

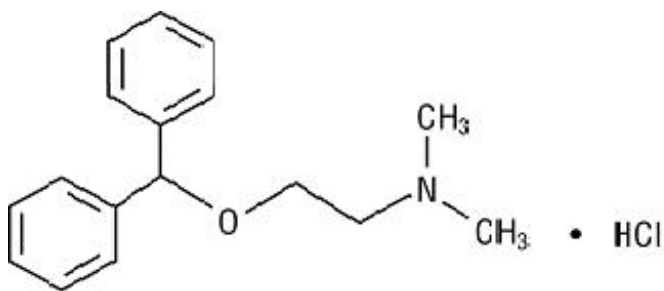
**DIPHENHYDRAMINE HYDROCHLORIDE- diphenhydramine hydrochloride injection**  
**Hikma Pharmaceuticals USA Inc.**

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**Diphenhydramine Hydrochloride Injection, USP**  
**Rx only**

**DESCRIPTION**

Diphenhydramine Hydrochloride Injection is a sterile, nonpyrogenic solution for intravenous or deep intramuscular use as an antihistaminic agent. Each mL contains diphenhydramine hydrochloride 50 mg and benzethonium chloride 100 mcg in Water for Injection. pH 4.0-6.5; sodium hydroxide and/or hydrochloric acid added, if needed, for pH adjustment.

The chemical name of diphenhydramine hydrochloride is 2-(Diphenylmethoxy)-N,N-dimethylethylamine hydrochloride. The structural formula is as follows:



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

Diphenhydramine hydrochloride occurs as a white crystalline powder and is freely soluble in water and alcohol.

**CLINICAL PHARMACOLOGY**

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

Diphenhydramine hydrochloride in the injectable form has a rapid onset of action. Diphenhydramine is widely distributed throughout the body, including the CNS. A portion of the drug is excreted unchanged in the urine, while the rest is metabolized via the liver. Detailed information on the pharmacokinetics of Diphenhydramine Hydrochloride Injection is not available.

**INDICATIONS AND USAGE**

Diphenhydramine Hydrochloride Injection is effective in adults and pediatric patients, other than premature infants and neonates, for the following conditions when the oral

form is impractical:

### **Antihistaminic**

For amelioration of allergic reactions to blood or plasma, in anaphylaxis as an adjunct to epinephrine and other standard measures after the acute symptoms have been controlled and for other uncomplicated allergic conditions of the immediate type when oral therapy is impossible or contraindicated.

### **Motion Sickness**

For active treatment of motion sickness.

### **Antiparkinsonism**

For use in parkinsonism, when oral therapy is impossible or contraindicated, as follows: parkinsonism in the elderly who are unable to tolerate more potent agents, mild cases of parkinsonism in other age groups and in other cases of parkinsonism in combination with centrally acting anticholinergic agents.

## **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.

### **Use as a Local Anesthetic**

Because of the risk of local necrosis, this drug should not be used as a local anesthetic.

### **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.

Local necrosis has been associated with the use of subcutaneous or intradermal use of intravenous diphenhydramine.

### **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 more 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**

Teratogenic Effects—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 should not be used in neonates and premature infants (see **CONTRAINDICATIONS**).

Diphenhydramine 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 italicized.

### **General**

Urticaria; drug rash; anaphylactic shock; photosensitivity; excessive perspiration; chills; dryness of 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.*

### **Gastrointestinal System**

*Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.*

### **Genitourinary System**

Urinary frequency, difficult urination, urinary retention, early menses.

### **Respiratory System**

*Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.*

## **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.

*Stimulants* should **not** be used.

Vasopressors may be used to treat hypotension.

## **DOSAGE AND ADMINISTRATION**

THIS PRODUCT IS FOR INTRAVENOUS OR INTRAMUSCULAR ADMINISTRATION ONLY.  
Diphenhydramine Hydrochloride Injection is indicated when the oral form is impractical.  
DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE  
RESPONSE OF THE PATIENT.

### **Pediatric Patients, Other Than Premature Infants and Neonates**

5 mg/kg/24 hours or 150 mg/m<sup>2</sup>/24 hours. Maximum daily dosage is 300 mg. Divide into four doses, administered intravenously at a rate generally not exceeding 25 mg/min, or deep intramuscularly.

### **Adults**

10 to 50 mg intravenously at a rate generally not exceeding 25 mg/min, or deep intramuscularly; 100 mg if required; maximum daily dosage is 400 mg.

**Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.**

### **HOW SUPPLIED**

Diphenhydramine Hydrochloride Injection, USP 50 mg/mL  
1 mL vials packaged in 25s (NDC 0641-6282-25)

### **Storage**

**Protect from light. Keep covered in carton until time of use. Store at 20° to 25°C (68° to 77°F), excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].**

To report SUSPECTED ADVERSE REACTIONS, contact Hikma Pharmaceuticals USA Inc. at 1-877-845-0689, or the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch). For Product Inquiry call 1-877-845-0689.

### **Manufactured by:**

Hikma Pharmaceuticals USA Inc.  
Berkeley Heights, NJ 07922

Novaplus is a registered trademark of Vizion, Inc.

**novaplus<sup>+</sup>**

Revised July 2023

463-027-00

### **PRINCIPAL DISPLAY PANEL**

NDC 0641-**6282-01**      Rx only  
**DiphenhydrAMINE**  
**Hydrochloride Injection, USP**

**50 mg/mL**  
**HIGH POTENCY**  
**For IM or IV use**  
**Protect from light**  
1 mL Vial

NDC 0641-6282-01 Rx ONLY  
**DiphenhydrAMINE**  
**HCl Injection, USP**  
**50 mg/mL**  
**HIGH POTENCY**  
**For IM or IV use**  
**Protect from light**  
1 mL Vial  
Manufactured by Hikma  
novaplus<sup>+</sup>  
463-026-00  
(01)00306416282017  
LOT  
EXP.

NDC 0641-**6282-25** Rx only  
**DiphenhydrAMINE**  
**Hydrochloride Injection, USP**  
**50 mg/mL**  
**HIGH POTENCY**  
**For deep Intramuscular**  
**or slow Intravenous use**  
25 x 1 mL Vials

LOT  
EXP.

**DiphenhydrAMINE**  
**HCl Injection, USP**  
**HIGH POTENCY 50 mg/mL**  
**For deep Intramuscular**  
**or slow Intravenous use**  
25 x 1 mL Vials

NDC 0641-6282-25 Rx ONLY  
Each mL contains diphenhydramine hydrochloride 50 mg and benzethonium chloride 100 mcg in Water for Injection. pH 4.0-6.5; sodium hydroxide and/or hydrochloric acid added, if needed, for pH adjustment.  
**Usual Dosage:** See package insert.  
**Protect from light:** Keep covered in carton until time of use.  
**Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].**  
Manufactured by Hikma  
Berkeley Heights, NJ 07922 463-026-00  
novaplus<sup>+</sup>  
463-026-00  
(01)00306416282253

**LIGHT SENSITIVE: Keep covered in carton until time of use. To open—Cut seal along dotted line.**

# DIPHENHYDRAMINE HYDROCHLORIDE

diphenhydramine hydrochloride injection

## Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:0641-6282
<b>Route of Administration</b>	INTRAMUSCULAR, INTRAVENOUS		

## Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>DIPHENHYDRAMINE HYDROCHLORIDE</b> (UNII: TC2D6JAD40) (DIPHENHYDRAMINE - UNII: 8GTS82S83M)	DIPHENHYDRAMINE HYDROCHLORIDE	50 mg in 1 mL

## Inactive Ingredients

Ingredient Name	Strength
<b>BENZETHONIUM CHLORIDE</b> (UNII: PH41D05744)	100 ug in 1 mL
<b>WATER</b> (UNII: 059QF0KO0R)	
<b>SODIUM HYDROXIDE</b> (UNII: 55X04QC32I)	
<b>HYDROCHLORIC ACID</b> (UNII: QTT17582CB)	

## Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0641-6282-25	25 in 1 PACKAGE	11/27/1972	
1	NDC:0641-6282-21	1 mL in 1 VIAL; Type 0: Not a Combination Product		

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA080817	11/27/1972	

**Labeler** - Hikma Pharmaceuticals USA Inc. (946499746)

**Registrant** - Hikma Pharmaceuticals USA Inc. (001230762)

## Establishment

Name	Address	ID/FEI	Business Operations
Hikma Pharmaceuticals USA Inc.		946499746	analysis(0641-6282) , label(0641-6282) , manufacture(0641-6282)