NDA 212887/S-004

SUPPLEMENT APPROVAL

ViiV Healthcare Company
c/o GlaxoSmithKline
Attention: Jeffrey S. Troughton, MS, RAC
Director, Global Regulatory Affairs
5 Moore Drive, P.O. Box 13398
5.5100.5B
Research Triangle Park, NC 27709

Dear Mr. Troughton:

Please refer to your supplemental new drug application (sNDA) dated and received July 23, 2021 and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Vocabria (cabotegravir) tablet.

This Prior Approval supplemental new drug application provides for expansion of the indication for Vocabria (cabotegravir) tablet to include use as an oral lead-in for Apretude (cabotegravir extended release injectable suspension) for HIV-1 pre-exposure prophylaxis (PrEP) for adults and pediatric patients 12 to less than 18 years of age weighing at least 35 kg and as short-term, oral therapy for HIV-1 PrEP for patients who will miss a planned injection dosing of Apretude (cabotegravir extended release injectable suspension).

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

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.[1] Content of labeling must be identical to the enclosed labeling (Prescribing Information and 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 *SPL Standard for Content of Labeling Technical Qs and As*.[2]

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 requirement for ages birth to less than 12 years of age because necessary studies are impossible or highly impracticable. This is because PrEP is intended to reduce the risk of sexually acquired HIV-1 infections. Clinical trials of PrEP would be highly impracticable in a pediatric population who are not sexually mature and active or in whom the likelihood of sexual behavior is very low.

We note that you have fulfilled the pediatric study requirement for ages 12 to 18 years for this application.

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[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] 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.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of antiretroviral drug resistance, including resistance in individuals experiencing pharmacologic failure

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk(s).

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4196-1 Conduct a study to collect and analyze data from adults and adolescents who take cabotegravir extended-release injectable suspension (CAB LA) for pre-exposure prophylaxis (PrEP) of sexually acquired HIV-1 infection and who become infected during PrEP use or within one year of discontinuing PrEP. As part of this study, collect and provide information on adherence, risk factors for non-adherence and HIV-1 acquisition. To compare tolerability and rates of HIV-1 acquisition among individuals who initiate CAB LA with an oral lead-in to those who directly initiate CAB LA injections, the following should be included in the study report:

a) Frequency of testing and methods used for HIV-1 diagnosis.
b) Frequency of prevalent HIV-1 infections that were detected, including those captured during screening.
c) Resistance analyses of viral isolates from those who acquire HIV-1, including a description of the methodologies used to evaluate resistance.
d) Description of subsequent antiretroviral therapy, including the time required to achieve virologic suppression and the durability of the

response (to cover 48-weeks from the time therapy is initiated, at minimum).

e) Information on adherence, select adverse events and treatment discontinuations.

The timetable you submitted on December 10, 2021, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 03/2022
Study Completion: 04/2027
Final Report Submission: 03/2028

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.[3]

Submit clinical protocol(s) to your IND 109678 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

[3] 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.

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.*[4]

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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, contact London Harrison, MBEE, Regulatory Project Manager, at 301-348-3926.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director
Division of Antivirals
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] 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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