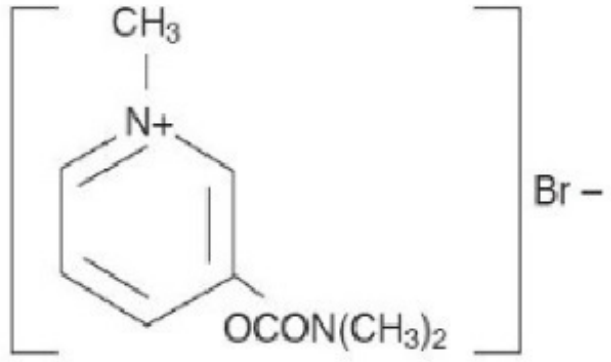
PYRIDOSTIGMINE - pyridostigmine bromide oral solution
Novitium Pharma LLC

Pyridostigmine Bromide Oral Solution, USP 60 mg/5 mL.

DESCRIPTION

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



Pyridostigmine Bromide Oral Solution, USP contains 60 mg pyridostigmine bromide per teaspoonful in a vehicle containing 5% alcohol, glycerin, lactic acid, sodium benzoate, sorbitol solution, sucrose, FD&C Red No. 40, FD&C Blue No. 1, raspberry flavor and water.

ACTION

Pyridostigmine Bromide Oral Solution 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.

INDICATIONS & USAGE

Pyridostigmine Bromide Oral Solution, USP is useful in the treatment of myasthenia gravis.

CONTRAINDICATIONS

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

PRECAUTIONS

GENERAL PRECAUTIONS

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 Oral Solution are most commonly related to over dosage 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 Novitium Pharma LLC at 1-855-204-1431 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DOSAGE & ADMINISTRATION

Pyridostigmine Bromide Oral Solution is available in the following form:

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.

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) and 5% alcohol - bottles of 16 fluid ounces (16 fl. oz.) (NDC 70954-148-10).

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

REFERENCES

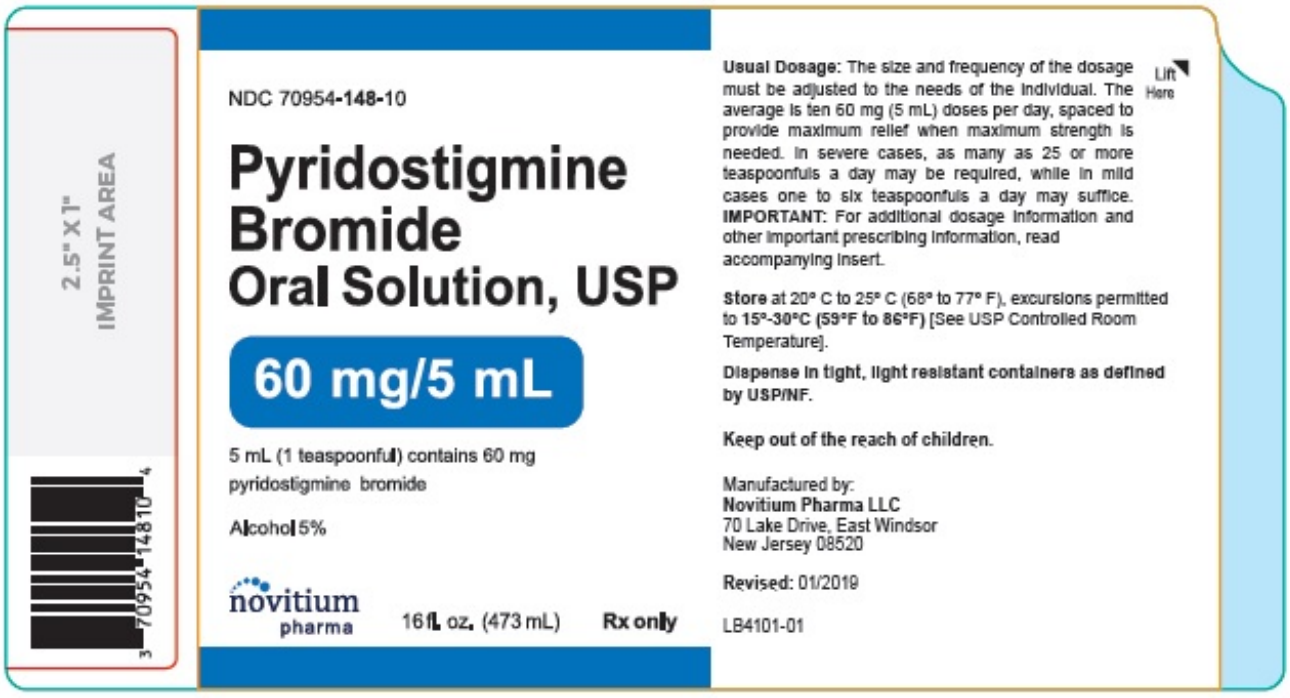
1. Osserman KE, Genkins G. Studies in myasthenia gravis: Reduction in mortality rate after crisis. JAMA. Jan 1963; 183:97-101.
2. Osserman KE, Genkins G. Studies in myasthenia gravis. NY State J Med. June 1961; 61:2076-2085.
3. Grob D. Myasthenia gravis. A review of pathogenesis and treatment. Arch Intern 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. Anaesthesialagy. (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

Manufactured by:
Novitium Pharma LLC
70 Lake Drive, East Windsor
New Jersey 08520

Revised: 01/2019

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Pyridostigmine Bromide Oral Solution, USP



PYRIDOSTIGMINE

pyridostigmine bromide oral solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:70954-148
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**
SUCROSE (UNII: C151H8M554)	

GLYCERIN (UNII: PDC6A3C0OX)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
LACTIC ACID (UNII: 33X04XA5AT)	
RASPBERRY (UNII: 4N14V5R27W)	
SORBITOL (UNII: 506T60A25R)	
ALCOHOL (UNII: 3K9958V90M)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	

Product Characteristics

Color	PINK	**Score**	
Shape		**Size**	
Flavor	RASPBERRY	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70954-148-10	473 mL in 1 BOTTLE; Type 0: Not a Combination Product	03/11/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA211694	03/11/2019	

Labeler - Novitium Pharma LLC (080301870)

Establishment

Name	Address	ID/FEI	Business Operations
Novitium Pharma LLC		080301870	MANUFACTURE(70954-148) , PACK(70954-148)

Revised: 3/2019 Novitium Pharma LLC