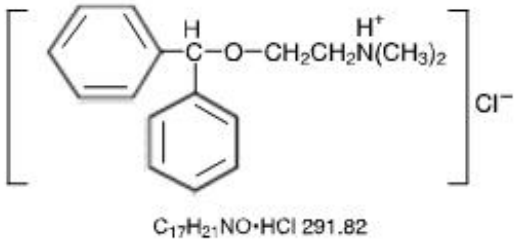
DIPHENHYDRAMINE HYDROCHLORIDE- diphenhydramine hydrochloride solution
PAI Holdings, LLC dba PAI Pharma

Diphenhydramine Hydrochloride Oral Solution USP

Rx ONLY

DESCRIPTION

Diphenhydramine hydrochloride is an antihistamine drug having the chemical name 2-(diphenylmethoxy)-N,N -dimethylethylamine hydrochloride and has the molecular formula $C_{17}H_{21}NO \cdot HCl$ (molecular weight 291.82). It occurs as a white odorless, crystalline powder and is freely soluble in water and alcohol. The structural formula is as follows:



$C_{17}H_{21}NO \cdot HCl$ 291.82

Each 5 mL contains 12.5 mg of diphenhydramine hydrochloride and alcohol 14% for oral administration. Inactive Ingredients: Citric acid, D&C Red No. 33, FD&C Red No. 40, flavoring, purified water, sodium citrate, and sucrose.

CLINICAL PHARMACOLOGY

Diphenhydramine hydrochloride is an antihistamine with anticholinergic (drying) and sedative effects. Antihistamines appear to compete with histamine for cell receptor sites on effector cells.

A single oral dose of diphenhydramine hydrochloride is quickly absorbed with maximum activity occurring in approximately one hour. The duration of activity following an average dose of diphenhydramine hydrochloride is from four to six hours. Diphenhydramine is widely distributed throughout the body, including the CNS. Little, if any, is excreted unchanged in the urine; most appears as the degradation products of metabolic transformation in the liver, which are almost completely excreted within 24 hours.

INDICATIONS AND USAGE

Diphenhydramine hydrochloride in the oral form is effective for the following indications:

Antihistaminic

For allergic conjunctivitis due to foods; mild, uncomplicated allergic skin manifestations of urticaria and angioedema; amelioration of allergic reactions to blood or plasma; dermatographism; as therapy for anaphylactic reactions *adjunctive* to epinephrine and other standard measures after the acute manifestations have been controlled.

Motion Sickness

For active and prophylactic treatment of motion sickness.

Antiparkinsonism

For parkinsonism (including drug-induced) in the elderly unable to tolerate more potent agents; mild cases of parkinsonism (including drug-induced) in other age groups; in other cases of parkinsonism (including drug-induced) in combination with centrally acting anticholinergic agents.

Nighttime Sleep-aid.

CONTRAINDICATIONS

Use in Neonates or Premature Infants

This drug should *not* be used in neonates or premature infants.

Use in Nursing Mothers

Because of the higher risk of antihistamines for infants generally, and for neonates and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Antihistamines are also contraindicated in the following conditions

Hypersensitivity to diphenhydramine hydrochloride and other antihistamines of similar chemical structure.

WARNINGS

Antihistamines should be used with considerable caution in patients with narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, or bladder-neck obstruction.

Use in Pediatric Patients

In pediatric patients, especially, antihistamines in *overdosage* may cause hallucinations, convulsions, or death. As in adults, antihistamines may diminish mental alertness in pediatric patients. In the young pediatric patient, particularly, they may produce excitation.

Use in the Elderly (approximately 60 years or older)

Antihistamines are most likely to cause dizziness, sedation, and hypotension in elderly

patients.

PRECAUTIONS

General

Diphenhydramine hydrochloride has an atropine-like action and therefore, should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease or hypertension. Use with caution in patients with lower respiratory disease including asthma.

Information for Patients

Patients taking diphenhydramine hydrochloride should be advised that this drug may cause drowsiness and has an additive effect with alcohol. Patients should be warned about engaging in activities requiring mental alertness such as driving a car or operating appliances, machinery, etc.

Drug Interactions

Diphenhydramine hydrochloride has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.). MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to determine mutagenic and carcinogenic potential have not been performed.

Pregnancy

Pregnancy Category B

Reproduction studies have been performed in rats and rabbits at doses up to 5 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to diphenhydramine hydrochloride. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Pediatric Use

Diphenhydramine hydrochloride should not be used in neonates and premature infants (see ***CONTRAINDICATIONS***).

Diphenhydramine hydrochloride may diminish mental alertness, or, in the young pediatric patient, cause excitation. Overdosage may cause hallucinations, convulsions, or death (see ***WARNINGS and OVERDOSAGE***).

See also DOSAGE AND ADMINISTRATION section.

ADVERSE REACTIONS

The most frequent adverse reactions are underscored.

- *General:* Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of the mouth, nose and throat.
- *Cardiovascular System:* Hypotension, headache, palpitations, tachycardia, extrasystoles.
- *Hematologic System:* Hemolytic anemia, thrombocytopenia, agranulocytosis.
- *Nervous System:* Sedation,sleepiness,dizziness,disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, neuritis, convulsions.
- *GI System:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.
- *GU System:* Urinary frequency, difficult urination, urinary retention, early menses.
- *Respiratory System:* Thickening of bronchial secretions, tightness of chest or throat and wheezing, nasal stuffiness.

To report SUSPECTED ADVERSE REACTIONS, contact Pharmaceutical Associates, Inc. at 1-800-845-8210 of FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in pediatric patients. Atropine-like signs and symptoms, dry mouth; fixed, dilated pupils; flushing and gastrointestinal symptoms may also occur.

If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precaution against aspiration 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 or cream were given beforehand. Isotonic or 1/2 isotonic saline is the lavage solution of choice.

Saline cathartics, as milk of magnesia, by osmosis draw water into the bowel and therefore are valuable for their action in rapid dilution of bowel content.

Stimulants should not be used.

Vasopressors may be used to treat hypotension.

DOSAGE AND ADMINISTRATION

DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT.

A single oral dose of diphenhydramine hydrochloride is quickly absorbed with maximum activity occurring in approximately one hour. The duration of activity following an average dose of diphenhydramine hydrochloride is from four to six hours.

Adults

25 to 50 mg three to four times daily. The nightime sleep aid dosage is 50 mg at

bedtime.

Pediatric Patients, other than premature infants and neonates

12.5 to 25 mg three or four times daily. Maximum daily dosage not to exceed 300 mg. For physicians who wish to calculate the dose on the basis of body weight or surface area, the recommended dosage is 5 mg/kg/24 hours or 150 mg/m2/24 hours.

Data are not available on the use of diphenhydramine hydrochloride as a nighttime sleep-aid in children under 12 years.

The basis for determining the most effective dosage regimen will be the response of the patient to medication and the condition under treatment.

In motion sickness, full dosage is recommended for prophylactic use, the first dose to be given 30 minutes before exposure to motion and similar doses before meals and upon retiring for the duration of exposure

STORAGE

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

HOW SUPPLIED

Each 5 mL of Diphenhydramine Hydrochloride Oral Solution USP (clear purple/red liquid, cinnamon/anise flavor) contains 12.5 mg diphenhydramine hydrochloride with 14% alcohol and is supplied in the following oral dosage forms:

NDC 0121-0489-05: 5 mL unit dose cup

NDC 0121-0489-00: Case contains 100 unit dose cups of 5 mL (0121-0489-05) packaged in 10 trays of 10 unit dose cups each.

NDC 0121-0978-10: 10 mL unit dose cup

NDC 0121-0978-00: Case contains 100 unit dose cups of 10 mL (0121-0978-10) packaged in 10 trays of 10 unit dose cups each.

MANUFACTURED BY

Pharmaceutical Associates, Inc.
Greenville, SC 29605
www.paipharma.com

R12/18

PRINCIPAL DISPLAY PANEL - 5 mL Unit Dose Cup Label

Delivers **5 mL**
NDC 0121-0489-05

DIPHENHYDRAMINE HCl
ORAL SOLUTION USP
12.5 mg/5 mL

Alcohol 14%
Package Not Child-Resistant

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

PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605

SEE INSERT

PRINCIPAL DISPLAY PANEL - 10 mL Unit Dose Cup Label

Delivers **10 mL**
NDC 0121-0978-10

DIPHENHYDRAMINE HCl
ORAL SOLUTION USP

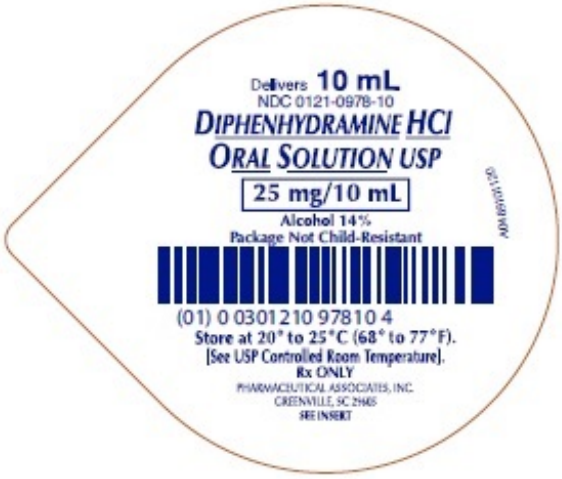
25 mg/10 mL

Alcohol 14%
Package Not Child-Resistant

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

PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605

SEE INSERT



DIPHENHYDRAMINE HYDROCHLORIDE

diphenhydramine hydrochloride solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0121-0489
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DIPHENHYDRAMINE HYDROCHLORIDE (UNII: TC2D6JAD40) (DIPHENHYDRAMINE - UNII:8GTS82S83M)	DIPHENHYDRAMINE HYDROCHLORIDE	12.5 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
D&C RED NO. 33 (UNII: 9DBA0SBB0L)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
WATER (UNII: 059QF0KO0R)	
SODIUM CITRATE (UNII: 1Q73Q2JULR)	
SUCROSE (UNII: C151H8M554)	

Product Characteristics

Color	pink	**Score**	
Shape		**Size**	
Flavor	CINNAMON	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0121-0489-00	10 in 1 CASE	02/10/1982	
1		10 in 1 TRAY		
1	NDC:0121-0489-05	5 mL in 1 CUP, UNIT-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA087513	02/10/1982	

DIPHENHYDRAMINE HYDROCHLORIDE

diphenhydramine hydrochloride solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0121-0978
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DIPHENHYDRAMINE HYDROCHLORIDE (UNII: TC2D6JAD40) (DIPHENHYDRAMINE - UNII:8GTS82S83M)	DIPHENHYDRAMINE HYDROCHLORIDE	25 mg in 10 mL

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
D&C RED NO. 33 (UNII: 9DBA0SBB0L)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
WATER (UNII: 059QF0KO0R)	
SODIUM CITRATE (UNII: 1Q73Q2JULR)	
SUCROSE (UNII: C151H8M554)	

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ANDA	ANDA087513	02/10/1982	

Labeler - PAI Holdings, LLC dba PAI Pharma (044940096)

Establishment

Name	Address	ID/FEI	Business Operations
PAI Holdings, LLC dba Pharmaceutical Associates, Inc. and dba PAI Pharma		097630693	manufacture(0121-0489, 0121-0978)