



NDA 022014/S-006

SUPPLEMENT APPROVAL

KV Pharmaceutical Company
Attention: Michael Jozwiakowski, Ph.D.
Vice President, Research and Development
16640 Chesterfield Grove Road, Suite 200
Chesterfield, MO 63005

Dear Dr. Jozwiakowski:

Please refer to your Supplemental New Drug Application (sNDA) dated March 20, 2009, received March 24, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Evamist[®] (estradiol transdermal spray).

We acknowledge receipt of your amendments dated December 16, 2011, September 7, 2012, July 30 and August 9, 2013, and January 30, 2014.

APPROVAL & LABELING

We have completed our review of this “Prior Approval” supplemental new drug application, as amended. Effective on the date of this letter, the following are included as approved in the attached, agreed-upon labeling text:

1. Contraindications:
 - Known anaphylactic reaction or angioedema
 - Known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders
2. Warnings and Precautions:
Subsection 5.16 Hereditary Angioedema
3. Adverse Reactions, Subsection 6.2 Postmarketing Experience
Skin: Nipple and areola discoloration, usually on the same side of the body as the inner forearm on which Evamist is applied, rash, pruritus, alopecia, urticaria, dry skin, skin discoloration, chloasma

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, text for the

patient package insert), 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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

PROMOTIONAL MATERIALS

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Kim Shiley, R.N., B.S.N., Regulatory Project Manager, at (301) 796-2117.

Sincerely,

{See appended electronic signature page}

Audrey Gassman, M.D.
Deputy Director
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/

AUDREY L GASSMAN
03/11/2014