DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 201917/S-007

SUPPLEMENT APPROVAL

Vertex Pharmaceuticals, Incorporated
Attention: Mark Swarz
Associate Director, Regulatory Affairs
130 Waverly Street
Cambridge, MA 02139

Dear Mr. Swarz:

Please refer to your Supplemental New Drug Application (sNDA) dated and received July 12, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for INCIVEK® (telaprevir), Film-Coated Tablets, 375 mg.

We acknowledge receipt of your amendments dated July 20, 2012, October 26, 2012, November 30, 2012, December 7, 2012, and December 13, 2012.

This "Prior Approval" supplemental new drug application proposes the following changes:

Package Insert

1. Addition of a **Boxed Warning** for serious skin reactions including Stevens Johnson Syndrome (SJS), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), and Toxic Epidermal Necrolysis (TEN).

   Revisions to the serious skin reactions information and addition of TEN to WARNINGS and PRECAUTIONS, *Serious Skin Reactions/Rash* (Section 5.1), ADVERSE REACTIONS, *Post-marketing Experience* (Section 6.2), and PATIENT COUNSELING INFORMATION, *Serious Skin Reactions/Rash* (Section 17.1).

2. Revisions to WARNINGS and PRECAUTIONS, *Anemia* (Section 5.2) including additional information on time to onset of anemia and the timing of and need for clinical interventions.

3. Addition of OATP1B1 and OATP2B1 information to DRUG INTERACTIONS, *Potential for INCIVEK to affect Other Drugs* (Section 7.1) and CLINICAL PHARMACOLOGY, *Pharmacokinetics* (Section 12.3), *Drug Interactions* subsection.

4. Addition of drug interaction information for fluvastatin, pitavastatin, pravastatin, rosuvastatin, and repaglinide to DRUG INTERACTIONS, Table 5 (Sections 7.3).

5. Addition of *in vitro* study data regarding recombinant aldo-ketoreductases effect on the metabolism of telaprevir to CLINICAL PHARMACOLOGY, Pharmacokinetics (Section 12.3), *Metabolism* subsection.

6. Addition of in vitro study data regarding BCRP, OATP1B1, OATP2B1, MRP2, MRP4, OCT2 and OAT1 to CLINICAL PHARMACOLOGY, Pharmacokinetics (Section 12.3), *Drug Interactions* subsection.

Medication Guide

7. Revisions to information about serious skin reactions and anemia as serious side effects.

8. Addition of fluvastatin, pitavastatin, pravastatin, rosuvastatin, and repaglinide under "Your healthcare provider may need to monitor your therapy more closely if you take INCIVEK with the following medicines."

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with revisions listed below.

1. Addition of "See full prescribing information for complete boxed warning" placed immediately following the title of the Boxed Warning in the Highlights section.

2. Retain the 6/2012 Warnings and Precautions (Section 5.5) as a Recent Major Change in the Highlights section. (b) (4) [redacted].

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 and 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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 questions, call Myung-Joo Patricia Hong, Regulatory Project Manager, at (301) 796-0807.

Sincerely,

{See appended electronic signature page}

Kendall A. Marcus, M.D.
Deputy Director of Safety
Division of Antiviral Products
Office of 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
12/14/2012