DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-011/S-001

Novartis Pharmaceuticals Corporation
Attention: Michael S. Buska
One Health Plaza
East Hanover, NJ 07936-1080

Dear Mr. Buska:

Please refer to your December 21, 2007 supplemental new drug application, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TYZEKA® (telbivudine) 600 mg tablets.

We acknowledge receipt of your submissions dated June 4, 2008, June 6, 2008, October 17, 2008(2) December 15, 2008, and January 9, 2009.

This supplemental new drug application for TYZEKA® (telbivudine) tablets provides the two year safety and efficacy data updates, primarily from the Globe NV-02B-007 and Chinese NV-02B-015 Phase III studies.

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) for an approved drug if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

Since TYZEKA® (telbivudine) tablets were approved in 2006, for the treatment of chronic hepatitis B in patients with evidence of viral replication and active liver inflammation, we have become aware that peripheral neuropathy, in some cases resulting in motor weakness, pain, sensory deficits and/or difficulty walking, has been reported in patients taking TYZEKA® (telbivudine) tablets alone or in combination with pegylated interferon-alfa-2a and other interferons. This information is from safety reports from study CLDT600A2406 and from postmarketing adverse event reports. This information was not available when TYZEKA® (telbivudine) tablets were granted marketing authorization. Therefore, we consider this information to be "new safety information" as defined under FDAAA.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part

208, FDA has determined that TYZEKA® (telbivudine) poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of TYZEKA® (telbivudine). FDA has determined that TYZEKA® (telbivudine) is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use, TYZEKA® (telbivudine).

Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed TYZEKA® (telbivudine).

Your proposed REMS, submitted on January 21, 2009, and appended to this letter, is approved. The REMS consists of the Medication Guide and the timetable for submission of assessments of the REMS included with this letter.

Your assessment of the REMS should include an evaluation of:

a. A survey of patients' understanding of the risk of peripheral neuropathy, as well as previously identified safety risks for TYZEKA®, including lactic acidosis, hepatomegaly, steatosis, myopathy, and worsening of hepatitis B.
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 22-011 REMS Assessment
NDA 22-011 Proposed REMS Modification

If you do not submit electronically, please send 5 copies of submissions containing REMS assessments or proposed modifications of the REMS.

Please note that:

- A Medication Guide must be reprinted immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];

- You are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208.24];

- The final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text; and

- You are responsible for ensuring that the label of each container or package includes a a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided [21 CFR 208.24(d)].

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert, text for the patient package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, **"SPL for approved NDA 22-011/S-001."**

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

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

HEALTHCARE PROVIDER LETTER

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fisher Lane
Rockville, MD 20857

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 Kenny Shade, Regulatory Project Manager, at (301) 796-0807.

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 (REMS, labeling)

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

/s/

Debra Birnkrant
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