Neostigmine Methylsulphate Fresenius 2.5mg/1ml Injection
Neostigmine Methylsulphate 2.5mg

Description
A clear and colourless sterile solution in amber glass ampoules.

Composition
Each ml ampoule contains 2.5mg of Neostigmine Methylsulphate.

Summary of Pharmacodynamics and Pharmacokinetics
Neostigmine is a reversible cholinesterase inhibitor. It is a quaternary ammonium compound and is absorbed poorly after oral administration. Neostigmine is destroyed by plasma esterases. The quaternary alcohol thus formed and the parent compounds are excreted in the urine.

Indications
Neostigmine Methylsulphate Fresenius 2.5mg/1ml Injection is indicated in the treatments of
- The symptomatic treatment of myasthenia gravis where oral therapy is impractical.
- Reversal of the effects of non-depolarising neuromuscular blocking agents such as tubocurarine and gallamine.
- The management of post-operative distension, paralytic ileus and urinary retention, where mechanical obstruction has been outruled.

Side Effects/Adverse Reaction
Side effects of Neostigmine Methylsulphate are
Salivation, anorexia, nausea and vomiting. Abdominal cramps and diarrhoea may occur. Muscle cramps, fasciculation and weakness may also occur.

Warning/Precautions
Neostigmine should be used with extreme caution in patients who have undergone recent intestinal or bladder surgery. When Neostigmine is given by injection, atropine should always be available to counteract any excessive reactions.

When Neostigmine Methylsulphate injection is used for myasthenia gravis; absence of clinical improvement may be indicative of overdosage or underdosage. Overdosage may lead to a cholinergic crisis characterised by muscle weakness affecting respiration. Increase in the severity of the disease may lead to myasthenic crisis also characterised by severe muscle weakness. Differential diagnosis can be aided by the edrophonium chloride test. If 0,1 ml (1 mg) or at most 0,2 ml (2 mg) of edrophonium chloride is given intravenously, a marked improvement indicates myasthenic crisis. Any other response, whether equivocal or exacerbation of symptoms, must be considered to be cholinergic in origin.

Should be used with caution in elderly patients and in patients with pre-existing cardiac rhythm disturbances. As Neostigmine is excreted mainly by the kidneys, caution is advised in cases of impaired renal function.

Should be used with caution in patients with bradycardia, bronchial asthma, recent coronary occlusion, epilepsy, hypotension, hyperthyroidism, Parkinsonism, peptic ulceration or vagotonia. Also to be used with caution in patients with myasthenia gravis to avoid provoking a cholinergic crisis with increased muscular weakness.

Contraindication
Neostigmine Methylsulphate is contraindicated in patients with
- Mechanical intestinal or urinary obstruction.
- In conjunction with depolarising muscle relaxants, such as suxamethonium.
- During cyclopropane or halothane anaesthesia, although it may be used after withdrawal of these agents.
- Diabetes
- Gangrene or peritonitis
- Pregnancy and lactation.

Recommended Dose and Directions for Use
Neostigmine Methylsulphate injections may be administered intramuscularly, subcutaneously or intravenously. When the intravenous route is used, administration must be by very slow injection.

I) Treatment of myasthenia gravis
Adults:
Doses of 1 to 2.5mg may be given by intramuscular or subcutaneous injection at intervals during the day when strength is most needed. The total daily dose is usually in the range of 5 to 20mg, but higher doses may be required by some patients.

Children:
Neonatal myasthenia can be treated with an initial dose of 0.1 mg intramuscularly.
Thereafter, the dosage should be titrated individually and is usually in the range of 0.05 to 0.25mg by injection.
Treatment is rarely needed beyond eight weeks of age.

II) Reversal of non-depolarising neuromuscular blocking agents
Adults and Children:
The usual dose is 0.05 to 0.07mg per kg body weight, given concomitantly with atropine sulphate, by slow intravenous injection over a period of 60 seconds.
Additional neostigmine may be required to restore normal muscle power but a total of 5mg for adults and 2.5mg for children should not be exceeded.
If preferred, the atropine sulphate may be administered prior to the neostigmine.

III) Management of post-operative distension, paralytic ileus and urinary retention
Adults:
The usual dose is 0.5 to 2.5mg by subcutaneous or intramuscular injection.

Children:
The usual dose is 0.125 to 1.0 mg by subcutaneous or intramuscular injection.

Incompatibilities
Neostigmine Methylsulphate should not be combined with other aqueous solutions of medicaments except with water for injection. The injection should be freshly prepared and unused portions should be discarded.

Use in Pregnancy and Lactation
The severity of myasthenia gravis often fluctuates considerably during pregnancy, particular care is needed to avoid cholinergic crisis caused by overdosage. It has been reported that neonatal myasthenia may follow administration of large doses during pregnancy. The amount of Neostigmine distributed into breast milk is very small but breast-fed infants need to be monitored.

Interaction With Other Medicaments/Drug Interactions
Certain antibiotics such as neomycin, streptomycin and kanamycin have a non-depolarising blocking action which may accentuate neuromuscular block. These agents must be used with care in conjunction with Neostigmine in patients with myasthenia gravis. Prolonged bradycardia has occurred in patients receiving beta-adrenoceptor blocking agents following administration of Neostigmine. Some antiarrhythmic agents such as quinidine may antagonise Neostigmine action by interfering with neuromuscular transmission.

Symptoms and Treatment of Overdose
Symptoms of overdosage include sweating, lachrymation, watery nasal discharge, eructation, involuntary defaecation and urination, flushing, miosis, conjunctival congestion, ciliary spasm, brow ache, nystagmus, restlessness, agitation, fear, excessive dreaming, hallucinations, increased bronchial secretion combined with bronchoconstriction, bradycardia and hypotension, scattered fasciculations and eventually severe weakness and paralysis, convulsions and coma. Paradoxical effects may also occur due to interaction between nicotinic and muscarinic actions. Accordingly there may be tachycardia and hypertension.

Death may follow due to cardiac arrest or central respiratory paralysis and pulmonary oedema. The major symptom of overdosage in myasthenia gravis is increased muscular weakness.

Treatment:
Give atropine sulphate 1 - 2 mg intravenously, intramuscularly, or subcutaneously to control the muscarinic effects. The dose may be repeated every 2 - 4 hours as necessary. Further treatment is symptomatic and supportive.

Presentation
This injection is available in 1ml ampoules
10 ampoules are packed into one outer carton.

Storage Condition
Protect from light and store below 30°Celsius. Keep out of reach of children.

Shelf Life
The injections can be used within 48 months from the date of manufacture if kept as recommended.

Registration number
Neostigmine Methylsulphate Fresenius 2.5mg/1ml Injection–
MAL06081214ARZ

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