



NDA 020164 S-100

## SUPPLEMENT APPROVAL

Sanofi-aventis U.S., LLC  
Attention: Joanne Robinett  
Sr. Director, U.S. Regulatory Affairs Marketed Products  
55 Corporate Drive, Mailstop: 55C-205A  
Bridgewater, NJ 08807

Dear Ms. Robinett:

Please refer to your Supplemental New Drug Application (sNDA) dated February 21, 2013, received February 21, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lovenox<sup>®</sup> (enoxaparin sodium) injection.

We acknowledge receipt of your amendments dated March 14 and May 10, 2013.

This "Changes Being Effected" supplemental new drug application proposes a revision of the Adverse Reactions section, subsection Post-marketing Experience by adding the following: headache, hemorrhagic anemia, eosinophilia, alopecia, hepatocellular and cholestatic liver injury, and osteoporosis following long-term therapy. It also adds the term "shock" to the examples of systemic allergic reactions.

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 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).

### **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 Janet Higgins, Regulatory Health Project Manager, at (240) 402-0330.

Sincerely,

*{See appended electronic signature page}*

Robert C. Kane, M.D.  
Deputy Division Director for Safety  
Division of Hematology Products  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ROBERT C KANE  
06/05/2013