DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 11287/S-023

SUPPLEMENT APPROVAL

sanofi-aventis U.S. LLC
Attention: Jo Beth Crimmins
55 Corporate Drive
Bridgewater, NJ 08807

Dear Ms. Crimmins:

Please refer to your supplemental new drug application dated June 17, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Kayexalate (sodium polystyrene sulfonate, USP) Powder.

We acknowledge receipt of your amendment dated December 1, 2010.

The December 1, 2010, submission constituted a complete response to our July 23, 2010, action letter.

This supplemental new drug application provides for the following labeling revisions to the **WARNINGS**, **PRECAUTIONS** and **ADVERSE REACTIONS** sections of the package insert.

1. In the **WARNINGS**, **Colonic Necrosis** paragraph, the word "Colonic" was replaced with "Intestinal" (two places). Also, the phrase, "which may be fatal" was added to describe the cases. The first part of this now reads, "**Intestinal Necrosis:** Cases of intestinal necrosis, which may be fatal, and other serious gastrointestinal adverse events (bleeding, ischemic colitis, perforation) have been reported in association with Kayexalate use.

2. In the **WARNINGS**, **Colonic Necrosis**, the following bullets were added:

    - Do not use in patients who do not have normal bowel function. This includes postoperative patients who have not had a bowel movement post surgery.
    - Do not use in patients who are at risk for developing constipation or impaction (including those with history of impaction, chronic constipation, inflammatory bowel disease, ischemic colitis, vascular intestinal atherosclerosis, previous bowel resection, or bowel obstruction).
    - Discontinue use in patients who develop constipation. Do not administer repeated doses in patients who have not passed a bowel movement.

3. Under **PRECAUTIONS, Sorbitol**, the word "Colonic" was replaced with "Intestinal." Also, the phrase, "which may be fatal" was added to describe the cases. The first part of

this section now reads, "**Sorbitol:** Concomitant use of Sorbitol with Kayexalate has been implicated in cases of colonic intestinal necrosis, which may be fatal."

4. In the second paragraph under **PRECAUTIONS, Pediatric Use**, the word "Colonic" was replaced with "Intestinal."

5. Under **PRECAUTIONS, Drug Interactions**, an outdated reference to **ADVERSE REACTIONS** was removed.

6. Under the 1st paragraph of the **ADVERSE REACTIONS** section, the word "hypomagnesemia" was added after the words "hypokalemia, hypocalcemia."

7. In the **ADVERSE REACTIONS** section, the word "colonic" was replaced with the word "intestinal" in the seventh sentence of the first paragraph.

8. In the **ADVERSE REACTIONS** section, the third bullet, the phrase, "Ischemic colitis" was added in front of the words, "gastrointestinal tract."

9. The last sentence under **ADVERSE REACTIONS**, just above **Drug Interactions**, was deleted. It read: "Magnesium-containing laxatives or sorbitol should not be used (See **PRECAUTIONS, Drug Interaction**)", and the sentence before it (In the event of clinically significant constipation...) now ends with a reference to **WARNINGS, Intestinal Necrosis**.

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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling text for the package insert and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements and any 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 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.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (*i.e.*, a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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, please call:

Russell Fortney, R.Ph.
Regulatory Project Manager
(301) 796-1068

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Agreed-upon labeling text)

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

/s/

MARY R SOUTHWORTH
01/03/2011