PYRIDOSTIGMINE BROMIDE- pyridostigmine bromide tablet, extended release
NuCare Pharmaceuticals,Inc.

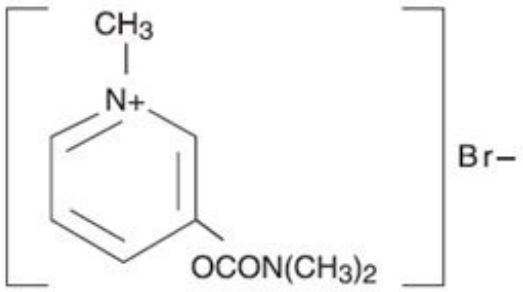
Pyridostigmine Bromide Extended-Release Tablets

(180 mg)

Rx only

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 extended-release tablets are available as extended-release tablets containing 180 mg pyridostigmine bromide; each tablet also contains carnauba wax, copovidone, lactose, magnesium stearate, and silicon dioxide.

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, 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 AND USAGE

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 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 Genkins [1] indicate that the differential diagnosis of the two types of crisis may require the use of 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 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.

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 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 Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION

Pyridostigmine bromide is available in extended-release dosage form:

Extended-Release Tablets — each containing 180 mg pyridostigmine bromide. This form provides uniformly slow release, hence prolonged duration of drug action; it facilitates control of myasthenic symptoms with fewer individual doses daily. The immediate effect of a 180 mg extended-release tablet is about equal to that of a 60 mg immediate-release tablet; however, its duration of effectiveness, although varying in individual patients, averages $2_{1/2}$ times that of a 60 mg dose.

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

Extended-Release Tablets — One to three 180 mg tablets, once or twice daily, will usually be sufficient to control symptoms; however, the needs of certain individuals may vary markedly from this average. The interval between doses should be at least 6 hours. For optimum control, it may be necessary to use the more rapidly acting regular tablets or syrup in conjunction with extended-release therapy.

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

HOW SUPPLIED

Pyridostigmine Bromide Extended-release Tablets, **180 mg** are available as light brown to pale yellow, capsule-shaped tablets, debossed with W1 on one side and single-scored on the other side.
NDC 68071-5032-3 BOTTLES OF 30

Note: Because of the hygroscopic nature of the extended-release tablets, mottling may occur. This does not affect their efficacy.

Store at 20° to 25°C (68° to 77°C) [see USP Controlled Room Temperature]. Dispense in a tight, light-resistant container. Keep pyridostigmine bromide extended-release tablets in a dry place with the silica gel enclosed.

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. *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.

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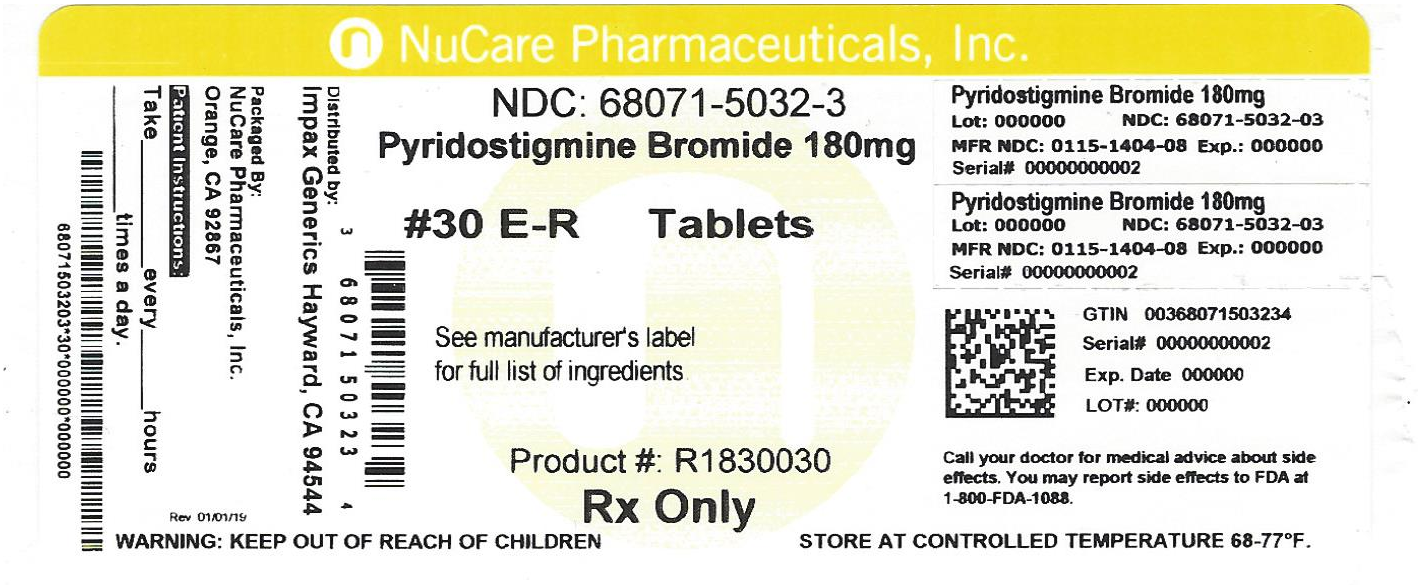
PRINCIPAL DISPLAY PANEL



PYRIDOSTIGMINE BROMIDE

pyridostigmine bromide tablet, extended release

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68071-5032(NDC:0115-1404)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
PYRIDOSTIGMINE BROMIDE (UNII: KVI301NA53) (PYRIDOSTIGMINE - UNII:19QM69HH21)	PYRIDOSTIGMINE BROMIDE	180 mg

Inactive Ingredients

Ingredient Name	Strength
CARNAUBA WAX (UNII: R12CBM0EIZ)	
COPOVIDONE K25-31 (UNII: D9C330MD8B)	
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	

Product Characteristics

Color	yellow (light brown to pale yellow)	**Score**	2 pieces
Shape	OVAL (capsule-shaped)	**Size**	19mm
Flavor		**Imprint Code**	W1
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68071-5032-3	30 in 1 BOTTLE; Type 0: Not a Combination Product	08/14/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA203184	09/18/2015	

Labeler - NuCare Pharmaceuticals,Inc. (010632300)

Establishment

Name	Address	ID/FEI	Business Operations
NuCare Pharmaceuticals,Inc.		010632300	relabel(68071-5032)