



NDA 202123/S-006

SUPPLEMENT APPROVAL

Gilead Sciences, Inc
Attention: Shalini Gidwani, M.Sc. RAC
Associate Director, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Gidwani:

Please refer to your Supplemental New Drug Application (sNDA) dated July 2, 2012, received July 3, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for COMPLERA[®] (emtricitabine/rilpivirine/tenofovir disoproxil fumarate) 200 mg/25 mg /300 mg fixed dose combination (FDC) tablets.

We also refer to our letter dated June 14, 2012, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for antiretroviral products. This information pertains to the risk of the autoimmune disorder as syndromes that can occur in the setting of immune reconstitution with the use of antiretroviral products.

This supplemental new drug application provides for revisions to the labeling for Complera[™] (emtricitabine/rilpivirine/tenofovir disoproxil fumarate) 200 mg/25 mg /300 mg fixed dose combination (FDC) tablets, consistent with our June 14, 2012 letter, and few additional editorial and grammatical revisions as follows (additions are noted by underline and deletions are noted by ~~strikethrough~~).

1. The Product name has been revised throughout the label as follows: ~~COMPLERA[™]~~
COMPLERA[®]
2. The **RECENT MAJOR CHANGES** in the **HIGHLIGHTS** section of the label has been added as follows:
-----RECENT MAJOR CHANGES-----
Warnings and Precautions
Immune Reconstitution Syndrome (5.9) XX/2012
3. The revision date has been changed from 8/2011 to [Month]/2012 at the end of the **HIGHLIGHTS** section and the last page of the label.
4. The **WARNINGS AND PRECAUTIONS/Immune Reconstitution Syndrome** sub-

section has been revised as follows:

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including COMPLERA. During the initial phase of combination antiretroviral treatment, patients whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections (such as *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia (PCP), or tuberculosis), which may necessitate further evaluation and treatment.

Autoimmune disorders (such as Graves' disease, polymyositis, and Guillain-Barré syndrome) have also been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

5. Patient Information Labeling:

a. The end of patient package insert has been revised as follows:

202123-DGS-0001 ~~02AUG2011~~ 26JUN2012

6. Few minor editorial and grammatical revisions were made throughout the label.

7. The phrase, “ and NRTI” was added in the footnote of the Table 8 and it now reads as follows:

a. This combination of NNRTI and NRTI substitutions is a subset of those with the E138K.

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, text for the Medication Guide), 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 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).

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/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. 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 Kyong Hyon, Safety Regulatory Project Manager, at (301) 796-0734.

Sincerely,

{See appended electronic signature page}

Kendall A. Marcus, MD
Deputy Director for Safety
Division of Antiviral Products
Office Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
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/

KENDALL A MARCUS
08/10/2012