



NDA 204671/S-001

SUPPLEMENT APPROVAL

Gilead Sciences, Inc.
Attention: Nicole Inocencio
Senior Manager, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Inocencio:

Please refer to your Supplemental New Drug Application (sNDA) dated May 15, 2014, received May 15, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sovaldi[®] (sofosbuvir) tablet, 400 mg.

We acknowledge receipt of your amendments dated August 6, 2014, October 20, 2014, October 27, 2014, and October 30, 2014.

This Prior Approval supplemental new drug application proposes the following changes:

1. To remove the hormonal contraceptive information from the WARNING AND PRECAUTIONS, *Pregnancy: Use with Ribavirin or Peginterferon Alfa/Ribavirin*, USE IN SPECIFIC POPULATIONS, *Pregnancy*, and PATIENT COUNSELING INFORMATION sections of labeling.
2. To update DRUG INTERACTIONS, *Drugs without Clinically Significant Interactions* and CLINICAL PHARMACOLOGY, *Pharmacokinetics*, Table 7, subsections of labeling with information regarding coadministration of SOVALDI with hormonal contraceptives.
3. To update CLINICAL PHARMACOLOGY, *Pharmacokinetics* subsection of labeling with data on enriched population PK analysis to define GS-331007 and SOF exposure parameters in patients with HCV infection.
4. To update NONCLINICAL TOXICOLOGY, *Carcinogenesis, Mutagenesis, Impairment of Fertility* subsection of labeling with information from the two year carcinogenicity studies in mice and rats.
5. To revise the Patient Information, "How Should I take Sovaldi" subsection by reordering the instructions on how to take Sovaldi.

6. To add the statement, “Take 1 tablet once daily” to the display panel of the container label.

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, 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).

IMMEDIATE CONTAINER LABELS

Submit final printed immediate container labels that are identical to the enclosed immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed**

Container Labels for approved NDA 204671/S-001.” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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
Office of Prescription Drug Promotion (OPDP)
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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

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 Linda C. Onaga, MPH Senior Regulatory Project Manager, at (301) 796-0759.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Container Labeling

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

/s/

WILLIAM B TAUBER
11/14/2014