DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021260/S-017

SUPPLEMENT APPROVAL

King Pharmaceuticals, Inc.
c/o: Pfizer Inc.
235 East 42nd Street, 219-9-24
New York, NY 10017

Attention: Catherine Maher, Ph.D.
Senior Director, Worldwide Safety and Regulatory

Dear Dr. Maher:

Please refer to your Supplemental New Drug Application (sNDA) dated October 8, 2012, received October 9, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for AVINZA (morphine sulfate extended-release) Capsules.

We acknowledge receipt of your amendments dated December 5, 2012, and March 28 and April 17, 2013.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the addition of banners/flags to the 90 and 120 mg strength carton and container labels containing the language, "For use in opioid-tolerant patients only," and changes to the package insert that include movement of text from section 12.1 to section 12.2, as requested by the Agency, typographical error corrections, and addition of the following text to the **CLINICAL PHARMACOLOGY**: **Pharmacodynamics** section:

> Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to hormonal changes that may manifest as symptoms of hypogonadism.

We have completed our review of this supplemental application, as amended, and 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 package insert, Medication

Guide), 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 includes 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).

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your October 8, 2012, submission containing final printed carton and container labels.

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 Lisa E. Basham, Senior Regulatory Health Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director,
Division of Anesthesia, Analgesia,
and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BOB A RAPPAPORT
05/06/2013