SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:

MYOSTIGMIN
Neostigmine Injection BP
Strength
0.5 mg/ ml- 5 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Sr. No.	Particulars	Grade	Qty./ml	Function
1.	Neostigmine Metilsulfate	B.P.	0.5 mg	Active

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM:

A clear, colourless solution.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

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 metabolized 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.

4.2 Posology and method of 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 1minute, 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 patient's response.

Method of administration :

Neostigmine Methylsulfate may be administered by IV, IM or SC injection. Please refer to the above text for the recommendedroute of administration according to indication.
Neostigmine Methylsulfate should be given slowly by the IV route (given over 1 minute).
A syringe of Atropine Sulfate should always be available to counteract severe cholinergic reactions should they occur.

4.3 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.

4.4 Special warnings and precautions for use:

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.

4.5 Interaction with other medicinal products and other forms of interaction:

Neostigmine Metilsulfate does not antagonize, and may in fact prolong, the phase I block of depolarizing 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.

4.6 Fertility, pregnancy and lactation:

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.

Lactation

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.

4.7 Effects on ability to drive and use machines:

Not applicable.

4.8 Undesirable effects or Adverse Reaction:

The following Adverse Events have been reported:

System Organ Class	Undesirable Effects	Frequency
Immune system disorders	Hypersensitivity, angioedema, anaphylactic reaction	Not known
Nervous system disorders	Cholinergic syndrome, especially at high doses. In patients with myasthenia gravis, cholinergic crisis may be difficult to distinguish from myasthenia crisis .	Not known
Eye disorders	Miosis, lacrimation increased	Not known
Cardiac disorders	Bradycardia, decreased cardiac conduction, in severe cases possibly leading to heart block or cardiac arrest	Not known
Vascular disorders	Hypotension	Not known
Respiratory, thoracic or mediastinal disorders	Increased bronchial secretion, bronchospasm	Not known
Gastrointestinal disorders	Nausea, vomiting, diarrhoea, abdominal cramps, salivary hypersecretion. Increased intestinal motility may result in involuntary defecation.	Not known
Skin and subcutaneous tissue disorders	Hyperhidrosis	Not known
Musculoskeletal, connective tissue and bone disorders	Muscle spasms	Not known
Renal and urinary disorders	Urinary incontinence	Not known

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose:

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.

5. PHARMACOLOGICAL PROPERTIES :

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group (ATC code): N07AA01

Neostigmine inhibits cholinesterase activity and prolongs and intensifies the muscarinic and nicotinic effects of acetylcholine. The anticholinesterase actions of Neostigmine are reversible. It is used mainly for its action on skeletal muscle and less frequently to increase the activity of smooth muscle. Neostigmine is used in the treatment of Myasthenia Gravis.

5.2 Pharmacokinetic properties:

Neostigmine is a quaternary ammonium compound and is poorly absorbed from the gastrointestinal tract. Following parenteral administration as the methylsulfate, neostigmine is metabolized partly by hydrolysis of the ester linkage and is excreted in the urine both as unchanged drug and as metabolites. The half-life of neostigmine is only one to two hours.

5.3 Pre-clinical Safety Data:

No further information other than that which is included in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Sodium Acetate BP
Glacial Acetic Acid BP
Water for injections (Bulk) BP

6.2 Incompatibilities:

Neostigmine may be diluted with Water for Injections. Stability of the injection cannot be guaranteed once it has been diluted.

6.3 Shelf – life:

24 Months

6.4 Special precautions for storage:

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

6.5 Nature and contents of container:

5 ml flint ampoule blue band snap off. Such 5 ampoules packed in a blister. Such 2 blisters packed in a carton along with package insert.

6.6 Special Precautions for Handling and Disposal:

Use as directed by a physician. If only part used discard the remaining solution.

7. MARKETING AUTHORIZATION HOLDER:

M/s. NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Indl. Estate, Mahakali Caves Road,
Andheri (East), Mumbai - 400 093

8. MARKETING AUTHORIZATION NUMBER:

08327/08359/REN/2022

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORISATION:

Date of first authorization: 07/02/2018

Date of Renewal of the Authorization:03/01/2023

10. DATE OF REVISION OF THE TEXT:

JULY 2023

11. REFERENCE

- Neostigmine Metisufate injection - Summary of Product Characteristics (SmPC) - (emc) - Summary of Product Characteristics (SmPC) https://www.medicines.org.uk/emc/product/6268/smpc