

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pyridostigmine 60 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 60mg of pyridostigmine bromide.

Each tablet also contains lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White to off white, flat faced, round, bevelled edges, uncoated tablet with cross scoring on one side and debossed 'NM' on the other side.

The tablet can be divided into four equal parts.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Myasthenia gravis, paralytic ileus and post-operative urinary retention.

4.2 Posology and method of administration

Myasthenia gravis Adults

Doses of 30 to 120mg are given at intervals throughout the day when maximum strength is needed (for example, on rising and before mealtimes). The usual duration of action of a dose is 3 to 4 hours in the daytime but a longer effect (6 hours) is often obtained with a dose taken on retiring for bed.

The total daily dose is usually in the range of 5 – 20 tablets but doses higher than these may be needed by some patients.

Children

Children under 6 years old should receive an initial dose of half a tablet (30mg) of pyridostigmine; children 6 – 12 years old should receive one tablet (60mg). Dosage should be increased gradually, in increments of 15 – 30mg daily, until maximum improvement is obtained. Total daily requirements are usually in the range to 30 – 360mg.

Other Indications Adults

The usual dose is 1 to 4 tablets (60 – 240mg).

Children

15 – 60mg.

The frequency of these doses may be varied according to the needs of the patient.

Elderly

There are no specific dosage recommendation for pyridostigmine in elderly patients.

Renal Impairment

Pyridostigmine is mainly excreted unchanged by the kidney, therefore lower doses may be required in patients with severe renal disease and treatment should be based on titration of drug dosage to effect.

4.3 Contraindications

Pyridostigmine should not be given to patients with mechanical gastro-intestinal or urinary obstruction. Pyridostigmine is contra-indicated in patients with known hypersensitivity to the drug and to bromides.

4.4 Special warnings and precautions for use

Extreme caution is required when administering pyridostigmine to patients with bronchial asthma.

Care should also be taken in patients with bradycardia, recent coronary occlusion, hypotension, vagotonia, peptic ulcer, epilepsy or Parkinsonism.

There is no evidence to suggest that pyridostigmine has any special effects on the elderly. However, elderly patients may be more susceptible to dysrhythmias than the young adult.

The requirement for pyridostigmine is usually markedly decreased after thymectomy or when additional therapy (steroids, immunosuppressant drugs) is given.

When relatively large doses of pyridostigmine are taken by myasthenic patients it may be necessary to give atropine or other anticholinergic drugs to counteract the muscarinic effects. It should be noted that the slower gastro-intestinal motility caused by these drugs may affect the absorption of pyridostigmine.

In all patients the possibility of "cholinergic crisis", due to overdosage of pyridostigmine, and its differentiation from "myasthenic crisis", due to increased severity of the disease, must be borne in mind. Both types of crisis are manifested by increased muscle weakness, but whereas myasthenic crisis may require more intensive anticholinesterase treatment, cholinergic crisis calls for immediate discontinuation of this treatment and institution of appropriate supportive measures, including respiratory assistance.

Pyridostigmine Lime TM tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Antimuscarinics:

Atropine and hyoscine antagonise the muscarinic effects of pyridostigmine bromide.

Anti-arrhythmics:

Procainamide, quinidine, and propranolol have been shown to antagonize the effects of pyridostigmine. There have been some reports of propafenone also being able to antagonize the effects of pyridostigmine.

Antibacterials:

Aminoglycoside antibiotics, clindamycin and also polymyxins antagonize the effects of pyridostigmine.

Antimalarials:

Chloroquine and hydroxychloroquine, by nature of their ability to increase myasthenic symptoms have also been shown to antagonize the effects of pyridostigmine.

Lithium:

The anti-myasthenic effects of pyridostigmine are antagonized by lithium .

Muscle Relaxants:

Pyridostigmine antagonises the effect of non-depolarising muscle relaxants (e.g. pancuronium and vecuronium). Pyridostigmine may prolong the effect of depolarising muscle relaxants (e.g. suxamethonium).

Methylcellulose:

Methylcellulose has been reported to prevent the absorption of pyridostigmine so should not be dosed concomitantly with it.

4.6 Fertility, pregnancy and lactation

The safety of pyridostigmine during pregnancy or lactation has not been established. Although the possible hazards to mother and child must be weighed against the potential benefits in every case, experience with pyridostigmine in pregnant patients with myasthenia gravis has revealed no untoward effect of the drug on the course of pregnancy. As the severity of myasthenia gravis often fluctuates considerably, particular care is required to avoid cholinergic crisis, due to overdosage of the drug, but otherwise management is no different from that in non-pregnant patients. Observations indicate that only negligible amounts of pyridostigmine are excreted in breast milk; nevertheless, due regard should be paid to possible effects on the breast-feeding infant.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

These are all gastrointestinal in nature.

Gastrointestinal:

Moderately serious effects include nausea and vomiting, increased salivation, diarrhoea and abdominal cramps.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: <http://www.hpra.ie/>; E-mail: medsafety@hpra.ie.

4.9 Overdose

Signs of overdosage due to muscarinic effects may include abdominal cramps, increased peristalsis, diarrhoea, nausea and vomiting, increased bronchial secretions, salivation, diaphoresis and miosis. Nicotinic effects consist of muscular cramps, fasciculations and general weakness. Bradycardia and hypotension may also occur. Artificial ventilation should be instituted if respiration is severely depressed. Atropine sulfate 1 to 2mg intravenously is an antidote to the muscarinic effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N07 AA 02, Pharmacotherapeutic group: Anticholinesterases

Pyridostigmine is an anticholinesterase. As an antagonist to cholinesterase, the enzyme which normally destroys acetylcholine, the action of pyridostigmine can briefly be described, therefore, as the potentiation of naturally occurring acetylcholine. Thus, it enhances the neuromuscular transmission in voluntary and involuntary muscles. Pyridostigmine has a more prolonged action than Prostigmin (neostigmine) although it is somewhat slower to take effect (generally taking 30 – 60 minutes). Because it has a weaker "muscarinic" action than Prostigmin, it is usually much better tolerated by myasthenic patients in whom the longer action is also an advantage. Although a positive correlation has

been demonstrated between the plasma concentrations of pyridostigmine and its pharmacological effects as measured by a decrement in muscle response to repetitive nerve stimulation in a single muscle, this relationship is less clear when a global evaluation of muscular function in myasthenia gravis is used.

5.2 Pharmacokinetic properties

One to two hours after oral administration of 60 mg pyridostigmine, peak plasma concentrations of 40 to 60 micrograms/L are observed. The oral bioavailability of pyridostigmine is low at approximately 10%. In spite of the short elimination half-life of pyridostigmine, intra-individual variations in plasma concentration during a dose interval are small in myasthenic patients receiving oral maintenance therapy, probably as a result of slow absorption from the gastrointestinal tract. Severely impaired renal function has been shown to prolong the elimination of pyridostigmine, and methylcellulose has been reported to inhibit the absorption completely. Elimination of pyridostigmine occurs via the kidney, as a largely unchanged molecule with a half-life of 3 to 4 hours.

5.3 Preclinical safety data

Not relevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silicon Dioxide
Lactose Monohydrate
Maize Starch
Purified Talc
Magnesium Stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months in amber glass bottle
36 months in white opaque HDPE bottle

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container and keep container tightly closed to protect from moisture and light.

6.5 Nature and contents of container

Type III amber glass bottle with PP child-resistant closure or white opaque HDPE bottle, containing HDPE desiccant (silica gel) canister, with a PP child-resistant closure. Each bottle contains 200 tablets.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031GA Haarlem
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1986/065/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21st November 2008

Date of last renewal: 29th February 2012

10 DATE OF REVISION OF THE TEXT

November 2017