DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-154/S-003 **SUPPLEMENT APPROVAL**
NDA 22-011/S-006 **FULFILLMENT OF POSTMARKETING COMMITMENT**

Novartis Pharmaceutical Corporation
Attention: Michael Buska
Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07856-1080

Dear Mr. Buska:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received January 29, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tyzeka® (telbivudine) 600 mg tablets and Tyzeka® (telbivudine) 100 mg/5 mL Oral Solution.

We acknowledge receipt of your amendments dated March 4, 2010, May 19, 2010, July 2, 2010 July 19, and July 27 2010, and your risk evaluation and mitigation strategy (REMS) assessment dated March 4, 2010 and July 22, 2010.

These Prior Approval supplemental new drug applications provide for new Oral Solution dose recommendations in patients with severe renal impairment and a new dosing cup that specifically corresponds to the dosing recommendations for the Oral Solution included in the prescribing information and for proposed modifications to the approved REMS.

We have completed our review of these supplemental applications, as amended. These supplements are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text. As discussed, we continue to encourage development of a dosing cup with higher contrast markings for improved readability as you proceed with your pediatric development program.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for package insert and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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 pending "Changes Being Effected" (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.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on July 19, 2010, 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 titled "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 Carton and Container Labels for approved NDA 22-011/S-006 and NDA 22-154/S-003.**" Approval of this submission by FDA is not required before the labeling is used.

We note, the "Rx only" on the carton labeling for the oral solution is between the dosage form (oral solution) and the strength (100mg/5mL) and refer to the [21 CFR 201.10], Drugs; statement of ingredients regulations. Please relocate the "Rx only" on the carton labeling in an area that does not intervene with written, printed or graphic matter and submit in the next annual report.

## POSTMARKETING COMMITMENTS

This supplement fulfills the postmarketing commitment established under NDA 22-154, on April 28, 2009, as listed below:

1078-4 Develop a dosing cup for distribution with Tyzeka oral solution that has clearly marked units of measure and contains only those units that correspond to dosing recommendations included in the prescribing information.

Because the trial is no longer feasible, the approval of this supplement releases you from the postmarketing commitment established under NDA 22-011, on October 25, 2006, as listed below:

7-4 Conduct and submit a final study report to evaluate the use of LdT in the treatment of HBV infection in minority racial/ethnic groups that were under-represented in the pivotal clinical trials (Blacks/African Americans, Hispanics).

## RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Tyzeka® (telbivudine) was originally approved on January 23, 2009, and a REMS modification to add Tyzeka® (telbivudine) oral solution was approved on April 28, 2009. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of revisions to the Patient Instructions for Use section of the Medication Guide for administration of the oral solution with the new dosing cup.

Your proposed modified REMS, submitted on July 22, 2010 and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on January 23, 2009.

There are no changes to the REMS assessment plan described in our January 23, 2009, letter.

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing the 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 as appropriate:

**NDA 22-154 & 22-011**
**REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 22-154 & 22-011 PRIOR APPROVAL SUPPLEMENT**
**PROPOSED REMS MODIFICATION**
**REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE) FOR NDA 22-154 & 22-011**
**REMS ASSESSMENT**
**PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see 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 CDERMedWatchSafetyAlerts@fda.hhs.gov, and 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, please contact Venessa M Perry, MPH, Regulatory Project Manager, at 301.796.4891.

Sincerely,

*{See appended electronic signature page}*

/Kendall Marcus/
for Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
REMS

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|---|---|---|---|
| NDA-22154 | SUPPL-3 | NOVARTIS PHARMACEUTICALS CORP | TYZEKA (TELBIVUDINE) ORAL |
| NDA-22011 | SUPPL-6 | NOVARTIS PHARMACEUTICALS CORP | TYZEKA |

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

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/s/

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VENESSA M PERRY
09/10/2010

KENDALL A MARCUS
09/10/2010