

For the use only of a Registered Medical Practitioners or a Hospital or a Laboratory.

NEOSTIGMINE INJECTION B.P. Myostigmin®

COMPOSITION

Each ml contains:

Neostigmine Metilsulfate B.P. 0.5mg / 2.5mg

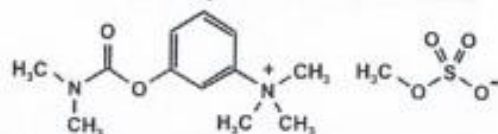
Water for Injections B.P. q.s.

DESCRIPTION

Myostigmin® (Neostigmine Injection B.P.) an anti-cholinesterase agent, is a sterile aqueous solution intended for intramuscular, intravenous or subcutaneous administration. Each ml contains Neostigmine Metilsulfate B.P. 0.5mg & 2.5mg.

Neostigmine Injection BP is a clear, colourless sterile solution of Neostigmine Metilsulfate with sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate and water for injections at pH 4.5 to 6.5.

Structural formula of Neostigmine Metilsulfate as follow:



Neostigmine Metilsulfate having molecular formula $C_{12}H_{18}N_2O_6S$ and molecular weight 334.4

CLINICAL PHARMACOLOGY

Neostigmine inhibits the hydrolysis of acetylcholine by competing with acetyl choline for attachment to acetyl-cholinesterase at sites of cholinergic transmission. It enhances cholinergic action by facilitating the transmission of impulses across neuromuscular junctions. Neostigmine undergoes hydrolysis by cholinesterase and is also metabolised by microsomal enzymes in the liver. Protein binding to human serum albumin ranges from 15 to 25%.

Following intramuscular administration, neostigmine is rapidly absorbed and eliminated. The clinical effects of Neostigmine usually begin within 20 to 30 minutes after intramuscular injection and last from 2.5 to 4 hours.

Following I.V. administration, plasma half-life ranges from 47 to 60 minutes have been reported with a mean half-life of 53 minutes.

INDICATIONS & USAGE

Neostigmine Injection is indicated for:

- * Reversal of effects of nondepolarising neuromuscular blocking agents (e.g. tubocurarine, metocurine, gallamine or Pancuronium) after surgery.
- * The prevention and treatment of postoperative distention and urinary retention after mechanical obstruction has been excluded.
- * The symptomatic control of myasthenia gravis when oral therapy is impractical.

CONTRAINDICATIONS

Neostigmine Injection B.P. is contraindicated in patients with known hypersensitivity to the drug. It is also contraindicated in patients with peritonitis or mechanical obstruction of the intestinal or urinary tract.

WARNINGS

Neostigmine Injection should be used with caution in patients with epilepsy, bronchial asthma, bradycardia, recent coronary occlusion, vagotonia, hyperthyroidism, cardiac arrhythmias or peptic ulcer. When large doses of neostigmine are administered, the prior or simultaneous injection of atropine sulfate may be advisable. Separate syringes should be used for Neostigmine and atropine because of the possibility of hypersensitivity in an occasional patient, atropine and antishock medication should always be readily available.

PRECAUTIONS

GENERAL: It is important to differentiate between myasthenic crisis and cholinergic crisis caused by overdosage of Myostigmin Injection. Both conditions result in extreme muscle weakness but require radically different treatment.

DRUG INTERACTIONS

Neostigmine Metilsulfate does not antagonize, and may in fact prolong, the phase I block of depolarising muscle relaxants such as Suxamethonium or decamethonium. Certain antibiotics, such as neomycin, streptomycin, kanamycin should be used in the myasthenic patient only where definitely indicated, and then and careful adjustment should be made of the anticholinesterase dosage. Local and some general anaesthetics, antiarrhythmic agents and other drugs that interfere with neuromuscular transmission should be used cautiously.

Carcinogenesis, mutagenesis and impairment of fertility: There have been no studies with Neostigmine Metilsulfate which would permit an evaluation of its carcinogenic or mutagenic potential. Studies on the effect of Neostigmine Metilsulfate on fertility and reproduction have not been performed.

PREGNANCY

Teratogenic Effects - Pregnancy category C.

There are no adequate or well controlled studies of Neostigmine in either laboratory animal or in pregnant women. It is not known whether Neostigmine Metilsulfate can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity.

Non-teratogenic effects- Anticholinesterase drugs may cause teratogenic uterine irritability and induce premature labour when given I.V. to pregnant woman near term.

Nursing Mothers: It is not known whether Neostigmine Metilsulfate is excreted in human milk. Because of the potential for serious adverse reactions from Neostigmine Metilsulfate, a decision should be made whether to discontinue nursing or to discontinue the drug.

Paediatric use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Side effects are generally due to an exaggeration of pharmacological effects of which salivation and fasciculation are the most common. Bowel cramps and diarrhoea may also occur. The following adverse reactions have been reported following use of Neostigmine Metilsulfate.

Allergic: Allergic reactions and anaphylaxis.

Neurologic: Dizziness, convulsions, headache, miosis and visual changes.

Cardiovascular: Cardiac arrhythmias, syncope and hypotension.

Respiratory: Increased oral, pharyngeal and bronchial secretions, respiratory depression, respiratory arrest and bronchospasm.

Dermatologic: Rash & Urticaria.

Gastrointestinal: Nausea, emesis, flatulence and increased peristalsis.

Musculoskeletal: Muscular cramps and spasms.

OVERDOSAGE

Overdosage of Neostigmine Injection can cause cholinergic crisis, which is characterized by increasing muscle weakness, and through involvement of the muscles of respiration, may result in death. Myasthenic crisis, accompanied by extreme muscle weakness and may be difficult to distinguish from cholinergic crisis on a symptomatic basis.

Treatment of the two conditions differs radically. Whereas the presence of myasthenic crisis requires more intensive anticholinest-

erase therapy, cholinergic crisis calls for the prompt withdrawal of all drugs of this type.

DOSAGE AND ADMINISTRATION

Reversal of Effects of nondepolarizing neuromuscular blocking agents: When Neostigmine Injection is administered Intravenously, it is recommended that Atropine Sulfate (0.6 to 1.2 mg) also administered simultaneously using separate syringes. The usual dose is 0.5 mg to 2.5 mg Neostigmine Injection given by Slow Intravenous, Intramuscular or Subcutaneous Injection, repeated as required. Reversal of non-depolarising neuromuscular blockade by intravenous injection over 1 minute, 50-70 micrograms/kg (Max.5mg) after or with glycopyrronium or atropine. It is recommended that the patient be well ventilated and a patent airway maintained until complete recovery. The drug should never be administered in the presence of high concentrations of Halothane or Cyclopropane. In Cardiac cases and severely ill patients, it is advisable to titrate the exact dose of Neostigmine required, using a peripheral nerve stimulator device. Parenteral drug products should be inspected visually for matter and discoloration prior to administration, whenever solution and container permit.

Treatment of postoperative distention - One ml of the 1:2000 solution (0.5mg) subcutaneously or intramuscularly, as required.

Treatment of urinary retention: 0.5 mg Neostigmine subcutaneously or intramuscularly. If urination does not occur within an hour, the patient should be catheterised. After the patient has voided, or the bladder has been emptied, continue the 0.5mg injection every three hours for atleast 5 injections.

Symptomatic control of myasthenia gravis: 0.5mg subcutaneously or intramuscularly. Subsequent doses should be based on the individual patients response.

STORAGE

Store below 30°C., protected from light. Do not freeze.

PRESENTATION

Myostigmin® (Neostigmine Injection B.P.) is available in a ampoule containing Neostigmine Metilsulfate B.P. 0.5mg/ml & 2.5mg/ml.

MADE IN INDIA BY:

NEON LABORATORIES LTD.
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Andheri (East), Mumbai - 400 093.

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