SUMMARY OF PRODUCT CHARACTERISTICS

Neox – Neostigmine Metilsulfate 2.5mg in 1ml solution for injection

Active Ingredient

Neostigmine Metilsulfate

1. Name of the medicinal product

Neox – Neostigmine Metilsulfate 2.5mg in 1ml solution for injection

2. Qualitative and quantitative composition

Each ml of solution for injection contains 2.5mg of Neostigmine Metilsulfate

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for injection

4. Clinical particulars

4.1. Therapeutic indications

Myasthenia Gravis, antagonist to non-depolarizing neuromuscular blockade, Paralytic Ileus, Post-operative Urinary Retention; Paroxysmal Supraventricular Tachycardia.

4.2. Posology and method of administration

Posology

Recommended doses are present by indication below but may be varied according to the individual needs of the patient.

Myasthenia Gravis

<table>
<tr><th colspan="2">Myasthenia Gravis</th></tr>
<tr><td>Patient population</td><td>Recommended dose (via subcutaneous or intramuscular injection)</td></tr>
<tr><td>Adults and Children</td><td>1mg – 2.5mg Neostigmine Metilsulfate repeated at suitable intervals throughout the day (usual total daily dose in adults is 5mg – 20mg).</td></tr>
<tr><td>(12 to 17 years)</td><td></td></tr>
<tr><td>Children (1 month to 11 years)</td><td>200micrograms to 500micrograms Neostigmine Metilsulfate repeated at suitable intervals throughout the day</td></tr>
<tr><td>Neonates (up to 1 month)</td><td>150 micrograms/kg Neostigmine Metilsulfate every 6 – 8 hours, to be given 30 minutes before feeds, then increased if necessary up to 300 micrograms/kg every 4 hours. Because of the self-limiting nature of the disease in neonates, the daily dosage should be reduced until the drug can be withdrawn.</td></tr>
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Antagonist to Non-depolarizing Neuromuscular Blockade

Reversal of Neuromuscular blockade with Neostigmine should not be attempted unless there is spontaneous recovery from paralysis.

Atropine and Neostigmine may be given simultaneously, but in patients with Bradycardia, the pulse rate should be increased to 80 per minute with Atropine before administering Neostigmine.

Antagonist to Non-depolarizing Neuromuscular Blockade	
Patient population	Recommended dose (via intravenous injection)
Adults	2.5mg Neostigmine Metilsulfate (maximum per dose 5mg), to be given over 1 minute, after or with glycopyrronium or atropine. Repeat if necessary.
Children (12 to 17 months)	50micrograms Neostigmine Metilsulfate per kg bodyweight (maximum per dose 2.5mg Neostigmine Metilsulfate) to be given over 1 minute after or with glycopyrronium or atropine, followed by a further dose of 25micrograms/kg Neostigmine Metilsulfate if required.
Children (1 month to 11 years)	50micrograms Neostigmine Metilsulfate per kg bodyweight (maximum per dose 2.5mg Neostigmine Metilsulfate) to be given over 1 minute after or with glycopyrronium or atropine, followed by a further dose of 25micrograms/kg Neostigmine Metilsulfate if required.
Neonates (up to 1 month)	50micrograms Neostigmine Metilsulfate per kg bodyweight to be given over 1 minute after or with glycopyrronium or atropine, followed by a further dose of 25micrograms/kg Neostigmine Metilsulfate if required.

Other Indications

Paralytic ileus and post-operative urinary retention	
Patient population	Recommended dose (via subcutaneous or intramuscular injection)
Adults	0.5mg – 2.5mg Neostigmine Metilsulfate.
Children	0.125mg – 1mg Neostigmine Metilsulfate.

Paroxysmal supraventricular tachycardia (via IV injection)

Treatment should be reserved for severe cases not responding to conventional treatment and under the close supervision of a specialist experienced with its use.

Use in special population groups

Pediatric population

A posology for use in the paediatric population is presented above by indication.

Use in the elderly

There are no specific dosage recommendations for Neostigmine Metilsulfate in the elderly (see section 4.4).

Method of Administration

Neostigmine Metilsulfate may be administered by IV, IM or SC injection. Please refer to the above text for the recommended route of administration according to indication.

Neostigmine Metilsulfate 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

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Neostigmine should not be administered to patients with mechanical obstruction of gastrointestinal or urinary tracts, peritonitis or doubtful bowel viability.

Neostigmine should not be used in conjunction with depolarising muscle relaxants such as suxamethonium as neuromuscular blockade may be potentiated.

4.4. Special warnings and precautions for use

Neostigmine should be used with extreme caution in patients with asthma as the parasympathomimetic action of neostigmine may cause bronchoconstriction.

Bradycardia, with the potential for progression to asystole, may occur in patients receiving neostigmine by intravenous injection unless atropine is given simultaneously. Extreme caution should be employed when treating patients with pre-existing bradycardia, cardiac arrhythmia or recent coronary occlusion.

Patients who are hyperreactive to neostigmine experience a severe cholinergic reaction to the drug. Atropine sulfate should always be available as an antagonist for the muscarinic effects of neostigmine.

Neostigmine should be used with caution in patients with epilepsy, vagotonia, hyperthyroidism, peptic ulceration or parkinsonism.

Administration of anticholinesterase agents to patients with intestinal anastomoses may produce rupture of the anastomosis or leakage of intestinal contents.

Elderly

Although there are no specific dosage requirements in the elderly, these patients may be more susceptible to dysrhythmias than younger patients.

Inhaledanaesthetics

Neostigmine Metilsulfate should not be given during cyclopropane or halothane anaesthesia; although it may be used after withdrawal of these agents.

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

Neuromuscular Blocking Agents

Neostigmine effectively antagonises the effect of non-depolarizing muscle relaxants (e.g., Tubocurarine,

Gallamine or Pancuronium) and this interaction is used to therapeutic advantage to reverse muscle relaxation after surgery. Neostigmine does not antagonise, and it may in fact prolong, the phase I block of depolarizing muscle relaxants such as Succinylcholine.

Other Drugs

Atropine antagonises the muscarinic effects of Neostigmine; the interaction is utilised to counteract the muscarinic symptoms of the Neostigmine toxicity.

Anticholinesterase agents are sometimes effective in reversing Neuromuscular Block induced by

Aminoglycoside Antibiotics. However, Aminoglycoside Antibiotics and other drugs that interfere with

Neuromuscular transmission should be used cautiously, if at all, in patients with Myasthenia Gravis and the dose of Neostigmine may have to be adjusted accordingly.

4.6. Fertility, pregnancy and lactation

The use of Neostigmine Metilsulfate 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 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 Neostigmine.

Only negligible amounts of Neostigmine Metilsulfate are excreted in breast milk. Nevertheless, attention should be paid to possible effects on the breast-feeding infant.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

Adverse effects of Neostigmine are chiefly those of exaggerated response to parasympathetic stimulation.

Tabulated summary of adverse reactions

Adverse reactions reported in the following table by MedDRA System Organ Class (SOC), Preferred Term and frequency. The following frequency categories are used:

Term	**Frequency of occurrence**
Very common	(≥1/10)
Common	(≥1/100 to <1/10)
Uncommon	(≥1/1 000 to <1/100)
Rare	(≥1/10 000 to <1/1 000)
Very rare	(<1/10 000)
Not known	(Cannot be estimated from the available data)

System Organ Class	**Frequency**	**Undesirable effects**
Immune System Disorders	Not Known	Hypersensitivity, angioedema, anaphylactic reaction
Nervous system disorders	Not Known	Cholinergic syndrome, especially at high doses. In patients with myasthenia gravis, cholinergic crisis may be difficult to distinguish from myasthenia crisis (see section 4.9).
Eye disorders	Not Known	Miosis, lacrimation increased
Cardiac disorders	Not Known	Bradycardia, decreased cardiac conduction, in severe cases possibly leading to heart block or cardiac arrest
Vascular disorders	Not Known	Hypotension
Respiratory, thoracic or mediastinal disorders	Not Known	Increased bronchial secretion, bronchospasm
Gastrointestinal disorders	Not Known	Nausea, vomiting, diarrhoea, abdominal cramps, salivary hypersecretion. Increased intestinal motility may result in involuntary defecation.
Skin and subcutaneous tissue disorders	Not Known	Hyperhidrosis
Musculoskeletal, connective	Not Known	Muscle spasms

tissue and bone disorders		
Renal and urinary disorders	Not Known	Urinary incontinence

Reporting of suspected adverse reactions

Health care professionals are asked to report any suspected adverse reactions via the https://pv.pharmacyboardkenya.org

4.9. Overdose

Symptoms

Neostigmine Metilsulfate overdosage may include Cholinergic Crisis, which is characterised by nausea, vomiting, diarrhoea, excessive salivation and sweating, increased bronchial secretions, miosis, bradycardia or tachycardia, cardio spasm, bronchospasm, incoordination, muscle cramps, fasciculation and paralysis.

Extremely high doses may produce CNS symptoms of agitation, fear or restlessness. Death may result from cardiac arrest or respiratory paralysis and pulmonary oedema. In patients with Myasthenia Gravis, in whom overdosage is most likely to occur, fasciculation and adverse parasympathomimetic effects may be mild or absent making cholinergic crisis difficult to distinguish from Myasthenia crisis.

Treatment

Maintenance of adequate respiration is of primary importance. Tracheostomy, Bronchial aspiration and postural drainage may be required; Respiration can be assisted mechanically or with oxygen, if necessary.

Neostigmine Metilsulfate should be discontinued immediately and 1mg – 4mg of Atropine Sulfate administered IV. Additional doses of Atropine may be given every 5minutes – 30minutes as needed to control muscarinic symptoms. Atropine overdosage should be avoided as tenacious secretions and bronchial plugs may result.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Anticholinesterase.

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 Metilsulfate, neostigmine is metabolised 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. Preclinical 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 citrate dihydrate

Citric acid anhydrous

Water for injections

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

Do not store above 30°C. Keep the ampoules in the outer carton to protect from light.

6.5. Nature and contents of container

Clear glass ampoules, glass type I, Ph. Eur.

Pack sizes: 5x 1ml and 10 x 1ml

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

For single use only. Discard any unused contents.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Tasa Pharma Ltd

Unit C1-C3, Kay complex,

Mombasa road, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER(S)

H2025/CTD11493/24867

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08.07.2025

10. DATE OF REVISION OF THE TEXT

08.07.2025