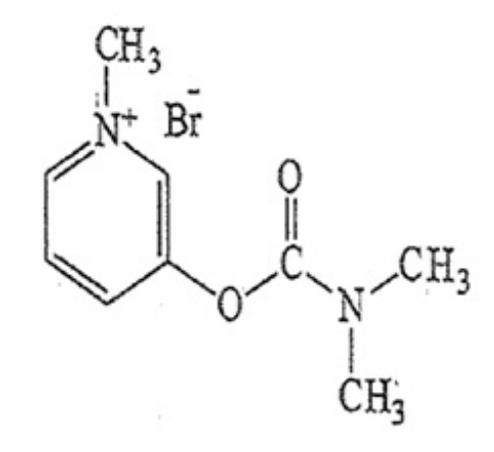


PYRIDOSTIGMINE BROMIDE - pyridostigmine bromide solution
Novadoz Pharmaceuticals LLC

Pyridostigmine Bromide Oral Solution, USP

DESCRIPTION:

Pyridostigmine bromide oral solution, USP is an orally active cholinesterase inhibitor. Chemically, pyridostigmine bromide, USP is 3-hydroxy-1-methylpyridinium bromide dimethylcarbamate. Its structural formula is:



The molecular formula of pyridostigmine bromide, USP is $C_9H_{13}BrN_2O_2$ having a molecular weight of 261.12.

Pyridostigmine bromide oral solution, USP contains 60 mg pyridostigmine bromide per teaspoonful in a vehicle containing 0.23% w/w alcohol, glycerin, lactic acid, sodium benzoate, sorbitol, sucrose, raspberry-flavor (propylene glycol, Nat & Art flavor) and water.

CLINICAL PHARMACOLOGY:

Pyridostigmine bromide inhibits the destruction of acetylcholine by cholinesterase and thereby permits freer transmission of nerve impulses across the neuromuscular junction. Pyridostigmine is an analog of neostigmine (Prostigmin), but differs from it in certain clinically significant respects; for example, pyridostigmine is characterized by a longer duration of action and fewer gastrointestinal side effects.

INDICATION:

Pyridostigmine bromide oral solution is useful in the treatment of myasthenia gravis.

CONTRAINDICATIONS:

Pyridostigmine bromide is contraindicated in mechanical intestinal or urinary obstruction, and particular caution should be used in its administration to patients with bronchial asthma. Care should be observed in the use of atropine for counteracting side effects, as discussed below.

WARNINGS:

Although failure of patients to show clinical improvement may reflect underdosage, it can also be indicative of overdosage. As is true of all cholinergic drugs, overdosage of pyridostigmine bromide may result in cholinergic crisis, a state characterized by increasing muscle weakness which, through involvement of the muscles of respiration, may lead to death. Myasthenic crisis due to an increase in the severity of the disease is also accompanied by extreme muscle weakness, and thus may be difficult to distinguish from cholinergic crisis on a symptomatic basis. Such differentiation is extremely important, since increases in doses of pyridostigmine bromide or other drugs of this class in the presence of cholinergic crisis or of a refractory or "insensitive" state could have grave consequences. Osserman and Genkins¹ indicate that the differential diagnosis of the two types of crisis may require the use of Tensilon (edrophonium chloride) as well as clinical judgment. The treatment of the two conditions obviously differs radically. Whereas the presence of myasthenic crisis suggests the need for more intensive anticholinesterase therapy, the diagnosis of cholinergic crisis, according to Osserman and Genkins¹, calls for the prompt *withdrawal* of all drugs of this type. The immediate use of atropine in cholinergic crisis is also recommended.

Atropine may also be used to abolish or obtund gastrointestinal side effects or other muscarinic reactions; but such use, by masking signs of overdosage, can lead to inadvertent induction of cholinergic crisis.

For detailed information on the management of patients with myasthenia gravis, the physician is referred to one of the excellent reviews such as those by Osserman and Genkins², Grob³ or Schwab.^{4,5}

Usage in Pregnancy:

The safety of pyridostigmine bromide during pregnancy or lactation in humans has not been established. Therefore, use of pyridostigmine bromide in women who may become pregnant requires weighing the drug's potential benefits against its possible hazards to mother and child.

PRECAUTION:

Pyridostigmine is mainly excreted unchanged by the kidney.^{6,7,8} Therefore, lower doses may be required in patients with renal disease, and treatment should be based on titration of drug dosage to effect.^{6,7}

Pediatric Use:

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS:

The side effects of pyridostigmine bromide are most commonly related to overdosage and generally are of two varieties, muscarinic and nicotinic. Among those in the former

group are nausea, vomiting, diarrhea, abdominal cramps, increased peristalsis, increased salivation, increased bronchial secretions, miosis and diaphoresis. Nicotinic side effects are comprised chiefly of muscle cramps, fasciculation and weakness. Muscarinic side effects can usually be counteracted by atropine, but for reasons shown in the preceding section the expedient is not without danger. As with any compound containing the bromide radical, a skin rash may be seen in an occasional patient. Such reactions usually subside promptly upon discontinuance of the medication.

To report SUSPECTED ADVERSE REACTIONS, contact Novadoz Pharmaceuticals LLC at 1-855-668-2369 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION:

Pyridostigmine Bromide Oral Solution, USP is available in following form:

Oral Solution -

raspberry-flavored, containing 60 mg pyridostigmine bromide per teaspoonful (5 mL). This form permits accurate dosage adjustment for children and "brittle" myasthenic patients who require fractions of 60 mg doses. It is more easily swallowed, especially in the morning, by patients with bulbar involvement.

Dosage:

The size and frequency of the dosage must be adjusted to the needs of the individual patient.

Oral Solution:

The average dose is ten 5 mL teaspoonfuls daily, spaced to provide maximum relief when maximum strength is needed. In severe cases as many as 25 teaspoonfuls a day may be required, while in mild cases one to six teaspoonfuls a day may suffice.

NOTE: For information on a diagnostic test for myasthenia gravis, and for the evaluation and stabilization of therapy, please see product literature on Tensilon (edrophonium chloride).

HOW SUPPLIED:

Pyridostigmine Bromide Oral Solution USP, 60 mg pyridostigmine bromide per teaspoonful (5 mL) is available as a clear, raspberry flavored solution and 0.23% w/w alcohol.

It is supplied as follows:

Bottles of 16 fluid ounces, (1 pint, 473 mL) NDC 72205-098-72

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

Dispense in tight, light-resistant containers as defined by the USP.

REFERENCES:

1. Osserman KE, Genkins G. Studies in myasthenia gravis: Reduction in mortality rate after crisis. *JAMA*. Jan 1963; 183:97-101.
2. Osserman KE, Genkins G. Studies in myasthenia gravis. *NY State J Med*. June 1961;

61:2076-2085.

3. Grob D. Myasthenia gravis. A review of pathogenesis and treatment. *Arch Intern Med.* Oct 1961; 108:615-638.
4. Schwab RS. Management of myasthenia gravis. *New Eng J Med.* Mar 1963; 268:596-597.
5. Schwab RS. Management of myasthenia gravis. *New Eng J Med.* Mar 1963; 268:717-719.
6. Cronnelly R, Stanski DR, Miller RD, Sheiner LB. Pyridostigmine kinetics with and without renal function. *Clin Pharmacol Ther.* 1980; 28: No. 1, 78-81.
7. Miller RD. Pharmacodynamics and pharmacokinetics of anticholinesterase. In: Ruegheimer E, Zindler M, ed. *Anesthesiology.* (Hamburg, Germany: Congress; Sep 14-21, 1980; 222-223.) (Int Congr. No. 538), Amsterdam, Netherlands: Excerpta Medica; 1981.
8. Breyer-Pfaff U, Maier U, Brinkmann AM, Schumm F. Pyridostigmine kinetics in healthy subjects and patients with myasthenia gravis. *Clin Pharmacol Ther.* 1985; 5:495-501.

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Manufactured by:

MSN Pharmaceuticals Inc.

Piscataway, NJ 08854

Distributed by:

Novadoz Pharmaceuticals LLC

Piscataway, NJ 08854 -3714

Issued on: 09/2023

PACKAGE LABEL PRINCIPAL DISPLAY PANEL

1 Pint (473 mL) Bottle Label

Rx only

NDC 72205-098-72

Pyridostigmine Bromide Oral Solution, USP

60 mg/5 mL

5 mL (one teaspoonful) contains **60 mg** pyridostigmine bromide, USP.

Alcohol 0.23% w/w

1 Pint (473 mL)



Usual Dosage: The size and frequency of the dosage must be adjusted to the needs of the individual. The average is ten 60 mg (5 mL) doses per day, spaced to provide maximum relief when maximum strength is needed. In severe cases, as many as 25 or more teaspoonfuls a day may be required, while in mild cases one to six teaspoonfuls a day may suffice.

IMPORTANT: For additional dosage information and other important prescribing information, read accompanying insert.

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

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

Keep out of the reach of children.

Manufactured by:
MSN Pharmaceuticals Inc.
Piscataway, NJ 08854

Distributed by:
Novadoz Pharmaceuticals LLC
Piscataway, NJ 08854-3714
TEL: 855 - NOVADOZ
(668-2369)

Issued: 06/2022



XXXXXX-XX

PYRIDOSTIGMINE BROMIDE

pyridostigmine bromide solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:72205-098
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
PYRIDOSTIGMINE BROMIDE (UNII: KVI301NA53) (PYRIDOSTIGMINE - UNII:19QM69HH21)	PYRIDOSTIGMINE BROMIDE	60 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
GLYCERIN (UNII: PDC6A3C0OX)	
LACTIC ACID (UNII: 33X04XA5AT)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
SORBITOL (UNII: 506T60A25R)	
SUCROSE (UNII: C151H8M554)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color		Score	
Shape		Size	

Flavor	RASPBERRY	Imprint Code		
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:72205-098-72	473 mL in 1 BOTTLE; Type 0: Not a Combination Product	09/26/2023	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
ANDA	ANDA216512	09/21/2023		

Labeler - Novadoz Pharmaceuticals LLC (081109687)

Establishment			
Name	Address	ID/FEI	Business Operations
MSN Pharmaceuticals Inc.		079229051	ANALYSIS(72205-098) , MANUFACTURE(72205-098)

Revised: 9/2023

Novadoz Pharmaceuticals LLC