NDA 208289/S-005

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Avadel Legacy Pharmaceuticals, LLC
c/o The Weinberg Group, Inc.
1129 Twentieth St. NW, Suite 600
Washington, DC 20036

Attention: Marla E Scarola, MS
Vice President, Regulatory Program Management

Dear Ms. Scarola:

Please refer to your supplemental new drug application (sNDA) dated and received October 26, 2018, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for AKOVAZ (ephedrine sulfate) injection.

This Prior Approval supplemental new drug application provides for changes to the USE IN SPECIAL POPULATIONS and NONCLINCAL TOXICOLOGY sections of the package insert as a result of your completed nonclinical studies noted below.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is 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]

[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.

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 REQUIREMENTS

We have received your submissions dated November 30, 2017, March 28, and June 26, 2018, and July 31, 2019, containing the final reports for the following postmarketing requirements listed in the April 29, 2016, approval letter.

3062-1	Conduct a juvenile toxicity study in rats to support treatment of children and adolescents with AKOVAZ (ephedrine sulfate) injection by IV administration.
3062-3	Conduct a fertility and early embryonic development toxicology study in the rat model for ephedrine sulfate.
3062-4	Conduct an embryo-fetal developmental toxicology study using the rat model for ephedrine sulfate.
3062-5	Conduct an embryo-fetal developmental toxicology study using the rabbit model for ephedrine sulfate.
3062-6	Conduct a pre- and post-natal developmental toxicology study in the rat model for ephedrine sulfate.

We have reviewed your submissions and conclude that the above requirements were fulfilled. The labeling being approved incorporates information obtained in the PMR studies.

We remind you that there is a postmarketing requirement listed in the April 29, 2016, approval letter that is still open.

REPORTING REQUIREMENTS

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

If you have any questions, call Kimberly Compton, RPh, RAC, Senior Regulatory Project Manager, at (301) 796-1191.

Sincerely,

{See appended electronic signature page}

Rigoberto Roca, MD
Director (Acting)
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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