DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021548 / S-040
NDA 022116 / S-024

SUPPLEMENT APPROVAL

ViiV Healthcare Company
Attention: Thomas F. Kline
Regulatory Executive, on behalf of GlaxoSmithKline
1250 S. Collegeville Road
Collegeville, PA 19426

Dear Mr. Kline:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted and received June 1, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for LEXIVA® (fosamprenavir calcium) tablets, 700 mg (NDA 021548), and LEXIVA® (fosamprenavir calcium) oral suspension, 50 mg/mL (NDA 022116).

These Prior Approval supplemental new drug applications provide the following updates to the prescription drug labeling for LEXIVA® (fosamprenavir calcium):

- Section 5, WARNINGS AND PRECAUTIONS: Subsection 5.7, Increase in Body Fat was updated.
- Section 7, DRUG INTERACTIONS: Table 7, entitled "Established and Other Potentially Significant Drug Interactions" was updated to add contraindicated drugs within the table, with cross-reference to Section 4.
- Section 8, USE IN SPECIFIC POPULATIONS: Subsections 8.1 Pregnancy and 8.2 Lactation were updated in accordance with the Pregnancy and Lactation Labeling Rule (PLLR).
- Section 17 PATIENT COUNSELING INFORMATION and PATIENT INFORMATION: Updated to correspond with changes in the Full Prescribing Information and to comply with current labeling practices.

APPROVAL & LABELING

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 the package insert, text for the patient 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 that include labeling changes 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:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. 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, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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 Suzanne Strayhorn, Regulatory Project Manager, at (240) 402-4247.

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(S):
Content of Labeling

PHARMACIST-DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

PATIENT INFORMATION

LEXIVA (lex-EE-vah) (fosamprenavir calcium) tablets	**LEXIVA (lex-EE-vah) (fosamprenavir calcium) oral suspension**

What is the most important information I should know about LEXIVA?

LEXIVA can interact with other medicines and cause serious side effects. It is important to know the medicines that should not be taken with LEXIVA. See the section "Who should not take LEXIVA?"

LEXIVA can cause serious side effects, including:

- **Severe skin reactions.** LEXIVA may cause severe or life-threatening skin reactions or rash.
  If you get a rash with any of the following symptoms, stop taking LEXIVA and call your healthcare provider or get medical help right away:
  - hives or sores in your mouth, or your skin blisters and peels
  - trouble swallowing or breathing
  - swelling of your face, eyes, lips, tongue, or throat

For more information about side effects, see "What are the possible side effects of LEXIVA?"

What is LEXIVA?

LEXIVA is a prescription medicine that is used together with other antiretroviral medicines to treat human immunodeficiency virus 1 (HIV-1) infection.

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

It is not known if LEXIVA is safe and effective in children younger than 4 weeks of age.

Do not take LEXIVA if you:

- **are allergic** to amprenavir, fosamprenavir calcium, or any of the ingredients in LEXIVA. See the end of this leaflet for a complete list of ingredients in LEXIVA.
- **take any of the following medicines:**
  - alfuzosin
  - rifampin
  - ergot including:
    - dihydroergotamine mesylate
    - ergotamine tartrate
    - methylergonovine
  - cisapride
  - St. John's wort (*Hypericum perforatum*)
  - lovastatin
  - simvastatin
  - pimozide
  - delavirdine mesylate
  - sildenafil (REVATIO), for treatment of pulmonary arterial hypertension

- triazolam
- midazolam, when taken by mouth

Serious problems can happen if you or your child take any of the medicines listed above with LEXIVA.

If you are taking LEXIVA with ritonavir, do not take the following medicines:

- flecainide
- propafenone
- lurasidone

Before taking LEXIVA, tell your healthcare provider about all of your medical conditions, including if you:

- are allergic to medicines that contain sulfa.
- have or have had liver problems, including hepatitis B or C virus infection.
- have kidney problems.
- have high blood sugar (diabetes).
- have hemophilia.
- have high cholesterol.
- are pregnant or plan to become pregnant. It is not known if LEXIVA will harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant during treatment with LEXIVA.
  - LEXIVA may reduce how well hormonal contraceptives (birth control pills) work. Females who may become pregnant should use a different form of birth control or an additional barrier method of birth control during treatment with LEXIVA.

  Pregnancy Registry. There is a pregnancy registry for women who take LEXIVA during pregnancy. The purpose of the registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. **Do not breastfeed if you take LEXIVA.**
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - It is not known if LEXIVA can pass to your baby in your breast milk.
  - Talk with your healthcare provider about the best way to feed your baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with LEXIVA.

Especially tell your healthcare provider if you take:

- quetiapine
- estrogen-based contraceptives (birth control pills). LEXIVA may reduce the effectiveness of estrogen-based contraceptives. During treatment with LEXIVA, you should use a different type of birth control.
- medicines to treat liver problems, including hepatitis C infection.

You can ask your healthcare provider or pharmacist for a list of medicines that interact with LEXIVA. **Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take LEXIVA with other medicines.

- Keep a list of your medicines to show your healthcare provider and pharmacist when you get a new medicine.

How should I take LEXIVA?

- **Take LEXIVA exactly as your healthcare provider tells you to take it.**
- If you miss a dose of LEXIVA, take it as soon as you remember. Do not take 2 doses at the same time or take more than your healthcare provider tells you to take.
- Stay under the care of a healthcare provider during treatment with LEXIVA.
- If your child is taking LEXIVA, your child's healthcare provider will decide the right dose based on your child's weight.
- LEXIVA tablets may be taken with or without food.
- **Adults should take LEXIVA oral suspension without food.**
- **Children should take LEXIVA oral suspension with food.** If your child vomits within 30 minutes after taking a dose of LEXIVA, the dose should be repeated.
- Shake LEXIVA oral suspension well before each use.
- Do not run out of LEXIVA. The virus in your blood may increase and the virus may become harder to treat. When your supply starts to run low, get more from your healthcare provider or pharmacy.
- If you take too much LEXIVA, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of LEXIVA?

LEXIVA may cause serious side effects including:

- **See "What is the most important information I should know about LEXIVA?"**
- **Liver problems.** Your healthcare provider should do blood tests before and during your treatment with LEXIVA to check your liver function. Some people with liver problems, including hepatitis B or C, may have an increased risk of developing worsening liver problems during treatment with LEXIVA.
- **Diabetes and high blood sugar (hyperglycemia).** Some people who take protease inhibitors, including LEXIVA, can get high blood sugar, develop diabetes, or your diabetes can get worse. Tell your healthcare provider if you notice an increase in thirst or urinate often during treatment with LEXIVA.
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Call your healthcare provider right away if you start having new symptoms after starting your HIV-1 medicine.
- **Increase in body fat.** An increase in body fat can happen in people who take protease inhibitors, including LEXIVA. The exact cause and long-term health effects of these conditions are not known.
- **Changes in blood tests.** Some people have changes in blood tests while taking LEXIVA. These include an increase in liver function tests, blood fat levels (cholesterol and triglycerides) and decrease in red blood cells. Your healthcare provider should do regular blood tests before and during your treatment with LEXIVA.
- **Increased bleeding problems in some people with hemophilia.** Some people with hemophilia have increased bleeding with protease inhibitors, including LEXIVA.
- **Kidney stones.** Some people have developed kidney stones during treatment with LEXIVA. Tell your healthcare provider right away if you develop any of the following signs or symptoms of kidney stones:
  - pain in your side
  - blood in your urine

- pain when you urinate

The most common side effects of LEXIVA in adults include:

- nausea
- vomiting
- rash
- diarrhea
- headache

The most common side effects of LEXIVA in children include vomiting and decrease in white blood cells.

These are not all the possible side effects of LEXIVA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LEXIVA?

- Store LEXIVA tablets at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep the bottle of LEXIVA tablets tightly closed.
- Store LEXIVA oral suspension at room temperature or in the refrigerator between 41°F to 86°F (5°C to 30°C). Refrigeration of LEXIVA oral suspension may improve taste for some people.
- Do not freeze.

Keep LEXIVA and all medicines out of the reach of children.

General information about the safe and effective use of LEXIVA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LEXIVA for a condition for which it was not prescribed. Do not give LEXIVA to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about LEXIVA that is written for health professionals.

For more information call 877-844-8872 or go to www.LEXIVA.com.

What are the ingredients in LEXIVA?

Active ingredient: fosamprenavir calcium

Inactive ingredients:

Tablets: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and povidone K30. The tablet film-coating contains the inactive ingredients hypromellose, iron oxide red, titanium dioxide, and triacetin.

Oral Suspension: artificial grape-bubblegum flavor, calcium chloride dihydrate, hypromellose, methylparaben, natural peppermint flavor, polysorbate 80, propylene glycol, propylparaben, purified water, and sucralose.

Manufactured for:

ViiV Healthcare
Research Triangle Park, NC 27709

Vertex Pharmaceuticals Incorporated
Cambridge, MA 02139

by:

GlaxoSmithKline
Research Triangle Park, NC 27709

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This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 12/2017