

PHENOXYBENZAMINE HYDROCHLORIDE- phenoxybenzamine hydrochloride capsule
Amneal Pharmaceuticals NY LLC

Phenoxybenzamine Hydrochloride Capsules, USP
(10 mg)
Rx only

Adrenergic, *alpha*-receptor-blocking agent

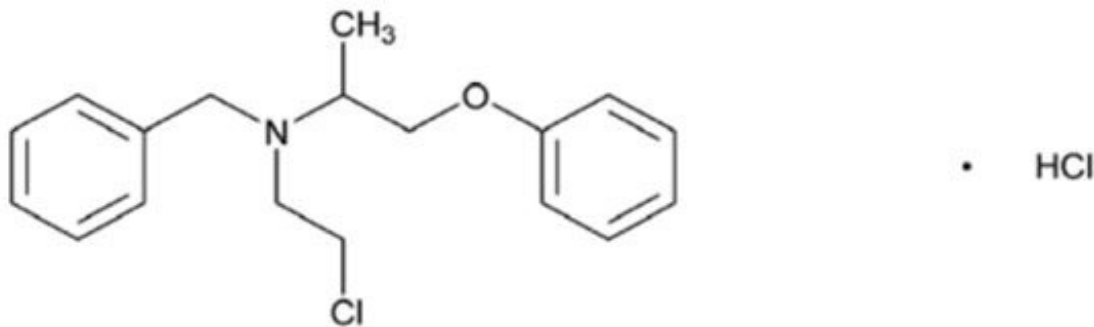
DESCRIPTION

Each phenoxybenzamine hydrochloride capsule, USP with red cap and body, is imprinted with “Amneal” on cap and “1502” on body, and contains 10 mg of phenoxybenzamine hydrochloride, USP. Inactive ingredients consist of colloidal silicon dioxide, D&C red 33, FD & C red 3, gelatin, iron oxide yellow, lactose monohydrate and sodium lauryl sulfate.

The capsule is imprinted with white pharmaceutical ink which contains butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac, strong ammonia solution and titanium dioxide.

Phenoxybenzamine hydrochloride is chemically known as *N*-(2-Chloroethyl)-*N*-(1-methyl-2-phenoxyethyl) benzylamine hydrochloride. Its molecular formula is C₁₈H₂₂ClNO·HCl.

The chemical structure is:



Phenoxybenzamine hydrochloride, USP is a white to almost white crystalline powder with a molecular weight of 340.29 g/mol, which melts between 136° and 141°C. It is freely soluble in ethanol (96%) and insoluble in diethyl ether.

CLINICAL PHARMACOLOGY

Phenoxybenzamine hydrochloride is a long-acting, adrenergic, *alpha*-receptor-blocking agent, which can produce and maintain “chemical sympathectomy” by oral administration. It increases blood flow to the skin, mucosa and abdominal viscera, and lowers both supine and erect blood pressures. It has no effect on the parasympathetic system.

20 percent to 30 percent of orally administered phenoxybenzamine appears to be absorbed in the active form¹.

The half-life of orally administered phenoxybenzamine hydrochloride is not known; however, the half-life of intravenously administered phenoxybenzamine hydrochloride is approximately 24 hours. Demonstrable effects with intravenous administration persist for at least 3 to 4 days, and the effects of daily administration are cumulative for nearly a week¹.

INDICATION AND USAGE

Phenoxybenzamine hydrochloride capsules are indicated in the treatment of pheochromocytoma, to control episodes of hypertension and sweating. If tachycardia is excessive, it may be necessary to use a *beta*-blocking agent concomitantly.

CONTRAINDICATIONS

Conditions where a fall in blood pressure may be undesirable; hypersensitivity to the phenoxybenzamine hydrochloride capsules, or any of its components.

WARNING

Phenoxybenzamine hydrochloride-induced *alpha*-adrenergic blockade leaves *beta*-adrenergic receptors unopposed. Compounds that stimulate both types of receptors may, therefore, produce an exaggerated hypotensive response and tachycardia.

PRECAUTIONS

General—Administer with caution in patients with marked cerebral or coronary arteriosclerosis or renal damage. Adrenergic blocking effect may aggravate symptoms of respiratory infections.

Drug Interactions²—Phenoxybenzamine hydrochloride may interact with compounds that stimulate both *alpha*- and *beta*-adrenergic receptors (i.e. epinephrine) to produce an exaggerated hypotensive response and tachycardia (see **WARNING**).

Phenoxybenzamine hydrochloride blocks hyperthermia production by levarterenol, and blocks hypothermia production by reserpine.

Carcinogenesis and Mutagenesis

Case reports of carcinoma in humans after long-term treatment with phenoxybenzamine have been reported. Hence long-term use of phenoxybenzamine is not recommended^{3, 4}. Carefully weigh the benefits and risks before prescribing phenoxybenzamine hydrochloride.

Phenoxybenzamine hydrochloride showed *in vitro* mutagenic activity in the Ames test and mouse lymphoma assay; it did not show mutagenic activity *in vivo* in the micronucleus test in mice. In rats and mice, repeated intraperitoneal administration of phenoxybenzamine hydrochloride (three times per week for up to 52 weeks) resulted in peritoneal sarcomas. Chronic oral dosing in rats (for up to 2 years) produced malignant tumors of the small intestine and non-glandular stomach, as well as ulcerative and/or erosive gastritis of the glandular stomach. Whereas squamous cell carcinomas of the non-glandular stomach were observed at all tested doses of phenoxybenzamine hydrochloride, there was a no-observed-effect-level of 10 mg/kg for tumors (carcinomas and sarcomas) of the small intestine. This dose is, on a body surface area basis, about twice the maximum recommended human dosage of 20 mg b.i.d.

Pregnancy - Teratogenic Effects

Adequate reproductive studies in animals have not been performed with phenoxybenzamine hydrochloride. It is also not known whether phenoxybenzamine hydrochloride can cause fetal harm when administered to a pregnant woman. Phenoxybenzamine hydrochloride should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether phenoxybenzamine hydrochloride is excreted in human milk. Because many

drugs are excreted in human milk, and because of the potential for serious adverse reactions from phenoxybenzamine hydrochloride, a decision should be made whether to discontinue nursing or to discontinue phenoxybenzamine hydrochloride, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The following adverse reactions have been observed, but there are insufficient data to support an estimate of their frequency.

Autonomic Nervous System*: Postural hypotension, tachycardia, inhibition of ejaculation, nasal congestion, miosis.

*These so-called "side effects" are actually evidence of adrenergic blockade and vary according to the degree of blockade.

Miscellaneous: Gastrointestinal irritation, drowsiness, fatigue.

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

SYMPTOMS - These are largely the result of blocking of the sympathetic nervous system and of the circulating epinephrine. They may include postural hypotension, resulting in dizziness or fainting; tachycardia, particularly postural; vomiting; lethargy; shock.

Treatment

When symptoms and signs of overdose exist, discontinue phenoxybenzamine hydrochloride capsules. Treatment of circulatory failure, if present, is a prime consideration. In cases of mild overdose, recumbent position with legs elevated usually restores cerebral circulation. In the more severe cases, the usual measures to combat shock should be instituted. Usual pressor agents are *not* effective. Epinephrine is contraindicated because it stimulates both *alpha*- and *beta*- receptors; since *alpha*-receptors are blocked, the net effect of epinephrine administration is vasodilation and a further drop in blood pressure (epinephrine reversal).

The patient may have to be kept flat for 24 hours or more in the case of overdose, as the effect of the drug is prolonged. Leg bandages and an abdominal binder may shorten the period of disability.

Intravenous infusion of levarterenol bitartrate** may be used to combat severe hypotensive reactions, because it stimulates *alpha*- receptors primarily. Although phenoxybenzamine hydrochloride is an *alpha*-adrenergic blocking agent, a sufficient dose of levarterenol bitartrate will overcome this effect.

The oral LD₅₀ for phenoxybenzamine hydrochloride is approximately 2,000 mg/kg in rats and approximately 500 mg/kg in guinea pigs.

DOSAGE AND ADMINISTRATION

The dosage should be adjusted to fit the needs of each patient. Small initial doses should be *slowly* increased until the desired effect is obtained or the side effects from blockade become troublesome. *After each increase, the patient should be observed on that level before instituting another increase.* The dosage should be carried to a point where symptomatic relief and/or objective improvement are obtained, but not so high that the side effects from blockade become troublesome.

Initially, 10 mg of phenoxybenzamine hydrochloride twice a day. Dosage should be increased every other day, usually to 20 mg to 40 mg 2 or 3 times a day, until an optimal dosage is obtained, as judged by blood pressure control.

Long-term use of phenoxybenzamine is not recommended (see **PRECAUTIONS - Carcinogenesis and Mutagenesis**).

HOW SUPPLIED

Phenoxybenzamine Hydrochloride Capsules USP, **10 mg** are supplied as size '3' red colored transparent hard gelatin capsule, imprinted with "Amneal" on cap and "1502" on body with white ink containing white to off-white powder.

They are available as follows:

Bottles of 100: NDC 69238-1502-1

STORAGE

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Dispense in tight container as defined in the USP.

REFERENCES

1. Weiner, N.: Drugs That Inhibit Adrenergic Nerves and Block Adrenergic Receptors, in Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics*, ed. 6, New York, Macmillan Publishing Co., 1980, p. 179; p. 182.
2. Martin, E.W.: *Drug Interactions Index 1978/1979*, Philadelphia, J.B. Lippincott Co., 1978, pp. 209-210.
3. Nettesheim O, Hoffken G, Gahr M, Breidert M: Haematemesis and dysphagia in a 20-year-old woman with congenital spine malformation and situs inversus partialis [German]. *Zeitschrift fur Gastroenterologie*. 2003;41(4):319-24.
4. Vaidyanathan S, Mansour P, Soni BM, Hughes PL, Singh G: Chronic lymphocytic leukaemia, synchronous small cell carcinoma and squamous neoplasia of the urinary bladder in a paraplegic man following long-term phenoxybenzamine therapy. *Spinal Cord*. 2006;44(3):188-91.

** Available as Levophed[®] Bitartrate (brand of norepinephrine bitartrate) from Abbott Laboratories.

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Manufactured by:

Amneal Pharmaceuticals Pvt. Ltd.
Oral Solid Dosage Unit
Ahmedabad 382213, INDIA

Distributed by:

Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807

Rev. 12-2020-01

PRINCIPAL DISPLAY PANEL

NDC 69238-1502-1

Phenoxybenzamine Hydrochloride Capsules USP, 10 mg
100 Capsules

Rx only
Amneal Pharmaceuticals LLC

NDC 69238-1502-1

Phenoxybenzamine Hydrochloride Capsules, USP

10 mg

Rx only
100 Capsules



Each capsule contains:

Phenoxybenzamine Hydrochloride, USP.....10 mg

Usual Dosage: See accompanying prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Dispense in a tight container as defined in the USP.

Mfg. Lic. No. G/25/2137

Manufactured by: **Amneal Pharmaceuticals Pvt. Ltd.**

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Non-Varnish Area
(For Lot And Exp. Date)
(20 X 51 mm)

PHENOXYBENZAMINE HYDROCHLORIDE

phenoxybenzamine hydrochloride capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:69238-1502
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
PHENOXYBENZAMINE HYDROCHLORIDE (UNII: X1IEG24OHL) (PHENOXYBENZAMINE - UNII:0TTZ664R7Z)	PHENOXYBENZAMINE HYDROCHLORIDE	10 mg

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
AMMONIA (UNII: 5138Q19F1X)	
BUTYL ALCOHOL (UNII: 8PJ61P6TS3)	
D&C RED NO. 33 (UNII: 9DBA0SBB0L)	
FD&C RED NO. 3 (UNII: PN2ZH5LOQY)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
ISOPROPYL ALCOHOL (UNII: ND2M416302)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SHELLAC (UNII: 46N107B71O)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	

SODIUM LAURYL SULFATE (UNII: 368GB5141J)

TITANIUM DIOXIDE (UNII: 15FIX9V2JP)

Product Characteristics

Color	RED (red cap and red body)	Score	no score
Shape	CAPSULE	Size	16mm
Flavor		Imprint Code	Amneal;1502
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69238-1502-1	100 in 1 BOTTLE; Type 0: Not a Combination Product	10/30/2020	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212568	10/30/2020	

Labeler - Amneal Pharmaceuticals NY LLC (123797875)

Registrant - Amneal Pharmaceuticals of New York, LLC (123797875)

Revised: 12/2020

Amneal Pharmaceuticals NY LLC