BROMPHENIRAMINE MALEATE, PSEUDOEPHEDRINE HYDROCHLORIDE, AND DEXTROMETHORPHAN HYDROBROMIDE- brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup
Taro Pharmaceuticals U.S.A., Inc.

Brompheniramine Maleate, Pseudoephedrine Hydrochloride, and Dextromethorphan Hydrobromide
Syrup

Rx only

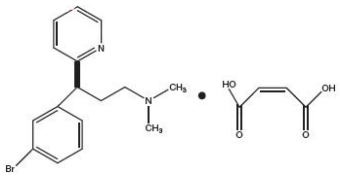
DESCRIPTION

Brompheniramine Maleate, Pseudoephedrine Hydrochloride, and Dextromethorphan Hydrobromide Syrup 2 mg/30 mg/10 mg per 5 mL is a clear, colorless to slightly yellowish grape flavored solution.

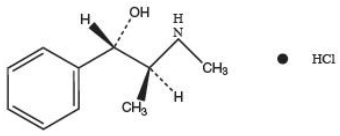
Each 5 mL (1 teaspoonful) contains:

Brompheniramine Maleate, USP	2 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Dextromethorphan Hydrobromide, USP	10 mg

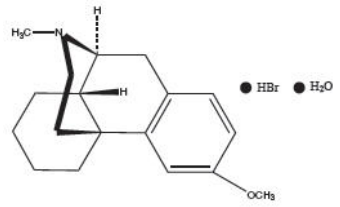
Inactive Ingredients: citric acid anhydrous, glycerin, grape flavor, methylparaben, propylene glycol, purified water, sodium benzoate and sucrose.



$C_{16}H_{19}BrN_2 \cdot C_4H_4O_4$
M.W. 435.31
Brompheniramine Maleate, USP
(±)-2- *p*-Bromo-α-2-(dimethylamino)ethylbenzylpyridine maleate (1:1)



$C_{10}H_{15}NO \cdot HCl$
M.W. 201.69
Pseudoephedrine Hydrochloride, USP
(+)-Pseudoephedrine hydrochloride



$C_{18}H_{25}NO \cdot HBr \cdot H_2O$
M.W. 370.32
Dextromethorphan Hydrobromide, USP
3-Methoxy-17-methyl-9α, 13α, 14α-morphinan hydrobromide monohydrate

Antihistamine/Nasal Decongestant/Antitussive syrup for oral administration.

CLINICAL PHARMACOLOGY

Brompheniramine maleate is a histamine antagonist, specifically an H_1-receptor-blocking agent belonging to the alkylamine class of antihistamines. Antihistamines appear to compete with histamine for receptor sites on effector cells. Brompheniramine also has anticholinergic (drying) and sedative effects. Among the antihistaminic effects, it antagonizes the allergic response (vasodilation, increased vascular permeability, increased mucus secretion) of nasal tissue. Brompheniramine is well absorbed

from the gastrointestinal tract, with peak plasma concentration after single, oral dose of 4 mg reached in 5 hours; urinary excretion is the major route of elimination, mostly as products of biodegradation; the liver is assumed to be the main site of metabolic transformation.

Pseudoephedrine acts on sympathetic nerve endings and also on smooth muscle, making it useful as a nasal decongestant. The nasal decongestant effect is mediated by the action of pseudoephedrine on a-sympathetic receptors, producing vasoconstriction of the dilated nasal arterioles. Following oral administration, effects are noted within 30 minutes with peak activity occurring at approximately one hour.

Dextromethorphan acts centrally to elevate the threshold for coughing. It has no analgesic or addictive properties. The onset of antitussive action occurs in 15 to 30 minutes after administration and is of long duration.

INDICATIONS AND USAGE

Brompheniramine Maleate, Pseudoephedrine Hydrochloride, and Dextromethorphan Hydrobromide Syrup is indicated for relief of coughs and upper respiratory symptoms, including nasal congestion, associated with allergy or the common cold.

CONTRAINDICATIONS

Hypersensitivity to any of the ingredients. Do not use in the newborn, in premature infants, in nursing mothers, or in patients with severe hypertension or severe coronary artery disease. Do not use dextromethorphan in patients receiving monoamine oxidase (MAOI) inhibitors (see **Drug Interactions**).

Antihistamines should not be used to treat lower respiratory tract conditions including asthma.

WARNINGS

Especially in infants and small children, antihistamines in overdosage may cause hallucinations, convulsions, and death.

Antihistamines may diminish mental alertness. In the young child, they may produce excitation.

PRECAUTIONS

General

Because of its antihistamine component, brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL should be used with caution in patients with a history of bronchial asthma, narrow angle glaucoma, gastrointestinal obstruction, or urinary bladder neck obstruction. Because of its sympathomimetic component, brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL should be used with caution in patients with diabetes, hypertension, heart disease, or thyroid disease.

Information for Patients

Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating dangerous machinery.

Drug Interactions

Monoamine oxidase (MAO) inhibitors

Hyperpyrexia, hypotension, and death have been reported coincident with the coadministration of MAO

inhibitors and products containing dextromethorphan. In addition, MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines and may enhance the effect of pseudoephedrine. Concomitant administration of brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL and MAO inhibitors should be avoided (see **CONTRAINDICATIONS**).

Central nervous system (CNS) depressants

Antihistamines have additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, antianxiety agents, etc.).

Antihypertensive drugs

Sympathomimetic may reduce the effects of antihypertensive drugs.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies of brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL to assess the carcinogenic and mutagenic potential or the effect on fertility have not been performed.

Pregnancy

Teratogenic Effects

Pregnancy Category C

Animal reproduction studies have not been conducted with brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL. It is also not known whether brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. It should be given to a pregnant woman only if clearly needed. Reproduction studies of brompheniramine maleate (a component of brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL) in rats and mice at doses up to 16 times the maximum human doses have revealed no evidence of impaired fertility or harm to the fetus.

Nursing Mothers

Because of the higher risk of intolerance of antihistamines in small infants generally, and in newborns and prematures in particular, brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL is contraindicated in nursing mothers.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 6 months have not been established (see **DOSAGE AND ADMINISTRATION**).

Geriatric Use

Clinical studies of brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. However, antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients. The elderly are also more likely to experience adverse reactions to sympathomimetics.

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, and of

concomitant disease or other drug therapy.

ADVERSE REACTIONS

The most frequent adverse reactions to brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup 2 mg/30 mg/10 mg per 5 mL are: sedation; dryness of mouth, nose and throat; thickening of bronchial secretions; dizziness.

Other adverse reactions may include:

Dermatologic: Urticaria, drug rash, photosensitivity, pruritus.

Cardiovascular System: Hypotension, hypertension, cardiac arrhythmias, palpitation.

CNS: Disturbed coordination, tremor, irritability, insomnia, visual disturbances, weakness, nervousness, convulsions, headache, euphoria, and dysphoria.

G.U. System: Urinary frequency, difficult urination.

G.I. System: Epigastric discomfort, anorexia, nausea, vomiting, diarrhea, constipation.

Respiratory System: Tightness of chest and wheezing, shortness of breath.

Hematologic System: Hemolytic anemia, thrombocytopenia, agranulocytosis.

OVERDOSAGE

Signs and Symptoms

Central nervous system effects from overdosage of brompheniramine may vary from depression to stimulation, especially in children. Anticholinergic effects may be noted. Toxic doses of pseudoephedrine may result in CNS stimulation, tachycardia, hypertension, and cardiac arrhythmias; signs of CNS depression may occasionally be seen. Dextromethorphan in toxic doses will cause drowsiness, ataxia, nystagmus, opisthotonos, and convulsive seizures.

Toxic Doses

Data suggest that individuals may respond in an unexpected manner to apparently small amounts of a particular drug. A 2½-year-old child survived the ingestion of 21 mg/kg of dextromethorphan exhibiting only ataxia, drowsiness, and fever, but seizures have been reported in 2 children following the ingestion of 13 to 17 mg/kg. Another 2½-year-old child survived a dose of 300 to 900 mg of brompheniramine. The toxic dose of pseudoephedrine should be less than that of ephedrine, which is estimated to be 50 mg/kg.

Treatment

Induce emesis if patient is alert and is seen prior to 6 hours following ingestion. Precautions against aspiration must be taken, especially in infants and small children. Gastric lavage may be carried out, although in some instances tracheostomy may be necessary prior to lavage. Naloxone hydrochloride 0.005 mg/kg intravenously may be of value in reversing the CNS depression that may occur from an overdose of dextromethorphan. CNS stimulants may counter CNS depression. Should CNS hyperactivity or convulsive seizures occur, intravenous short-acting barbiturates may be indicated. Hypertensive responses and/or tachycardia should be treated appropriately. Oxygen, intravenous fluids, and other supportive measures should be employed as indicated.

DOSAGE AND ADMINISTRATION

Adults and pediatric patients 12 years of age and over: 10 mL (2 teaspoonfuls) every 4 hours. Children 6 to under 12 years of age: 5 mL (1 teaspoonful) every 4 hours. Children 2 to under 6 years of age: 2.5

mL (½ teaspoonful) every 4 hours. Infants 6 months to under 2 years of age: Dosage to be established by a physician.

Do not exceed 6 doses during a 24-hour period.

HOW SUPPLIED

Brompheniramine Maleate, Pseudoephedrine Hydrochloride, and Dextromethorphan Hydrobromide Syrup 2 mg/30 mg/10 mg per 5 mL is a clear, colorless to slightly yellowish grape flavored solution containing in each 5 mL (1 teaspoonful) brompheniramine maleate 2 mg, pseudoephedrine hydrochloride 30 mg and dextromethorphan hydrobromide 10 mg, available in the following sizes:

4 fl oz (118 mL) - NDC 51672-4165-8
16 fl oz (473 mL) - NDC 51672-4165-9

RECOMMENDED STORAGE

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

KEEP TIGHTLY CLOSED

Dispense in a tight, light-resistant container as defined in the USP.

Mfd. by: Taro Pharmaceutical Industries Ltd., Haifa Bay, Israel 2624761
Dist. by: **Taro Pharmaceuticals U.S.A., Inc.,** Hawthorne, NY 10532
Revised: June, 2017
20430-0617-2

PRINCIPAL DISPLAY PANEL - 118 mL Bottle Label

NDC 51672-4165-8

4 fl oz (118 mL)

**Brompheniramine
Maleate,
Pseudoephedrine
Hydrochloride, and
Dextromethorphan
Hydrobromide
Syrup**

**Keep this and all medications
out of the reach of children.**

TARO

Rx only

BROMPHENIRAMINE MALEATE, PSEUDOEPHEDRINE HYDROCHLORIDE, AND DEXTROMETHORPHAN HYDROBROMIDE

brompheniramine maleate, pseudoephedrine hydrochloride, and dextromethorphan hydrobromide syrup

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51672-4165
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Brompheniramine Maleate (UNII: IXA7C9ZN03) (Brompheniramine - UNII:H57G17P2FN)	Brompheniramine Maleate	2 mg in 5 mL
Pseudoephedrine Hydrochloride (UNII: 6V9V2RYJ8N) (Pseudoephedrine - UNII:7CUC9DDI9F)	Pseudoephedrine Hydrochloride	30 mg in 5 mL
Dextromethorphan Hydrobromide (UNII: 9D2RTI9KYH) (Dextromethorphan - UNII:7355X3ROTS)	Dextromethorphan Hydrobromide	10 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
anhydrous citric acid (UNII: XF417D3PSL)	
glycerin (UNII: PDC6A3C0OX)	
methylparaben (UNII: A2I8C7HI9T)	
propylene glycol (UNII: 6DC9Q167V3)	
water (UNII: 059QF0KO0R)	
sodium benzoate (UNII: OJ245FE5EU)	
sucrose (UNII: C151H8M554)	

Product Characteristics

Color	YELLOW (clear, colorless to slightly yellowish)	**Score**	
Shape		**Size**	
Flavor	GRAPE	**Imprint Code**	

Contains	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51672-4165-8	118 mL in 1 BOTTLE; Type 0: Not a Combination Product	02/27/2017	
2	NDC:51672-4165-9	473 mL in 1 BOTTLE; Type 0: Not a Combination Product	02/27/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205112	02/27/2017	

Labeler - Taro Pharmaceuticals U.S.A., Inc. (145186370)

Establishment

Name	Address	ID/FEI	Business Operations
Taro Pharmaceutical Industries Ltd.		600072078	MANUFACTURE(51672-4165)

Revised: 2/2018 Taro Pharmaceuticals U.S.A., Inc.