Merck Announces FDA Acceptance of Resubmission of New Drug Application for Sugammadex Sodium Injection

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WHITEHOUSE STATION, N.J.--(BUSINESS WIRE)--Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the resubmission of the New Drug Application (NDA) for sugammadex sodium injection has been accepted for review by the U.S. Food and Drug Administration (FDA). Merck expects the FDA’s review to be completed in the first half of 2013.

Sugammadex sodium injection is the company’s investigational agent for the reversal of neuromuscular blockade (NMB) induced by rocuronium or vecuronium (neuromuscular blocking agents). NMB is used in anesthesiology to induce muscle relaxation during surgery. Sugammadex is designed to work by inactivating rocuronium or vecuronium molecules directly by encapsulation. If approved, it would be the first in a new class of medicines in the U.S. known as selective relaxant binding agents to be used in the surgical setting.

In 2008, the FDA did not approve the original NDA for sugammadex sodium injection, requesting additional data related to hypersensitivity (allergic) reactions and coagulation (bleeding) events. Merck submitted this requested data within the NDA resubmission, which the FDA has now deemed complete for review.

“We are pleased the FDA has accepted our resubmission of sugammadex sodium injection for review, as this was a key milestone in our effort to bring this medicine to the U.S.,” said Darryle D. Schoepp, Ph.D., senior vice president and head of Neuroscience and Ophthalmology, Merck Research Laboratories. “Sugammadex sodium injection is an example of Merck’s ongoing commitment to developing new medicines for patients in hospital-based settings.”

Indication for ZEMURON® (rocuronium bromide) Injection

ZEMURON Injection, from Merck, is indicated for inpatients and outpatients as an adjunct to general anesthesia to facilitate both rapid sequence and routine tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation.

Important safety information about ZEMURON

ZEMURON is contraindicated in patients known to have hypersensitivity (e.g., anaphylaxis) to rocuronium bromide or other neuromuscular blocking agents.

ZEMURON should be administered in carefully adjusted dosages by or under the supervision of experienced clinicians who are familiar with the drug’s actions and the possible complications of its use. The drug should not be administered unless facilities for intubation, mechanical ventilation, oxygen therapy, and an antagonist are immediately available. It is recommended that clinicians administering neuromuscular blocking agents, such as ZEMURON, employ a peripheral nerve stimulator to monitor drug effect, need for additional doses, adequacy of spontaneous recovery or antagonism, and to decrease the complications of overdosage if additional doses are administered.

Severe anaphylactic reactions to neuromuscular blocking agents, including ZEMURON, have been reported. These reactions have, in some cases (including cases with ZEMURON), been life threatening and fatal. Due to the potential severity of these reactions, the necessary precautions, such as the immediate availability of appropriate emergency treatment, should be taken. Precautions should also be taken in those patients who have had previous anaphylactic reactions to other neuromuscular blocking agents, since cross-reactivity between neuromuscular blocking agents, both depolarizing and non-depolarizing, has been reported.

ZEMURON has no known effect on consciousness, pain threshold, or cerebration. Therefore, its administration must be accompanied by adequate anesthesia or sedation.

In order to prevent complications resulting from residual paralysis, it is recommended to extubate only after the patient has recovered sufficiently from neuromuscular block. Other factors, which could cause residual paralysis after extubation in the post-operative phase, (such as drug interactions or patient condition) should also be considered. If not used as part of standard clinical practice, the use of a reversal agent should be considered, especially in those cases where residual paralysis is more likely to occur.
ZEMURON has not been studied for long-term use in the intensive care unit (ICU). As with other non-depolarizing neuromuscular blocking drugs, apparent tolerance to ZEMURON may develop during chronic administration in the ICU. While the mechanism for development of this resistance is not known, receptor up-regulation may be a contributing factor. It is strongly recommended that neuromuscular transmission be monitored continuously during administration and recovery with the help of a nerve stimulator. Additional doses of ZEMURON (rocuronium bromide) or any other neuromuscular blocking agent should not be given until there is a definite response (one twitch of the train-of-four) to nerve stimulation. Prolonged paralysis and/or skeletal muscle weakness may be noted during initial attempts to wean from the ventilator patients who have chronically received neuromuscular blocking drugs in the ICU.

Myopathy after long-term administration of other non-depolarizing neuromuscular blocking agents in the ICU alone or in combination with corticosteroid therapy has been reported. Therefore, for patients receiving both neuromuscular blocking agents and corticosteroids, the period of use of the neuromuscular blocking agent should be limited as much as possible and only used in the setting where in the opinion of the prescribing agent, the specific advantages outweigh the risk.

ZEMURON has not been studied in malignant hyperthermia-susceptible patients. Because ZEMURON is always used with other agents, and the occurrence of malignant hyperthermia during anesthesia is possible even in the absence of known triggering agents, clinicians should be familiar with early signs, confirmatory diagnosis and treatment of malignant hyperthermia prior to the start of any anesthetic.

Conditions associated with an increased circulatory delayed time, e.g., cardiovascular disease or advanced age, may be associated with a delay in onset time.

The overall analysis of ECG data in pediatric patients indicates that the concomitant use of ZEMURON with general anesthetic agents can prolong the QTc interval.

Non-depolarizing neuromuscular blocking agents have been found to exhibit profound neuromuscular blocking effects in cachetic or debilitated patients, patients with neuromuscular diseases and patients with carcinomatosis. Certain inhalation anesthetics, particularly enflurane and isoflurane, antibiotics, magnesium salts, lithium, local anesthetics, procainamide and quinidine, have been shown to increase the duration of neuromuscular block and decrease infusion requirements of neuromuscular blocking agents. In these or other patients in whom potentiation of neuromuscular block or difficulty with reversal may be anticipated, a decrease from the recommended initial dose of ZEMURON should be considered.

Resistance to non-depolarizing agents, consistent with up-regulation of skeletal muscle acetylcholine receptors, is associated with burns, disuse atrophy, denervation, and direct muscle trauma. Receptor up-regulation may also contribute to the resistance to non-depolarizing muscle relaxants, which sometimes develops in patients with cerebral palsy, patients chronically receiving anticonvulsant agents, such as carbamazepine or phenytoin, or with chronic exposure to non-depolarizing agents. When ZEMURON (rocuronium bromide) is administered to these patients, shorter durations of neuromuscular block may occur, and infusion rates may be higher due to the development of resistance to non-depolarizing muscle relaxants.

Severe acid-base and/or electrolyte abnormalities may potentiate or cause resistance to the neuromuscular blocking action of ZEMURON. No data are available in such patients, and no dosing recommendations can be made.

ZEMURON, which has an acid pH, should not be mixed with alkaline solutions (e.g. barbiturate solutions) in the same syringe or administered simultaneously during intravenous infusion through the same needle.

ZEMURON may be associated with increased pulmonary vascular resistance, so caution is appropriate in patients with pulmonary hypertension or valvular heart disease.

In patients with myasthenia gravis or myasthenic (Eaton-Lambert) syndrome, small doses of non-depolarizing neuromuscular blocking agents may have profound effects. In such patients, a peripheral nerve stimulator and use of a small test dose may be of value in monitoring the response to administration of muscle relaxants.

If extravasation occurs, it may be associated with signs or symptoms of local irritation. The injection or infusion should be terminated immediately and restarted in another vein.

In clinical trials, the most common adverse reactions (2 percent) are transient hypotension and hypertension.

There are no controlled studies documenting the use of ZEMURON before or after other non-depolarizing muscle relaxants. Interactions have been observed when other non-depolarizing muscle relaxants have been administered in succession.

The use of ZEMURON before succinylcholine, for the purpose of attenuating some of the side effects of succinylcholine, has not been studied.


**Merck's Commitment to Hospital-Based Medicine**

Merck is committed to scientific excellence, and the discovery and development of innovative treatments for patient care in hospitals. We strive to develop new solutions to help our hospital-based customers deliver quality care to their patients.

**About Merck**

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on Twitter, Facebook and YouTube.

**Forward-Looking Statement**
This news release includes “forward-looking statements” within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of Merck’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost-containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; Merck’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of Merck’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck’s 2011 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).

Please see Prescribing Information for ZEMURON (rocuronium bromide) at http://www.merck.com/product/usa/pi_circulars/z/zemuron/zemuron_pi.pdf.

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