



NDA 021629/S-028

SUPPLEMENT APPROVAL

sanofi-aventis U.S. LLC
Attention: Kristina Civile
Sr. Manager, U.S. Regulatory Affairs Marketed Products
55 Corporate Drive, Mailstop: 55c-205A
Bridgewater, New Jersey 08807

Dear Ms. Civile:

Please refer to your Supplemental New Drug Application (sNDA) dated and received June 5, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Apidra (insulin glulisine [rDNA origin]) injection.

We acknowledge receipt of your amendment dated June 12, 2013.

This "Changes Being Effected" supplemental new drug application proposes to revise the Dosage and Administration (2.3), Warnings and Precautions (5.7), How Supplied/Storage and Handling and Patient Counseling Information (17.2) sections of the package insert, and to the 10 ml vial patient instructions for use to add further information pertaining to subcutaneous insulin infusion pumps. The revision of the Warnings and Precautions and the Patient Counseling Information sections include that, in addition to hyperglycemia and ketosis, insulin pump or infusion set handling errors or insulin degradation can rapidly lead to diabetic ketoacidosis.

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 the package insert, patient package insert, 3 mL prefilled pen patient instructions for use, 3 mL cartridge patient instructions for use, and and 10 mL vial patient instructions for use), 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).

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 Richard Whitehead, Regulatory Project Manager, at (301) 796-4945.

Sincerely,

{See appended electronic signature page}

Jean-Marc Guettier, M.D.
Director (Acting)
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling:

Package Insert

Patient Package Insert (version approved with S-008, on February 24, 2009)

3 mL Prefilled Pen Patient Instructions for Use (version approved with S-008)

3 mL Cartridge System Patient Instructions for Use (version approved with S-008)

10 mL vial Patient Instructions for Use

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

/s/

JEAN-MARC P GUETTIER
09/06/2013