DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22128/S-009

SUPPLEMENT APPROVAL

ViiV Healthcare Company c/o GlaxoSmithKline
Attention: Andrew Gustafson, Ph.D.
Senior Director, Global Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709-3398

Dear Dr. Gustafson:

Please refer to your Supplemental New Drug Application (sNDA) dated July 13, 2012, received July 13, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Selzentry® (maraviroc) Tablets, 150mg and 300mg.

We acknowledge receipt of your amendments dated July 27, 2012.

We also refer to our letter dated June 14, 2012, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for antiretroviral products. This information pertains to the risk of the autoimmune disorder as syndromes that can occur in the setting of immune reconstitution with the use of antiretroviral products.

In addition, we refer to non-safety labeling changes in our June 14, 2012 letter for all antiretroviral products based on recent studies demonstrating decreased transmission of HIV when HIV-infected patients or their uninfected partners take antiretroviral medication.

This supplemental new drug application provides for revisions to the labeling for Selzentry® (maraviroc) Tablets, 150mg and 300mg, consistent with our June 14, 2012 letter, and few additional editorial revisions as follows (additions are noted by underline and deletions are noted by ~~strikethrough)~~.

1. The **RECENT MAJOR CHANGES** in the **HIGHLIGHTS** section of the label has been revised as follows:

---**RECENT MAJOR CHANGES**---

~~Boxed Warning, Hepatotoxicity~~	~~July 2011~~
~~Warnings and Precautions, Hepatotoxicity (5.1)~~	~~July 2011~~
Warnings and Precautions, Immune Reconstitution Syndrome (5.3)	mo/year

2. The end of the **HIGHLIGHTS** section has been revised as follows:

Revised: ~~11/2011~~

3. The **PRECAUTIONS/Immune Reconstitution Syndrome** sub-section has been revised as follows:

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including SELZENTRY~~maraviroc~~. During the initial phase of combination antiretroviral treatment, patients whose immune system responds may develop an inflammatory response to indolent or residual opportunistic infections (such as infection with *Mycobacterium avium* infection, cytomegalovirus, *Pneumocystis jirovecii* pneumonia [PCP], or ~~*Mycobacterium*~~ tuberculosis, or reactivation of *Herpes* simplex and *Herpes* zoster), which may necessitate further evaluation and treatment.

Autoimmune disorders (such as Graves' disease, polymyositis, and Guillain-Barré syndrome) have also been reported to occur in the setting of immune reconstitution; however, the time to onset is more variable, and can occur many months after initiation of treatment.

4. The referenced Table number in the first sentence of the third paragraph in the **CLINICAL PHARMACOLOGY/Pharmacokinetics/Effect of Maraviroc on the Pharmacokinetics of Concomitant Drugs** has been changed from 6 to 10 and now it reads as, "(see Table 10).

5. The word, HIV, has been revised as HIV-1 for consistency with FDA requested new text throughout the label.

6. The second, third, fourth, and fifth paragraphs in the **PATIENT COUNSELING INFORMATION** section has been revised as follows:

Patients should be informed that SELZENTRY is not a cure for HIV-1 infection and patients may ~~still develop~~continue to experience illnesses associated with HIV-1 infection, including opportunistic infections. ~~The use of SELZENTRY has not been shown to reduce the risk of transmission of HIV to others through sexual contact, sharing needles, or blood contamination.~~

Patients should remain under the care of a physician when using SELZENTRY. ~~be advised that it is important to:~~
Patients should be advised to avoid doing things that can spread HIV-1 infection to others.

- **Do not share needles or other injection equipment.**
- **Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.**
- **Do not have any kind of sex without protection.** Always practice safe sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

- **Do not breastfeed.** We do not know if SELZENTRY can be passed to your baby in your breast milk and whether it could harm your baby. Also, mothers with HIV-1 should not breastfeed because HIV-1 can be passed to the baby in the breast milk.
- ~~remain under the care of a physician when using SELZENTRY;~~
- ~~take SELZENTRY every day as prescribed and in combination with other antiretroviral drugs;~~
- ~~report to their physician the use of any other prescription or nonprescription medication or herbal products;~~
- ~~inform their physician if they are pregnant, plan to become pregnant or become pregnant while taking SELZENTRY;~~
- ~~not change the dose or dosing schedule of SELZENTRY or any antiretroviral medication without consulting their physician.~~

Patients should be advised that it is important to take all their anti-HIV medicines as prescribed and at the same time(s) each day. SELZENTRY must always be used in combination with other antiretroviral drugs. Patients should not alter the dose or discontinue therapy without consulting their physician. If a dose is missed, patients should take the next dose of SELZENTRY as soon as possible and then take their next scheduled dose at its regular time. If it is less than 6 hours before their next scheduled dose, they should not take the missed dose and should instead wait and take the next dose at the regular time.

Patients should be advised that when their supply of SELZENTRY starts to run low, they should ask their doctor or pharmacist for a refill.

~~Patients should be advised that if they forget to take a dose, they should take the next dose of SELZENTRY as soon as possible and then take their next scheduled dose at its regular time. If it is less than 6 hours before their next scheduled dose, they should not take the missed dose and should instead wait and take the next dose at the regular time.~~

7. The end section of package insert has been revised as follows:

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~~November 2011~~Month Year
SEL: ~~5PI~~XPI

8. **MEDICATION GUIDE**:

a. "**Does Selzentry lower the risk of passing HIV to other people?"** section has been revised as follows:

~~**Does SELZENTRY lower the risk of passing HIV to other people?**~~

~~**No, SELZENTRY does not lower the risk of passing HIV to other people** through sexual contact, sharing needles, or being exposed to your blood.~~

- ~~Continue to practice safer sex.~~

- ~~Use latex or polyurethane condoms or other barrier methods to lower the chance of sexual contact with any body fluids. This includes semen from a man, vaginal secretions from a woman, or blood.~~
- ~~Never re-use or share needles.~~
- ~~Ask your healthcare provider if you have any questions about safer sex or how to prevent passing HIV to other people.~~

General information about SELZENTRY

SELZENTRY does not cure HIV-1 infection and you may continue to experience illnesses associated with HIV-1 infection, including opportunistic infections. You should remain under the care of a doctor when using SELZENTRY.

Avoid doing things that can spread HIV-1 infection.

- **Do not share needles or other injection equipment.**
- **Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.**
- **Do not have any kind of sex without protection.** Always practice safe sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

b. The seventh bulleted paragraph in the "**Before you take SELZENTRY, tell your healthcare provider if you:**" section has been revised as follows:

- are breastfeeding or plan to breastfeed. ~~It is recommended that HIV-positive women should not breastfeed their babies. This is because of the chance of passing HIV to your baby. You should not breastfeed if you are taking SELZENTRY because the risk to your baby is unknown. Talk with your healthcare provider about the best way to feed your baby.~~ **Do not breastfeed.** We do not know if SELZENTRY can be passed to your baby in your breast milk and whether it could harm your baby. Also, mothers with HIV-1 should not breastfeed because HIV-1 can be passed to the baby in the breast milk. Talk with your healthcare provider about the best way to feed your baby.

c. The end of the **MEDICATION GUIDE** has been revised as followed:

©2012~~0~~, ViiV Healthcare. All rights reserved.

~~November 2010~~month year
SEL:~~-2~~MG

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.

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, text for the Patient Information), 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.

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 Kyong Hyon, Safety Regulatory Project Manager, at (301) 796-0734.

Sincerely,

{See appended electronic signature page}

Kendall A. Marcus, MD
Deputy Director for Safety
Division of Antiviral Products
Office 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
08/10/2012