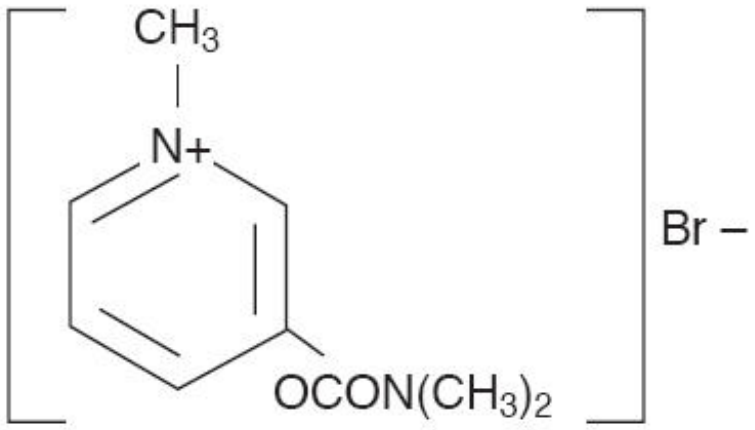
PYRIDOSTIGMINE BROMIDE- pyridostigmine bromide solution
Acella Pharmaceuticals, LLC

Pyridostigmine Bromide Oral Solution USP

DESCRIPTION

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



Pyridostigmine bromide is available as an oral solution containing 60 mg pyridostigmine bromide per teaspoonful in a vehicle containing 5% alcohol, glycerin, lactic acid, sodium benzoate, sorbitol, sucrose, FD&C Red No. 40, FD&C Blue No. 1, flavors and water.

ACTIONS

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 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 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 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 Genkins [1] 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 Genkins, [1] 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 Genkins [2], Grob [3] or Schwab. [4,5]

Usage in Pregnancy

The safety of pyridostigmine during pregnancy or lactation in humans has not been established. Therefore, use of pyridostigmine 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]

ADVERSE REACTIONS

The side effects of pyridostigmine 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 FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or Acella Pharmaceuticals, LLC at 1-800-541-4802.

DOSAGE AND ADMINISTRATION

Pyridostigmine bromide oral solution is available as raspberry-flavored oral solution, 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.

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.

HOW SUPPLIED

Pyridostigmine Bromide Oral Solution, USP, 60 mg pyridostigmine bromide per teaspoonful (5 mL) and 5% alcohol — bottles of 16 fluid ounces (1 pint) (NDC 42192-626-16)

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

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 patho-genesis 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. *Anaesthesiology*. (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.

Distributed by:
Acella Pharmaceuticals, LLC
Alpharetta, GA 30005
1-800-541-4802

201138-01

L-0003 Rev. 0925-01

PRINCIPAL DISPLAY PANEL - 473 mL Bottle

42192-**626**-16

Pyridostigmine Bromide Oral Solution USP 60 mg/5 mL

Alcohol 5%

Rx Only
1 Pint (473 mL)
L-0399 Rev. 0723-01 401143-01

3 42192 62616 4

42192-**626**-16
Pyridostigmine Bromide Oral Solution USP 60 mg/5 mL

Each 5 mL (teaspoonful) contains:
Pyridostigmine Bromide USP ..... 60 mg
Alcohol 5%

Usual Dosage: The size and frequency of the dosage must be adjusted to the needs of the individual. The average dose 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).

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

Distributed by:
Acella Pharmaceuticals, LLC
Alpharetta, GA 30005
1-800-541-4802

Acella PHARMACEUTICALS, LLC

NDC 42192-626-16
Rx Only

Pyridostigmine Bromide Oral Solution USP 5 mL = 60 mg
1 Pint (473 mL)

5 mL (1 teaspoonful)
contains 60 mg pyridostigmine bromide.

Alcohol 5%

Acella Pharmaceuticals, LLC
Alpharetta, GA 30005

PYRIDOSTIGMINE BROMIDE

pyridostigmine bromide solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:42192-626
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)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
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:42192-626-	473 mL in 1 BOTTLE; Type 0: Not a Combination	10/09/2023	

1	16	Product	10/09/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212405	10/09/2023	

Labeler - Acella Pharmaceuticals, LLC (825380939)