PYRIMINE TABLET 60 MG

DESCRIPTION
Orange round biconvex film coated tablet.

CONTENTS
Each tablet contains 60 mg of Pyridostigmine bromide.

PROPERTIES
Pyridostigmine is an anticholinesterase agent that reversibly inhibits the hydrolysis of acetylcholine by competing for attachment to acetylcholinesterase. Acetylcholine then accumulates at cholinergic synapses and its effects are prolonged and enhanced. Therefore, pyridostigmine produces generalised cholinergic responses including miosis, increased tonus of intestinal and skeletal musculature, constriction of bronchi and ureters, bradycardia and stimulation of secretion by salivary and sweat glands. It also has a direct cholinomimetic effect on skeletal muscle.

A Pyridostigmine action is similar to neostigmine but is slower in onset (generally, 30 - 60 minutes) and longer duration of action.

Pyridostigmine bromide is poorly absorbed from the gastrointestinal tract. The bioavailability after oral administration of pyridostigmine bromide is about 10 – 20%. It generally has an onset of action of 30 – 45 minutes with duration of action of 3 – 6 hours upon oral administration. A variable duration of action has been seen in patients with Myasthenia Gravis, depending on the physical and emotional stress suffered by the patient and the severity of the disease.

Pyridostigmine has been reported to cross the placental and very small amounts are distributed into breast milk. It does not cross blood brain barrier and no information on protein binding is available.

Following oral administration, the elimination half-life of pyridostigmine is 3 hours in patients with normal renal function. However, this can be prolonged up to three times over in individual cases. It has been reported in anephric patients the elimination half-life is 6.3 hours.

Pyridostigmine undergoes hydrolysis by cholinesterases and is also metabolised in the liver. Approximately 80 – 90% of pyridostigmine is excreted unchanged via kidney and found in the urine with its major metabolite, 3-hydroxy-N-methylpyridine.

INDICATIONS
Pyrimine Tablet 60 mg is indicated in the treatment of Myasthenia Gravis.

DOSAGE & ADMINISTRATION
Myasthenia Gravis

Adult: 60 - 180 mg (1 - 3 tablets of Pyrimine Tablet 60 mg) 2 - 4 times daily, or higher doses if necessary. The total daily dosage ranges from 300 - 1200 mg (5 - 20 tablets of Pyrimine Tablet 60 mg) but doses higher than these dosages may be required in other patients. Children: For children under the age of 6 years old, the initial dose of 30 mg (½ of Pyrimine Tablet 60 mg) should be given, while children between 6 and 12 years old should receive 60 mg (1 tablet of Pyrimine Tablet 60 mg). The dosage will be increased gradually, in increments of 15 – 30 mg daily until a satisfactory response is obtained, which is usually within the dosage range of 30 – 360 mg daily.

In Myasthenia gravis, one dose is effective for approximately four hours during the day whilst at night (owing to reduced physical activity), a longer duration of effect of around 6 hours can be expected. It is recommended that the times of administration be chosen so that the maximum effect coincides with the most strenuous physical exertion, e.g. when getting up and at mealtimes.

Special dosage instructions

The required dose must be carefully titrated when used in paediatrics. In cases of neonatal myasthenia, generally one treatment with neostigmine is preferred. However, if this appears unsuitable due to excessively cholinergic side effects, then *Pyrimine Tablet 60 mg* can be administered. In these cases, the following serves as a rough guideline: 5-10 mg by mouth in tablet form, 30 - 60 minutes before food. Treatment over the eighth week of life is required only in extremely rare cases of congenital and familial infantile myasthenia.

Pyridostigmine is mainly eliminated unchanged via the kidneys. Lower doses may therefore be indicated in patients presenting with kidney disease. The dose should be adjusted in line with the desired effect.

CONTRAINDICATIONS
Pyrimine Tablet 60 mg is contraindicated in patients with mechanical obstruction of the intestinal or urinary tract and in patients who are hypersensitive to pyridostigmine and bromides.

WARNINGS & PRECAUTIONS

Overdosage of pyridostigmine may result in cholinergic crisis, a state described by increasing muscle weakness that may lead to death if it affects the respiratory muscles. Myasthenia crisis due to an increase in the severity of the disease is also associated by muscle weakness which may be hard to differentiate from cholinergic crisis on a symptomatic basis. Hence, it is important to perform a diagnosis to distinguish between these two crisis. Treatment for these two conditions obviously differ as in myasthenia crisis, demand for intensive anti-cholinesterase therapy while in cholinergic crisis, immediate withdrawal of this type of drugs is required.

Atropine may abolish or reduce the muscarinic side effects. However, such use that is by masking the signs and symptoms of the indication of pyridostigmine overdose may prevent early detection of cholinergic crisis.

Pyridostigmine should be used with caution in patients with bronchial asthma, cardiac dysrhythmias, chronic obstructive pulmonary disease and bradychardia.

Pyridostigmine is mainly excreted unchanged by the kidney. Hence, in patients with renal disease, only lower dosage of pyridostigmine may be required and it should be titrated carefully to produce the desired effect.

Interactions with other medicaments

Atropine and hyoscine antagonise the muscarinic effects of pyridostigmine. Pyridostigmine antagonises the effect of non-depolarising muscle relaxants, such as pancuronium and vecuronium. It may also prolong the effect of depolarising muscle relaxants for example suxamethonium.

Concomitant therapy with beta-adrenergic blocking agent should be used with caution for the treatment of hypertension or glaucoma.

Pregnancy & lactation

Pregnancy: The safety use of pyridostigmine during pregnancy has not been established. Hence, use of pyridostigmine in pregnant women requires that all possible benefits be weighed against the potential risk.

Lactation: There is a possibility of pyridostigmine diffusing into breast milk; the drug should be used with caution in nursing women.

ADVERSE REACTIONS

The most common adverse effects with pyridostigmine are usually muscarinic or nicotinic effects.

Muscarinic effects include nausea, vomiting, diarrhoea, abdominal cramps, increased peristalsis, increased salivation, increased bronchial secretion, miosis, diaphoresis, bradycardia and branchospasm. Muscarinic adverse effects occur less frequently with pyridostigmine treatment than with neostigmine.

The most common nicotinic effects encountered consist mainly of muscle cramps, fasciculations and muscle weakness.

As with other drugs containing bromide, therapy with pyridostigmine bromide may cause skin rash. This condition usually resolves promptly upon discontinuation of the therapy.

SYMPTOMS & TREATMENTS OF OVERDOSAGE

Symptoms: Overdose of Pyrimine Tablet 60 mg may induce cholinergic crisis, which symptoms include nausea, vomiting, diarrhoea, excessive salivation and sweating, increased bronchial secretions, miosis, lacrimation, bradycardia or tachycardia, cardiospasm, bronchospasm, hypotension, incoordination, blurred vision, muscle cramps, weakness, fasciculation and paralysis. Very high doses may produce CNS agitation, restlessness, confusion, visual hallucinations and paranoid delusions.

Treatment: Execute withdrawal of Pyrimine Tablet 60 mg or other cholinergic drugs immediately and maintain an adequate airway, if necessary, assist respiration mechanically or with oxygen. Slow intravenous administration of 1 – 2 mg atropine sulphate should be given to control the muscarinic symptoms. This dose is to be repeated at intervals of two to four hours if required.

STORAGE CONDITIONS & PHARMACEUTICAL PRECAUTIONS

Store in a cool dry place, below 30°C.
Protect from light.
Keep out of reach of children.
Jauhi daripada kanak-kanak.

PACKING/PACK SIZES

Aluminium foil pack strip of 10.
Box of 10, 30, 50, 100, 150 and 200 tablets.

Manufactured by:
SRIPRASIT PHARMA CO. LTD.
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Samut Sakhon 74110, Thailand.

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