesin and Hydrocodone
Bitartrate Syrup

2 mg/ 5 mg/ 100 mg/1.8 mg: per 5 mL of syrup

Antihistamine/ Decongestant/ Expectorant/ Antitussive

Pfizer Consumer Healthcare,
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DIMETANE[®] EXPECTORANT DC

Brompheniramine Maleate, Phenylephrine Hydrochloride, Guaifenesin and Hydrocodone Bitartrate Syrup

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

| Route of Administration | Dosage Form / Strength | Nonmedicinal Ingredients |
|-------------------------|--|--|
| Oral | Syrup, each 5 mL of which contains: brompheniramine maleate 2 mg, phenylephrine hydrochloride 5 mg, guaifenesin 100 mg and hydrocodone bitartrate 1.8 mg | Alcohol, citric acid, cola flavour, D&C Red No. 33, FD&C Red No. 40, glycerin, invert sugar, menthol flavour, raspberry flavours, sodium benzoate and water. |

INDICATIONS AND CLINICAL USE

Adults and Children 12 years and older

Dimetane[®] Expectorant DC is indicated for:

- the temporary relief of coughing and the complications of allergic states including manifestations such as perennial and seasonal allergic rhinitis
- the symptomatic relief of cough, nasal stuffiness and rhinitis accompanying the common cold and other upper respiratory tract infections.

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 (<12 years of age)

The safety and efficacy of Dimetane[®] Expectorant DC has not been studied in the pediatric population. Therefore the use of Dimetane[®] Expectorant DC is not recommended in patients under 12 years of age. The use of hydrocodone in patients below the age of 6 years has been associated with increased safety concerns (i.e. respiratory depression) regardless of clinical setting (see **WARNINGS AND PRECAUTIONS, Neurologic, Respiratory and Special Populations, Pediatrics**).

CONTRAINDICATIONS

Dimetane[®] Expectorant DC is contraindicated in:

- Patients who are hypersensitive to the active substance brompheniramine maleate, phenylephrine hydrochloride, guaifenesin and 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 persistent or chronic cough (as occurs with smoking), 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, convulsive disorders.
- Patients with diabetes, high blood pressure, heart or thyroid disease, glaucoma or trouble urinating due to an enlarged prostate and bladder neck obstruction.
- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure, head injury or suffer from seizures.
- 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 also 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, DIMETANE[®] EXPECTORANT DC (hydrocodone bitartrate and phenylephrine HCl) 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

DIMETANE[®] EXPECTORANT DC 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 DIMETANE[®] EXPECTORANT DC and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS, Abuse and Misuse). DIMETANE[®] EXPECTORANT DC 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 Dimetane[®] Expectorant DC. 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 Dimetane[®] Expectorant DC or following a dose increase. Further, instruct patients of the hazards related to taking opioids, including fatal overdose.

Accidental Exposure

Accidental ingestion of DIMETANE[®] EXPECTORANT DC, 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 DIMETANE[®] EXPECTORANT DC 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 hydrocodone bitartrate 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).

- Reserve concomitant prescribing of DIMETANE[®] EXPECTORANT DC 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 (see DOSAGE AND ADMINISTRATION, disposal, for instructions on proper disposal).

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

Patients should be cautioned not to consume alcohol while taking Dimetane[®] Expectorant DC as it may increase the chance of experiencing serious adverse events, including death.

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

Abuse and Misuse

Like all opioids, **Dimetane[®] Expectorant DC** is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, **Dimetane[®] Expectorant DC** 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

DIMETANE[®] EXPECTORANT DC 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 DIMETANE[®] EXPECTORANT DC; extreme caution and awareness are warranted to mitigate the risk.

Cardiovascular

Hydrocodone administration may result in hypotension and dizziness.

Dependence/Tolerance

As with other opioids, tolerance and physical dependence may develop upon repeated administration of Dimetane[®] Expectorant DC 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 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 may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Neonatal Opioid Withdrawal Syndrome (NOWS)

Use of Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC, 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 Dimetane® Expectorant DC is used with benzodiazepines, alcohol, or other CNS depressants.

Dimetane® Expectorant DC 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 **Dimetane® Expectorant DC** may aggravate convulsions in patients with convulsive disorders, and may induce or aggravate seizures in some clinical settings. Therefore, **Dimetane® Expectorant DC** should not be used in these patients (see **CONTRAINDICATIONS**).

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

Serotonin Syndrome: Dimetane® Expectorant DC could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs (e.g. antidepressants, 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. Dimetane® Expectorant DC should not be used in combination with MAO inhibitors or serotonin-precursors (such as L-tryptophan, oxitriptan) and should be used with caution in combination with other serotonergic drugs (triptans, certain tricyclic antidepressants, lithium, tramadol, St. John's Wort) due to the risk of serotonergic syndrome (see **DRUG INTERACTIONS**).

Psychomotor Impairment

Dimetane® Expectorant DC 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 with other CNS depressants, including other opioids, phenothiazine,

sedative/hypnotics and alcohol.

Respiratory

Hydrocodone, including Dimetane[®] Expectorant DC 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.

The use of hydrocodone is not recommended 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 Dimetane[®] Expectorant DC 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. The 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 pre-existing respiratory depression for respiratory depression, particularly when initiating therapy and titrating with Dimetane[®] Expectorant DC, as in these patients, even usual therapeutic doses of Dimetane[®] Expectorant DC may decrease respiratory drive to the point of apnea. The use of Dimetane[®] Expectorant DC 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 lead to a decrease in sex hormone levels. It may also lead to low libido (desire to have sex), erectile dysfunction or being infertile.

Special Populations

Special Risk Groups: Hydrocodone 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. Dimetane[®] Expectorant DC 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**).

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, Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC is used in this population.

Pediatrics (< 18 years of age): The use of Dimetane Expectorant DC is not recommended in patients under 12 years of age (see **DOSAGE AND ADMINISTRATION**).

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

Hypersensitivity reactions to brompheniramine maleate, including skin rashes, urticaria, hypotension and thrombocytopenia may occur rarely. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered.

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

Overview

Do not use with a monoamine oxidase inhibitor (MAOI) or for 2 weeks after stopping the MAOI drug (see CONTRAINDICATIONS).

Do not use if you have taken medication in the last 14 days for high blood pressure or depression, including other antihistamines, other products that contain codeine or cough suppressants, decongestants, expectorants, tranquilizers, sedating drugs, or if you consumer 3 or more alcoholic beverages per day.

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**). Dimetane[®] Expectorant DC should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

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**).

Drug Laboratory Interactions

Guaifenesin has been shown to produce a color interference with certain clinical laboratory determinations of 5-hydroxyindoleacetic acid (5-HIAA) and vanillylmandelic acid (VMA).

Drug-Lifestyle Interactions

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

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

DOSAGE AND ADMINISTRATION

Dosing Considerations

Dimetane[®] Expectorant DC may be taken with or without food, with a glass of water.

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 DIMETANE[®] EXPECTORANT DC is 40 mL (14 morphine milligram equivalent). Each patient should be assessed for their risk prior to prescribing DIMETANE[®] EXPECTORANT DC, 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 DIMETANE[®] EXPECTORANT DC

Recommended Dose and Dosage Adjustment

Adults and Children 12 years and over:

Take 10 mL (2 tsp) every 6 hours. Do not exceed 4 doses (8tsp.) in a 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. Dimetane[®] Expectorant DC 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 DIMETANE[®] EXPECTORANT DC. 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

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

Dimetane[®] Expectorant DC should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired Dimetane[®] Expectorant DC 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: May vary from CNS depression to stimulation. Stimulation is particularly likely in children as a result of antihistamine overdosage. Atropine-like signs and symptoms such as dry mouth, fixed, dilated pupils, flushing and gastrointestinal symptoms may also occur.

Treatment: If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by administering syrup of ipecac. Precautions against aspirations must be taken, especially in infants and children. If vomiting is unsuccessful, gastric lavage is indicated within 3 hours after ingestion and even later if large amounts of milk and cream were given beforehand. Emesis or lavage should be followed by the administration of activated charcoal. Stimulants should not be used. Vasopressors may be used to treat hypotension. Naloxone may be used to treat hydrocodone toxicity.

ACTION AND CLINICAL PHARMACOLOGY

Pharmacodynamics

Endocrine System:

Opioids may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical signs and symptoms may be manifest from these hormonal changes.

Mechanism of Action

Brompheniramine Maleate: The mechanism of action of brompheniramine and other similar antihistamines is competition with histamine for histamine receptor sites. By occupying the histamine receptor sites, they prevent histamine from activating the site. Brompheniramine is an H-1 histamine receptor antagonist, acting on the H-1 histamine receptors to block histamine-induced responses.

Guaifenesin: Guaifenesin is thought to act as an expectorant by increasing the volume and reducing the viscosity of secretions in the trachea and bronchi. Thus, it may increase the efficiency of the cough reflex and facilitate removal of the secretions. However, objective evidence for this is limited and conflicting.

Phenylephrine Hydrochloride: Phenylephrine is used orally to stimulate alpha-adrenergic receptors on the nasal mucosa (direct effect) causing vasoconstriction of local vessel. The vasoconstrictive action decreases mucosal edema, thereby leading to a decongestant effect.

Hydrocodone Bitartrate: Hydrocodone is a semisynthetic opioid agonist that acts as a full agonist, binding to and activating opioid receptors at sites in the peri-aqueductal and periventricular gray matter, the ventromedial medulla, and the spinal cord to produce analgesia. Although relatively selective for the mu-opioid receptor, it can interact with other opioid receptors at higher doses. The analgesia, as well as the euphorant, respiratory depressant and physiologic dependence properties result because of the agonist action at the mu receptors.

Special Populations and Conditions

Pediatrics:

Regardless of clinical setting, the use of DIMETANE[®] EXPECTORANT DC is not recommended in patients below the age of 12 years due to increased safety concern (see Warnings and Precautions/Use in Children)

STORAGE AND STABILITY

Dimetane[®] Expectorant DC should be stored at room temperature (15-30°C)

Others:

Keep in a safe place out of the reach of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Composition:

Each 5 mL of cherry-red liquid, menthol and raspberry taste and odor, contains: hydrocortisone bitartrate 1.8 mg, brompheniramine maleate 2 mg, phenylephrine hydrochloride 5 mg and guaifenesin 100 mg.

Non-medicinal Ingredients: Alcohol, citric acid, cola flavour, D&C Red No. 33, FD&C Red No. 40, glycerin, invert sugar, menthol flavour, raspberry flavours, sodium benzoate and water.

Energy: 13.92 kcal / 5mL, Sodium: 0.8 mg / 5mL.

Packaging:

Bottles of 1 L.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:

Brompheniramine Maleate
Phenylephrine Hydrochloride
Guaifenesin
Hydrocodone Bitartrate

Chemical name:

Brompheniramine Maleate:

Brompheniramine Chemical name:

IUPAC Name: 3-(4-bromophenyl)-*N,N*-dimethyl-3-pyridin-2-yl-propan-1-amine

Phenylephrine Hydrochloride:

Phenylephrine Chemical name:

IUPAC Name: 3-[(1*R*)-1-hydroxy-2-(methylamino)ethyl]phenol;hydrochloride

CAS Name: (α *R*)-3-Hydroxy- α -[(methylamino)methyl]benzenemethanol

Additional Names: (-)-*m*-hydroxy- α -[(methylamino)methyl]benzyl alcohol; *l*-1-(*m*-hydroxyphenyl)-2-methylaminoethanol; *l*- α -hydroxy- β -methylamino-3-hydroxy-1-ethylbenzene; *m*-methylaminoethanolphenol; metaoxedrin

Guaifenesin:

IUPAC Name: (*RS*)-3-(2-methoxyphenoxy)propane-1,2-diol

CAS Name: 3-(2-Methoxyphenoxy)-1,2-propanediol

Additional Names: glycerol mono(2-methoxyphenyl) ether; glycerol α -(2-methoxyphenyl) ether; guaiacyl glyceryl ether; glyceryl guaiacyl ether; glycerol guaiacolate; α -glyceryl guaiacol ether; *o*-methoxyphenyl glyceryl ether; 1,2-dihydroxy-3-(2-methoxyphenoxy)propane; guaiacol glyceryl ether; guaiphenesin; guaiacuran

Hydrocodone Bitartrate:

Hydrocodone Chemical name:

IUPAC Name: 4,5 α -epoxy-3-methoxy-17-methylmorphinan-6-one

CAS Name: (5 α)-4,5-Epoxy-3-methoxy-17-methylmorphinan-6-one

Additional Names: dihydrocodeinone

Hydrocodone Bitartrate Chemical name:

IUPAC Name: 4R,4aR,7aR,12bS)-9-methoxy-3-methyl-

1,2,4,4a,5,6,7a,13-octahydro-4,12-methanobenzofuro[3,2-e]isoquinoline-7-one;2,3-dihydroxybutanedioic acid

CAS Name: (5 α)-4,5-Epoxy-3-methoxy-17-methylmorphinan-6-one

Molecular formula and molecular mass:

Brompheniramine Maleate:

Molecular Formula: C₁₆H₁₉BrN₂·C₄H₄O₄

Molecular Weight: 435.32

Phenylephrine Hydrochloride:

Molecular Formula: C₉H₁₃NO₂·HCl

Molecular Weight: 203.67

Guaifenesin:

Molecular Formula: C₁₀H₁₄O₄

Molecular Weight: 198.22

Hydrocodone Bitartrate:

Hydrocodone:

Molecular Formula: C₁₈H₂₁NO₃

Molecular Weight: 299.37

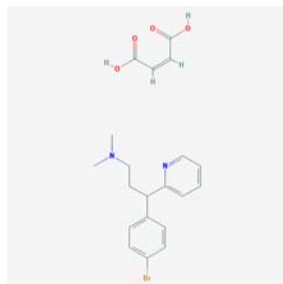
Hydrocodone Bitartrate:

Molecular Formula: C₂₂H₂₇NO₉

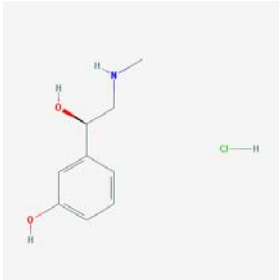
Molecular Weight: 397.36 449.45108 g/mol

Structural formula:

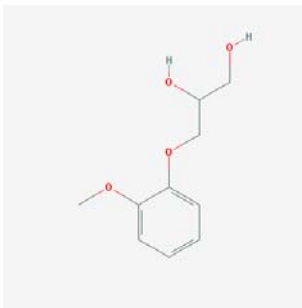
Brompheniramine Maleate:



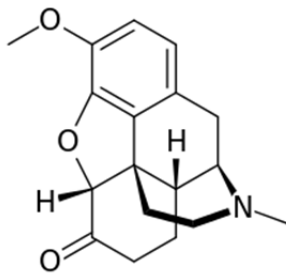
Phenylephrine Hydrochloride:



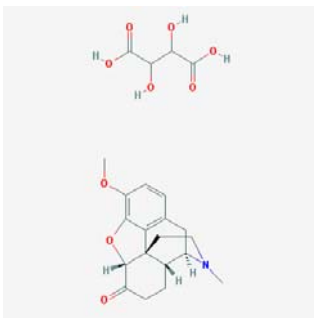
Guaifenesin:



Hydrocodone:



Hydrocodone Bitartrate



Physicochemical Properties:

Brompheniramine Maleate: Crystals, melting point 132-134 °C. Freely soluble in water; soluble in alcohol, chloroform. pH of a 2% aqueous solution about 5. Slightly soluble in ether, benzene.

Phenylephrine Hydrochloride: Odorless white microcrystalline powder. Bitter taste. pH (1% aqueous solution) about 5 with melting point 140-145 °C. $[\alpha]_D -44.0$ (c = 2.16 in H₂O). pK₁ 8.77; pK₂ 9.84. uv max (0.05N HCl): 216, 274, 279 nm ($\epsilon \times 10^{-3}$ 5.91, 1.81, 1.65). uv max (0.05N NaOH): 239, 292.5 ($\epsilon \times 10^{-3}$ 8.95, 3.04). Freely soluble in water, alcohol. LD₅₀ in rats (mg/kg): 17 ±1.1 i.p.; 33 ±2.0 s.c. (Warren, Werner).

Guaifenesin: Crystals, melting point 132-134 °C. Freely soluble in water; soluble in alcohol, chloroform. pH of a 2% aqueous solution about 5. Slightly soluble in ether, benzene.

Hydrocodone: Prisms from alcohol, melting point 197-198 °C. $[\alpha]_D^{25} -203$ (c = 0.41 in CHCl₃). Soluble in alcohol, acetone, ethyl acetate, chloroform. Insoluble in water. uv max: 280 nm (ϵ 1310). LD₅₀ s.c. in mice: 85.7 mg/kg (Eddy, Reid).

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

DIMETANE[®] EXPECTORANT DC

Brompheniramine Maleate 2 mg, Phenylephrine Hydrochloride 5 mg, Guaifenesin 100 mg and Hydrocodone Bitartrate Syrup 1.8 mg: per 5mL of syrup

Read this carefully before you start taking **Dimetane[®] Expectorant DC** 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 **Dimetane[®] Expectorant DC**.

Serious Warnings and Precautions

- **Even if you take Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC. 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 Dimetane[®] Expectorant DC. If a person has not been prescribed DIMETANE[®] EXPECTORANT DC, they could die from taking it. This is especially true for children. This is especially true for children.**
- **If you took DIMETANE[®] EXPECTORANT DC 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 Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC used for?

Dimetane[®] Expectorant DC is indicated for use in adults and children 12 years of age and over for the temporary relief of cough, runny nose, stuffy nose associated with:

- allergies, or
- the common cold

How does Dimetane[®] Expectorant DC work?

Brompheniramine Maleate helps stop runny noses and sneezing

Phenylephrine Hydrochloride helps clear nasal congestion

Guaifenesin helps loosen phlegm

Hydrocodone Bitartrate acts on the brain to suppress cough.

What are the ingredients in Dimetane[®] Expectorant DC?

Medicinal ingredients: Brompheniramine Maleate, Phenylephrine Hydrochloride, Guaifenesin and Hydrocodone Bitartrate

Non-medicinal ingredients: Alcohol, citric acid, cola flavour, D&C Red No. 33, FD&C Red No. 40, glycerin, invert sugar, menthol flavour, raspberry flavours, sodium benzoate and water.

Dimetane[®] Expectorant DC comes in the following dosage forms:

Brompheniramine Maleate 2 mg, Phenylephrine Hydrochloride 5 mg, Guaifenesin 100 mg and Hydrocodone Bitartrate Syrup 1.8 mg: per 5mL of syrup

Do not use Dimetane[®] Expectorant DC if:

- your doctor did not prescribe it for you
- you are allergic to brompheniramine maleate, phenylephrine hydrochloride, guaifenesin or hydrocodone bitartrate or to any of the other ingredients in Dimetane[®] Expectorant DC
- you have severe asthma, trouble breathing, or other breathing problems
- you have any heart problems
- you have bowel blockage or narrowing of the stomach or intestines
- you have severe pain in your abdomen
- have a head injury
- you are at risk for having seizures
- 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)
- you are going to have, or recently had, a planned surgery
- you are pregnant or planning to become pregnant or in labour

- are breastfeeding

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

- have a history of illicit or prescription drug or alcohol abuse
- have severe kidney, liver or lung disease
- have low blood pressure
- have past or current depression
- suffer from chronic or severe constipation
- have persistent or chronic cough (as occurs with smoking), glaucoma, diabetes, high blood pressure, heart disease
- have problems with your thyroid, adrenal or prostate gland
- have, or had in the past hallucinations or other severe mental problems
- suffer from migraines
- or under a physician's care

Other warnings you should know about:

Use in Children

Young children are at greater risk of the sedating effects of narcotic cough drugs. The use of hydrocodone in children less than 6 years of age has led to slow, shallow or weak breathing that has been fatal. Dimetane Expectorant DC should be given with caution to children. This is especially true for children who have difficulty breathing. **DO NOT** give **Dimetane Expectorant[®] DC** to young children. **Dimetane[®] Expectorant DC** is not recommended for children under 12.

Opioid dependence and addiction:

There are important differences between physical dependence and addiction. It is important that you talk to your doctor if you have any questions or concerns about abuse, addiction or physical dependence. As with all opioids, taking hydrocodone may cause you to become dependent on it. Do not take more than the dose prescribed to you by your doctor.

Pregnancy, nursing, labour and delivery:

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

Driving and using machines: Before you do tasks which may require special attention, you should wait until you know how you react to Dimetane[®] Expectorant DC. Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC.

Serotonin Syndrome: Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC with certain antidepressants 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 Dimetane[®] Expectorant DC:

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking Dimetane[®] Expectorant DC. 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 Dimetane[®] Expectorant DC
- 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 Dimetane[®]
- Expectorant DC 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
- warfarin (such as coumadin) and other anticoagulants (used to prevent or treat blood clots)
- anti-retroviral drugs (used 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 (eg. triptans)
- grapefruit juice
- St. John's Wort

How to take Dimetane[®] Expectorant DC:

Usual Dose:

Adults and Children 12 years and over:

Take 10 mL (2 tsps.) every 6 hours. Do not exceed 4 doses (8 tsps.) in a 24-hour period.

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 Dimetane[®] Expectorant DC. Be sure to use Dimetane[®] Expectorant DC only for the condition for which it was prescribed.

If you develop any side effect as a result of taking Dimetane[®] Expectorant DC, tell your doctor immediately.

Stopping your Medication

If you have been taking Dimetane[®] Expectorant DC for more than a few days you may experience some of the following uncomfortable symptoms when you stop taking it:

- 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 {added for consistency with ER wording}
- an unexplained fever
- weakness
- yawning

Refilling your Prescription for Dimetane[®] Expectorant DC:

A new written prescription is required from your doctor each time you need more Dimetane[®] Expectorant DC.

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 Dimetane [®] Expectorant DC, 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 Dimetane® Expectorant DC?

These are not all the possible side effects you may feel when taking Dimetane® Expectorant DC. 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
- Mild mental stimulation
- Convulsions
- Urinary retention
- Low sex drive, impotence (erectile dysfunction), infertility

Talk with your doctor or pharmacist about ways to prevent constipation when you start using **BRAND NAME**.

| 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: 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

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](https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html): <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>
- 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 1908C
Ottawa, ON
K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect \(https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html\)](https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html).

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:

- Store at room temperature (15-30°C).
- **Keep Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC, get emergency help right away.**

Disposal:

Dimetane[®] Expectorant DC 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 Dimetane[®] Expectorant DC:

- 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): (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>), or by calling Pfizer Consumer Healthcare, a division of Pfizer Canada Inc., Mississauga, Ontario L5R 4B2 at 1-888-275-9938.

This leaflet was prepared by Pfizer Consumer Healthcare, a division of Pfizer Canada Inc.

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