Neostigmine methylsulfate

500 mcg/mL Solution for Injection(I.M./I.V./S.C.)

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Anticholinesterase

Product Description:

Neostigmine methylsulfate injection is a clear colourless solution in water for injection filled in a 1mL amber glass bottle.

Formulation/Composition:

Each mL contains:
Neostigmine Methylsulfate, BP.....500 mcg

PHARMACODYNAMICS

Neostigmine is an anticholinesterase agent, and inhibits the hydrolysis of acetylcholine by competing with acetylcholine for binding to acetylcholinesterase at sites of cholinergic transmission. By reducing the breakdown of acetylcholine,neuromuscular transmission is facilitated. Neostigmine also has direct postsynaptic cholinomimetic effects which can be managed clinically by the co-administration of atropine or glycopyrrolate

PHARMACOKINETIC PROPERTIES:

After absorption or IV administration, 80% of a single neostigmine dose is excreted by the kidney in the unchanged (50%) and metabolized (30%) forms in 24 hours. The elimination half-life is approximately 51 to 91 minutes. Protein binding in human serum albumin is reported to range from 15 to 25%.

Distribution: Protein binding of neostigmine to human serum albumin ranges from 15 to 25%. The observed volume of distribution is between 0.12 and 1.4 L/kg following intravenous injection.

Elimination: Neostigmine is metabolized by microsomal enzymes in the liver and the observed elimination half-life reported is between 24 and 113 minutes.

Metabolism: Neostigmine is metabolized by microsomal enzymes in the liver.

Excretion: The observed elimination half-life reported is between 24 and 113 minutes following intravenous injection.

Specific Populations:

Pediatric Population: After intravenous administration as a 2-minute infusion (infants 2 to 10 months old: 100 mcg/kg; children 1 to 6 years old: 70 mcg/kg), the elimination half-life for infants and children were 39 ± 5 min and 48 ± 16 min (mean ± SD), respectively.

Clearance for infants and children were 13.6 ± 2.8 and 11.1 ± 2.7 mL/min/kg (mean ± SD), respectively.

Renal Impairment: Elimination half-life was prolonged in anephric patients compared to normal subjects; elimination half-life for normal, transplant and anephric patients were 79.8 ± 48.6, 104.7 ± 64 and 181 ± 54 min (mean ± SD), respectively.

Hepatic Impairment: The pharmacokinetics of neostigmine in patients with hepatic impairment has not been studied. Neostigmine is metabolized by microsomal enzymes in the liver and its concentration may increase in patients with impaired hepatic functions.

INDICATIONS:

Neostigmine Methylsulfate, a cholinesterase inhibitor, is indicated for reversal of the effects of nondepolarizing neuromuscular blocking agents (NMBA) after surgery

Myasthenia gravis, antagonist to non-depolarising neuromuscular blockade, paralytic ileus, post-op distension, urinary retention, paroxysmal supraventricular tachycardia.

DOSAGE

Intestinal atony, postoperative: Prophylaxis: 250 mcg as for intestinal atony.

Treatment: 500 mcg SC, IM (or possibly slow IV) repeated at intervals of 4 to 5 hours.

Urinary retention: Prophylaxis: 250 mcg as for intestinal atony.

Treatment: 500 mcg SC or IM and apply heat to the lower abdomen. If urination does not occur within one hour, the patient should be catheterized. After the patient has voided, continue the 0.5 mg injections at 3-hour intervals for at least 5 additional injections.

Myasthenia gravis: Occasionally parenteral therapy is needed in seriously ill patients and up to 1 mg IM every hour may be necessary in myasthenic crises. Curare antagonist (to neutralize the effect of curare in surgical anesthesia and shock therapy); 0.5 to 2 mg slow IV Atropine sulfate 0.6 to 1.2 mg IV should be given.

CONTRAINDICATION:

Neostigmine should be used with caution in patients with epilepsy, bronchial asthma, bradycardia, recent coronary occlusion, vagotonia, hyperthyroidism, cardiac arrhythmias or peptic ulcer.

Neostigmine should not be administered to patients with peritonitis, mechanical obstruction of the intestinal or urinary tracts or doubtful bowel viability. Patients with a known sensitivity to neostigmine should not be treated with the drug.

WARNINGS AND PRECAUTIONS:

Bradycardia: Atropine or glycopyrrolate should be administered prior to administration of neostigmine methylsulfate injection to lessen risk of bradycardia

Coexisting Conditions: patients with known cardiac disease, cardiac arrhythmias, or recent coronary artery occlusion may be particularly sensitive to the hemodynamic effects of neostigmine; their blood pressure and electrocardiogram should be continuously monitored with the initiation of neostigmine treatment and for a duration sufficient to assure hemodynamic stability.

Neuromuscular Dysfunction: Can occur if large doses of neostigmine methylsulfate are administered when there is minimal neuromuscular blockade; reduce the dose if recovery from neuromuscular blockade is nearly complete.

When large doses are given, simultaneous administration of atropine sulfate may be advisable. Because of the possibility of hypersensitivity in an occasional patient, atropine should always be at hand, together with antishock medications. Hypotension and bradycardia may occur if the effect of gallamine of curare is antagonized by neostigmine.

ADVERSE DRUG REACTIONS:

The untoward effects of neostigmine are most commonly related to overdosage and generally are of two varieties: muscarinic and nicotinic. Among the former group are nausea, vomiting, diarrhea, abdominal cramps, increased salivation, increased bronchial secretions, miosis and diaphoresis. Muscarinic untoward effects can usually be counteracted by atropine. Nicotinic adverse effects are chiefly muscle cramps, fasciculation and weakness, which can be difficult to distinguish from exacerbation of underlying myasthenia gravis.

Allergic: Allergic reactions and anaphylaxis.
Neurologic: Dizziness, convulsions, loss of consciousness, drowsiness, headache, dysarthria, miosis and visual changes.
Cardiovascular: Cardiac arrhythmias (including bradycardia, tachycardia, A V block and nodal rhythm) and nonspecific EKG changes have been reported, as well as cardiac arrest, syncope and hypotension.These have been predominantly noted following the use of the injectable form of Neostigmine Methylsulfate (neostigmine methylsulfate (neostigmine methylsulfate injection) injection)
Respiratory: Increased oral, pharyngeal and bronchial secretions, dyspnea, respiratory depression, respiratory arrest and bronchospasm.
Dermatologic: Rash and urticaria.
Gastrointestinal: Nausea, emesis, flatulence and increased peristalsis.
Genitourinary: Urinary frequency.
Musculoskeletal: Muscle cramps and spasms, arthralgia.
Miscellaneous: Diaphoresis, flushing and weakness.

DRUG INTEREACTIONS:

Neostigmine should not be used in conjunction with depolarizing muscle relaxants such as Suxamethonium. It should not be used during cyclopropane or halothane anesthesia, although it may be used after withdrawal of these agents. Prolonged bradycardia has occurred in patients receiving beta-adrenoceptor blocking agents following administration of neostigmine. The action of neostigmine may be antagonized by agents such as the aminoglycoside antibiotics, that possess non-depolarising blocking actions.

Neostigmine's action may also be antagonized by other agents that interfere with neuromuscular transmission including some anti-arrhythmic agents such as quinidine.

OVERDOSAGE AND TREATMENT:

Muscarinic symptoms (nausea, vomiting, diarrhea, sweating, increased with other drugs which may alter the activity of metabolizing enzymes or bronchial and salivary secretions, and bradycardia) may appear with transporters. Overdosage of Neostigmine methylsulfate (cholinergic crisis), but may be managed by the use of additional atropine or glycopyrrolate. The possibility of iatrogenic overdose can be lessened by carefully monitoring the muscle twitch response to peripheral nerve stimulation. Should overdosage occur, ventilation should be supported by artificial means until the adequacy of spontaneous respiration is assured, and cardiac function should be monitored.

PREGNANCY CATEGORY: C

INCOMPATIBILITIES: None known
SHELF LIFE: 24 months
STORAGE CONDITIONS: **Protect from light. Store below 30°C.**
AVAILABILITY: 500 mcg/mL Solution for injection
USP Type I amber glass bottle x 1 mL (Box of 10's, 20's,100's)

CAUTION: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Date of First Authorization: 6 March 2017
Date of Revision of Package Insert: 15 March 2023
Reg. No.: DRP-7064

ADR REPORTING
For suspected adverse drug reaction, please report to FDA: www.fda.gov.ph and BIOCARE: pv@biocarelifesciences.com.

Seek medical attention immediately at the first sign of any adverse drug reaction.

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