DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-011/S-009
NDA 22-154/S-006

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Ilham Benassou
Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Benassou:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received February 8, 2011, submitted under 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tyzeka® (telbivudine) 600 mg tablets and Tyzeka® (telbivudine) oral solution 100 mg/5 mL.

We acknowledge receipt of your amendments dated February 24, 2011 and March 14, 2011.

We also refer to our letter dated November 19, 2010, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Tyzeka® (telbivudine) 600 mg tablets and Tyzeka® (telbivudine) oral solution 100 mg/5 mL. This information pertains to the higher risk of development of resistance-associated substitutions in treated patients. We also acknowledge receipt of your December 17, 2010, response to this request.

These supplemental new drug applications provides for revisions to the labeling for Tyzeka® (telbivudine), consistent with the agreed upon changes to the language included in our November 19, 2010, letter are as follows (additions are noted by underline and deletion are noted by ~~strikethrough)~~. In addition, to avoid medication errors, all ≤ or ≥ symbols have been spelled out throughout the package insert (PI).

Indications and Usage-Under Section 1.1 Chronic Hepatitis B, "The following points should be considered when initiating therapy with Tyzeka":

- For HBeAg-positive patients, Tyzeka should only be initiated in patients with HBV DNA less than 9 $\log_{10}$ copies/mL and ALT greater than or equal to 2x Upper Limit of Normal (ULN) prior to treatment.
- For HBeAg-negative patients, Tyzeka should only be initiated in patients with HBV DNA less than 7 $\log_{10}$ copies/mL prior to treatment.
- On-treatment response should guide continued therapy [*see Dosage and Administration (2.1) and Microbiology (12.4)*].

Dosage and Administration-Under Section 2.1 Adults and Adolescents (≥16 years of age and older):

Due to higher rates of resistance that may develop with longer term treatment among patients with incomplete viral suppression, treatment should only be initiated, if pre-treatment HBV DNA and ALT measurements are known, in the following patient populations:

For HBeAg-positive patients, HBV DNA should be less than 9 $\log_{10}$ copies/mL and ALT should be greater than or equal to 2x ULN prior to treatment with Tyzeka.

For HBeAg-negative patients, HBV DNA should be less than 7 $\log_{10}$ copies/mL prior to treatment with Tyzeka.

HBV DNA levels should be monitored at 24 weeks of treatment to assure complete viral suppression (HBV DNA less than 300 copies/mL). Alternate therapy should be initiated for patients who have detectable HBV DNA after 24 weeks of treatment. Optimal therapy should be guided by further resistance testing.

Dosage and Administration-Under Section 2.4-Duration of Therapy:

For patients with incomplete viral suppression (HBV DNA greater than or equal to 300 copies/mL) after 24 weeks of treatment, alternate therapy should be instituted. HBV DNA should be monitored every 6 months to assure continued response. If patients test positive for HBV DNA at any time after their initial response, alternate treatment should be instituted. Optimal therapy should be guided by resistance testing.

We have completed our review of these supplemental applications, as amended. They are 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 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 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
Division of Drug Marketing, Advertising, and Communications
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 Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 Stacey Min, Pharm.D., Regulatory Project Manager, at (301) 796-4253.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral 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/

KENDALL A MARCUS
03/29/2011