



NDA 21945/S-005

SUPPLEMENT APPROVAL

KV Pharmaceuticals, Inc.
Attention: Mary Beth Placht
Regulatory Affairs Manager
16640 Chesterfield Grove Road, Suite 200
Chesterfield, MO 63005

Dear Ms. Placht:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 11, 2013, submitted under section 505(b) (2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Makena (hydroxyprogesterone caproate injection) 250ml/mg.

We acknowledge receipt of your amendments dated August 9, September 5 and 6, 2013.

This "Prior Approval" supplemental new drug application provides for:

- 1) Revisions to the Drug Interactions and Clinical Pharmacology sections of labeling to describe the results of an *in vitro* study in human hepatocytes to determine the potential of hydroxyprogesterone caproate to induce or alter the metabolic activities of CYP1A2, 2A6 and 2B6 and
- (2) Addition of Section 6.2, Postmarketing Experience, in labeling to include adverse outcomes related to pregnancy, puerperium, and perinatal conditions and reproductive and breast disorders.

During the review of the supplement, agreement was reached that the existing Limitation of Use statement "Makena is not intended for use in women with multiple gestations or other risk factors for preterm birth" in Highlights and Indications and Use of labeling be bolded to increase its prominence.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. 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 package insert) with the addition of any labeling changes in pending “Changes Being Effectuated” (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).

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 Charlene Williamson, Regulatory Project Manager, at (301) 796-1025.

Sincerely,

{See appended electronic signature page}

Christine P. Nguyen, M.D.
Deputy Director for Safety
Division of Bone, Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

CHRISTINE P NGUYEN
09/16/2013