NDA 212888/S-003

SUPPLEMENT APPROVAL

ViiV Healthcare Company
Attention: Elizabeth Austin, PhD
Senior Director, Global Regulatory Affairs
Five Moore Drive
PO Box 13398
Research Triangle, NC 27709

Dear Dr. Austin:[1]

Please refer to your supplemental new drug application (sNDA) dated and received May 27, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Cabenuva (cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension).

- This Prior Approval supplemental new drug application updates the USPI with Week 124 data from the FLAIR Extension Phase study and provides for the following:
    - Supports a new dosage regimen for Cabenuva that allows patients to proceed directly to injection dosing without the use of oral cabotegravir and oral rilpivirine lead-in dosing.
    - Adds Week 124 data from FLAIR to DOSAGE and ADMINISTRATION, ADVERSE REACTIONS, Clinical Trials Experience, CLINICAL PHARMACOLOGY, Pharmacokinetics and Microbiology, and CLINICAL STUDIES, Clinical Trials in Adults sections of the USPI.

- Updates the DOSAGE and ADMINISTRATION section to allow the use of any other fully suppressive oral antiretroviral regimen if a patient plans to miss a scheduled injection visit.

APPROVAL & LABELING

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

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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 FDA.gov.[2] Content of labeling must be identical to the enclosed labeling (Prescribing Information, Patient Package Insert and Instructions for Use), 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 *SPL Standard for Content of Labeling Technical Qs and As*.[3]

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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study(ies) requirement for this application from birth to less than 2 years of age because necessary studies are impossible or highly impractical due to the success of interventions preventing mother to child transmission of HIV-1 infections and limited population available for recruitment in this age group.

[2] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[3] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

We are deferring submission of your pediatric studies for ages 2 to less than 18 years of age and weighing at least 10 kg and higher for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act/FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act/FDCA. These required studies are listed below.

4232-1 Conduct a study in subjects weighing 35 kg and higher (approximately 12 to less than 18 years of age) who are HIV-1 infected, virologically suppressed (HIV-1 RNA <50 copies/mL) and on a stable antiretroviral regimen at the time of enrollment, to assess the pharmacokinetics, safety and tolerability, and antiviral activity of Cabenuva. Study participants must be monitored for a minimum of 24 weeks to assess safety and durability of antiviral response.

Final Protocol Submission:	N/A
Study Completion:	7/2022
Final Report Submission:	1/2023

4232-2 Conduct a study in subjects weighing 25 kg to less than 35 kg (approximately 6 to less than 12 years of age) who are HIV-1 infected, virologically suppressed (HIV-1 RNA <50 copies/mL) and on a stable antiretroviral regimen at the time of enrollment, to assess the pharmacokinetics, safety and tolerability, and antiviral activity of Cabenuva. Study participants must be monitored for a minimum of 24 weeks to assess safety and durability of antiviral response.

Final Protocol Submission:	8/2022
Study Completion:	6/2023
Final Report Submission:	12/2023

4232-3	Conduct a study in subjects weighing 10 kg to less than 25 kg (approximately 2 to less than 6 years of age) who are HIV-1 infected, virologically suppressed (HIV-1 RNA <50 copies/mL) and on a stable antiretroviral regimen at the time of enrollment, to assess the pharmacokinetics, safety and tolerability, and antiviral activity of Cabenuva. Study participants must be monitored for a minimum of 24 weeks to assess safety and durability of antiviral response.	
	Final Protocol Submission:	8/2022
	Study Completion:	12/2025
	Final Report Submission:	6/2026

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Submit the protocol(s) to your IND 109678, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[5]

[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[5] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

You must submit final promotional materials and Prescribing Information, 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 FDA.gov.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

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 Andrew Gentles, PharmD, BCPS, Senior Regulatory Project Manager, at (240) 402-5708 or the mainline at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

Yodit Belew, MD
Deputy Director (Acting)
Division of Antivirals
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
  - Instructions for Use

[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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