DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 208289/S-002

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Flamel Ireland Limited
c/o The Weinberg Group, Inc.
1129 Twentieth St. NW, Suite 600
Washington, DC 20036

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

Dear Ms. Scarola:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 8, 2017, 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 proposes labeling changes to Section 13 NONCLINCAL TOXICOLOGY of the package insert based on the results of the postmarketing requirement study titled *In Vivo Mammalian Erythrocyte Micronucleus Assay in Rats*, regarding the genotoxicity of the product.

APPROVAL & LABELING

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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 February 8, 2017, containing the final report for the postmarketing requirement listed in our April 29, 2016, NDA Approval Letter:

3062-7 Conduct an in vivo micronucleus genotoxicity assay with ephedrine sulfate.

We have reviewed your submission and conclude that the above requirement has been fulfilled.

We remind you that there are postmarketing requirements listed in our April 29, 2016, letter that are 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, Senior Regulatory Project Manager, at (301) 796-1191.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, MD
Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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 on behalf of SHARON H HERTZ
08/10/2018