DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 50705/S-011

SUPPLEMENT APPROVAL

sanofi-aventis U.S. LLC., A SANOFI COMPANY
Attention: John Cook
Director, U.S. Regulatory Affairs Marketed Products
55 Corporate Drive
Bridgewater, NJ 08807

Dear Mr. Cook:

Please refer to your Supplemental New Drug Application (sNDA) dated October 24, 2016, received October 24, 2016, and your amendment dated April 14, 2017, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for RIFATER (rifampin, isoniazid, and pyrazinamide USP) Tablets.

This "Changes Being Effected" supplemental new drug application provides for revisions to the **WARNINGS**, **PRECAUTIONS**, and **ADVERSE REACTIONS** sections of the package insert as follows:

WARNINGS

(1) Revised to include information on Drug Reaction with Eosinophilia and Systemic Symptoms syndrome (DRESS) and to update signs and symptoms of drug-induced hypersensitivity reactions.

(2) **Isoniazid** subsection has been revised to include Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) and provides information on monitoring for skin reactions.

PRECAUTIONS

The **Information for Patients** subsection has been revised to include more descriptive information for patients related to hypersensitivity reactions and rash.

ADVERSE REACTIONS

Adverse Reactions Reported for Individual Components subsections**, Rifampin and Isoniazid Hypersensitivity reaction** subsections were updated accordingly with the safety information about DRESS and TEN and for **Pyrazinamide,** the **Other** subsection was revised to include DRESS.

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), 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 include 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 Mr. Gregory DiBernardo, Regulatory Project Manager, at (301) 796-4063.

Sincerely,

{See appended electronic signature page}

Joseph G. Toerner, M.D., M.P.H.
Deputy Director for Safety
Division of Anti-Infective Products
Office of Antimicrobial Products
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/

JOSEPH G TOERNER
04/24/2017