For Immediate Release

May 16, 2018

Harsher Singh
Vice President and Chief Commercial Officer
American Regent
Ph: 631-924-4000
corpcommunications@americanregent.com

American Regent Announces the Availability of Neostigmine Methylsulfate Injection, USP; AP Rated and Therapeutically Equivalent to Bloxiverz®[1]*

Shirley, NY - American Regent today announced the introduction of Neostigmine Methylsulfate Injection, USP. **Product is available for immediate shipment and customers can order through their wholesaler/distributor or by contacting our Customer Support Group at 1-800-645-1706.**

Neostigmine Methylsulfate Injection, USP is a cholinesterase inhibitor indicated for the reversal of the effects of nondepolarizing neuromuscular blocking agents after surgery.

Neostigmine Methylsulfate Injection, USP is supplied as follows:

PACK NDC#	Strength	Supplied As	Shelf Pack
0517-1133-05	5 mg/10 mL (0.5 mg/mL)	10 mL MDV	5
0517-1134-05	10 mg/10 mL (1 mg/mL)	10 mL MDV	5

*Bloxiverz® is a trademark of Avadel Legacy Pharmaceuticals LLC.

See the following Important Safety Information in addition to the Full Prescribing Information.

Reference: 1. US Food and Drug Administration. Neostigmine Methylsulfate Injection, USP ANDA 209182 Approval Letter. May 2018.

Neostigmine Methylsulfate Injection, USP

For Intravenous Use

INDICATIONS AND USAGE

Neostigmine methylsulfate injection is a cholinesterase inhibitor indicated for the reversal of the effects of nondepolarizing neuromuscular blocking agents after surgery.

IMPORTANT SAFETY INFORMATION

Important Dosage Information: Doses of neostigmine methylsulfate injection should be individualized, and a peripheral nerve stimulator should be used to determine the time of initiation of neostigmine methylsulfate injection and should be used to determine the need for additional doses.

CONTRAINDICATIONS

Neostigmine methylsulfate injection is contraindicated in patients with known hypersensitivity to neostigmine methylsulfate and in patients with peritonitis or mechanical obstruction of the intestinal or urinary tract.

WARNINGS AND PRECAUTIONS

Bradycardia: Neostigmine has been associated with bradycardia.

Serious Adverse Reactions in Patients with Certain Coexisting Conditions: Neostigmine methylsulfate injection should be used with caution in patients with: coronary artery disease, cardiac arrhythmias, recent acute coronary syndrome or myasthenia gravis.

Hypersensitivity: Because of the possibility of hypersensitivity, atropine and medications to treat anaphylaxis should be readily available.

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

Cholinergic Crisis: It is important to differentiate between myasthenic crisis and cholinergic crisis caused by overdosage of neostigmine methylsulfate injection.

ADVERSE REACTIONS

Clinical Trials Experience: The following table lists the adverse reactions that occurred with an overall frequency of 1% or greater.

System Organ Class	Adverse Reaction
Cardiovascular Disorders	bradycardia, hypotension, tachycardia/heart rate increase
Gastrointestinal Disorders	dry mouth, nausea, post-procedural nausea, vomiting
General Disorders and Administration Site Conditions	incision site complication, pharyngolaryngeal pain, procedural complication, procedural pain
Nervous System Disorders	dizziness, headache, postoperative shivering, prolonged neuromuscular blockade
Psychiatric Disorders	insomnia
Respiratory, Thoracic and Mediastinal Disorders	dyspnea, oxygen desaturation <90%
Skin and Subcutaneous Tissue Disorders	pruritus

Post Marketing Experience: The following adverse reactions have been identified during parenteral use of neostigmine methylsulfate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

System Organ Class	Adverse Reaction
Allergic Disorders	allergic reactions, anaphylaxis
Nervous System Disorders	convulsions, drowsiness, dysarthria, fasciculation, loss of consciousness, miosis, visual changes
Cardiovascular Disorders	cardiac arrest, cardiac arrhythmias (A-V block, nodal rhythm), hypotension, nonspecific EKG changes, syncope
Respiratory, Thoracic and Mediastinal Disorders	bronchospasm; increased oral, pharyngeal and bronchial secretions; respiratory arrest; respiratory depression
Skin and Sub-cutaneous Tissue Disorders	rash, urticaria
Gastrointestinal Disorders	bowel cramps, diarrhea, flatulence, increased peristalsis
Renal and Urinary Disorders	urinary frequency
Musculoskeletal and Connective Tissue Disorders	arthralgia, muscle cramps, spasms, weakness
Miscellaneous	diaphoresis, flushing

USE IN SPECIFIC POPULATIONS

Pregnancy: There are no adequate or well-controlled studies of neostigmine methylsulfate injection in pregnant women.

Neostigmine methylsulfate injection should be given to a pregnant woman only if clearly needed.

Labor and Delivery: The effect of neostigmine methylsulfate injection on the mother and fetus with regard to labor and delivery is not known. Cholinesterase inhibitor drugs may induce premature labor when given intravenously to pregnant women near term.

Nursing Mothers: It is not known whether neostigmine methylsulfate is excreted in human milk. Caution should be exercised when neostigmine methylsulfate injection is administered to a nursing woman.

Pediatric Use: Recovery of neuromuscular activity occurs more rapidly with smaller doses of cholinesterase inhibitors in infants and children than in adults. However, infants and small children may be at greater risk of complications from incomplete reversal of neuromuscular blockade due to decreased respiratory reserve. The risks associated with incomplete reversal outweigh any risk from giving higher doses of neostigmine methylsulfate injection.

Geriatric Use: Neostigmine methylsulfate injection should be used with caution and monitored for a longer period in elderly patients.

Renal Impairment: Elimination half-life of neostigmine methylsulfate was prolonged in anephric patients compared to normal subjects.

Hepatic Impairment: The pharmacokinetics of neostigmine methylsulfate in patients with hepatic impairment have not been studied.

OVERDOSAGE

Muscarinic symptoms may appear with overdosage of neostigmine methylsulfate injection (cholinergic crisis), but may be managed by the use of additional atropine or glycopyrrolate. Ventilation should be supported by artificial means until the adequacy of spontaneous respiration is assured, and cardiac function should be monitored.

Cholinergic crisis, may result in death. Myasthenic crisis, may be difficult to distinguish from cholinergic crisis on a symptomatic basis. The presence of myasthenic crisis requires more intensive anticholinesterase therapy; cholinergic crisis calls for the prompt withdrawal of all drugs of this type.

You are encouraged to report Adverse Drug Events (ADEs) to American Regent:
Email: pv@luitpold.com; Fax: 1-610-650-0170;
Phone: 1-800-734-9236

ADEs may also be reported to the FDA at 1-800-FDA-1088 or to
www.fda.gov/Medwatch

Drug Information:
1-888-354-4855
(9:00 am - 5:00 pm Eastern Time, Monday - Friday)

1-877-845-6371
(Available outside of normal business hours)

About American Regent

American Regent is a leader in the development, manufacturing and sales of generic and branded IV products. With a history of 50 years in generic specialty injectables, American Regent has sales approaching one billion dollars.

American Regent strives for continuous improvement to bring to market high quality innovative medications to meet unmet medical needs, and produces high quality accessible generic medications covering a wide array of therapeutic areas. American Regent is a member of the Daiichi Sankyo Group; and is headquartered in Shirley, NY.

For more information, please visit www.americanregent.com.

About Daiichi Sankyo

Daiichi Sankyo is a global pharmaceutical company with corporate origins in Japan. We provide innovative products and services in more than 20 countries around the world. With more than 100 years of scientific expertise, our company draws upon a rich legacy of innovation and a robust pipeline of promising new medicines to help patients.

Through the outstanding knowledge and commitment of our 15,000 employees worldwide, we create innovative new and generic medicines, and new methods of drug discovery and delivery. We share a passion for innovation, as well as compassion for the patients around the world who are in need of our medicines.

For more information, please visit: www.daiichisankyo.com. Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit: www.dsi.com.

PP-NM-US-0006 4/2018