NDA 022225/S-007/S-009

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
126 E. Lincoln Avenue, PO Box 2000
RY34-B188
Rahway, NJ 07065

Attention: Dori Glassner
Director, Global Regulatory Affairs

Dear Ms. Glassner:

Please refer to your supplemental new drug applications (sNDAs) dated and received, March 24, 2020, and January 13, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bridion (sugammadex) Injection.

We also refer to our letter dated October 5, 2020, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Bridion, pertaining to the risk of Kounis Syndrome (allergic coronary artery vasospasm). However, we also refer to your rebuttal statement dated and received November 4, 2020, in which you detailed the reasons why you believed such a change was not warranted. Finally, we refer to our letter dated November 19, 2020, extending the discussion period to February 2, 2021.

The Prior Approval supplemental new drug application (S-007) proposes changes to the package insert based on data from study entitled, *A Phase 4 Randomized, Active-Comparator Controlled Clinical Trial to Study the Safety of Sugammadex (MK-8616) for the Reversal of Neuromuscular Blockade Induced by Either Rocuronium Bromide or Vecuronium Bromide in American Society of Anesthesiologists (ASA) Class 3 or 4 Subjects*, to fulfill the requirements of PMR 3003-3.

The Changes Being Effected (CBE) Supplement, S-009, provides for Safety Labeling Changes required under Section 505(o)(4) of the FDCA, consistent with labeling negotiations through discussions following our October 5, 2020, letter. The October 5, 2020, letter required additions of new safety information to the Warnings and Precaution and Adverse Reactions sections of labeling; the final labeling includes an addition only to 6.2, Post-Marketing Experience, and omits the term “Kounis Syndrome”.

APPROVAL & LABELING

We have completed our review of Supplement S-007, as amended, and Supplement S-009. These are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information) , with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated March 24, 2020, containing the final report for the following postmarketing requirement listed in the December 15, 2015, approval letter.

3003-3: Conduct a postmarketing clinical trial comparing sugammadex to placebo and/or drugs approved for the management of the reversal of the effects of neuromuscular blockade induced by rocuronium or vecuronium in a population of American Society of Anesthesiologists Class 3 and 4 patients. The goal of the trial is characterization of the risks of bradycardia and other cardiac arrhythmias after sugammadex administration in this

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

population that may have more severe outcomes related to cardiac arrhythmias experienced during reversal of neuromuscular blockade. Prespecify the case definition of bradycardia, tachycardia, and the other cardiac arrhythmias of interest.

We have reviewed your submission and conclude that the above commitment was fulfilled.

We remind you that there are postmarketing requirements listed in the December 15, 2015, postapproval postmarketing requirement letter that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, call Allison Meyer, Senior Regulatory Health Project Manager, at (301) 796-1258.

Sincerely,

{See appended electronic signature page}

Rigoberto Roca, MD
Director
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
  - Prescribing Information

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

RIGOBERTO A ROCA
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