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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-500

Approval Letter(s)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-500

Martine Kraus, Ph.D.
Director, Regulatory Affairs
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Dear Dr. Kraus:

Please refer to your new drug application (NDA) dated September 3, 2002, received September 3, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Emtriva™ (emtricitabine) 200 mg capsules.

We acknowledge receipt of your submissions dated July 22, 2002, July 30, 2002, August 20, 2002 (2), September 26, 2002, October 1, 2002, October 4, 2002, October 15, 2002, November 26, 2002, December 16, 2002, December 27, 2002, February 25, 2003 (2), February 26, 2003, March 25, 2003, April 1, 2003, April 4, 2003, April 7, 2003, April 15, 2003 (2), April 16, 2003, April 18, 2003, April 25, 2003, April 28, 2003 (2), April 29, 2003, May 8, 2003, May 9, 2003, May 15, 2003 (2), May 16, 2003 (2), May 20, 2003, May 23, 2003, June 2, 2003, June 3, 2003, June 6, 2003, June 10, 2003, June 18, 2003, June 19, 2003, June 20, 2003 (2), June 25, 2003, June 26, 2003, and July 1, 2003.

This new drug application provides for the use of Emtriva™ (emtricitabine) capsules for the treatment of HIV infection in adults.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted July 1, 2003, patient package insert submitted July 1, 2003, immediate container and carton labels submitted April 28, 2003). 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.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "FPL for approved NDA 21-500." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated June 20, 2003. These commitments are listed below.

1. Conduct a study to assess the mechanism of action and clinical significance of skin discoloration observed in patients in emtricitabine clinical trials.

Protocol Submission: Within 3 months of the date of this letter
Study Start: Within 6 months of the date of this letter
Final Report Submission: Within 30 months of the date of this letter

2. Submit the final study report for study TPI DOC #15396 within one month of the date of this letter.

3. Identify the enzymes responsible for emtricitabine metabolism.

Protocol Submission: Within 3 months of the date of this letter
Study Start: Within 5 months of the date of this letter
Final Report Submission: Within 11 months of the date of this letter

4. Determine the potential for enzyme inducers to decrease emtricitabine plasma concentrations.

Protocol Submission: Within 3 months of the date of this letter
Study Start: Within 5 months of the date of this letter
Final Report Submission: Within 11 months of the date of this letter

5. Submit the final study reports from your ongoing carcinogenicity studies.

Final Report Submission: Within 10 months of the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Virginia L. Yoerg, Regulatory Health Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Mark J. Goldberger, M.D., M.P.H.
Director
Office of Drug Evaluation 4
Center for Drug Evaluation and Research

Enclosure: Package Insert and Patient Package Insert.

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

/s/

Mark Goldberger
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