CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212887Orig1s000
212888Orig1s000

OTHER ACTION LETTERS

NDA 212887

COMPLETE RESPONSE

ViiV Healthcare Company
Attention: Beth Austin, PhD
Senior Director, Global Regulatory Affairs
5 Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709

Dear Dr. Austin:

Please refer to your new drug application (NDA) dated April 29, 2019, received April 29, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for VOCABRIA® (cabotegravir) 30 mg tablets.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendation to address the issue.

PRODUCT QUALITY

We have identified deficiencies in the product quality information for CABENUVA® (cabotegravir extended release injectable suspension + rilpivirine extended release injectable suspension) 600 mg/900 mg co-pack NDA. As the approval of the VOCABRIA (cabotegravir) NDA is contingent on the approval of the CABENUVA NDA, the CABENUVA NDA deficiencies must be adequately addressed before this application can be approved.

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

[1] http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm
[2] http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm

If you revise labeling, use the SRPI checklist to ensure that the Prescribing Information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at FDA.gov.[3]

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 include annotations that support any proposed changes.

CARTON AND CONTAINER LABELING

Submit latest draft carton and container labeling based on your proposed revision dated December 18, 2019.

PROPRIETARY NAME

Please refer to correspondence dated, July 1, 2019 which addresses the proposed proprietary name, VOCABRIA. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

(2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
- Present tabulations of the new safety data combined with the original application data.

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

- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.

- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

(3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

(4) Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.

(5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.

(6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

(7) Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

(8) Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call LCDR Andrew Gentles, PharmD, BCPS AQ-ID, Regulatory Project Manager, at (240) 402-5708 or the mainline at (301) 796-1500.

Sincerely,

{See appended electronic signature page}

John Farley, MD, MPH
Director (Acting)
Office of Infectious Diseases
Center for Drug Evaluation and Research

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/

JOHN J FARLEY
12/19/2019 05:19:04 PM

NDA 212888

COMPLETE RESPONSE

ViiV Healthcare Company
Attention: Beth Austin, PhD
Senior Director, Global Regulatory Affairs
5 Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709

Dear Dr. Austin:

Please refer to your new drug application (NDA) dated April 29, 2019, received April 29, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CABENUVA® (cabotegravir extended release injectable suspension + rilpivirine extended release injectable suspension) 600 mg/900 mg co-pack.

We also acknowledge receipt of your amendment dated December 17, 2019. A formal review of this amendment is deferred to the next review cycle. You may incorporate applicable sections of the amendment by specific reference as part of your response to the deficiencies cited in this letter.

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY/FACILITY INSPECTIONS

1. During a recent inspection of the GLAXO OPERATIONS UK LIMITED (FEI: 3002807078) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved. Note that as a follow-up to the pre-approval inspection, a Post-Action Memorandum with outstanding concerns will be sent to the inspected drug product facility. Ensure that a future resubmission includes updates to the relevant modules of application in response to these deficiencies.

2. (b) (4)

(b) (4)

3. Your application referenced the Drug Master File (DMF) (b) (4). This DMF was found inadequate to support your submission and a DMF Deficiency Letter was sent to the DMF holder on December 18, 2019. These deficiencies must be adequately addressed before this application can be approved. As part of your response to this letter, include the date the DMF holder amended their DMF to address the deficiencies.

ADDITIONAL COMMENTS

We have the following comments/recommendations that are not approvability issues:

PRODUCT QUALITY

1. The proposed upper limit for the median drug product particle size acceptance range is significantly higher than that of that of pivotal clinical batches. We request that you tighten and further justify this limit.

2. We request that you provide full details of the test for (b) (4)

3. Although we have deferred review of the December 17, 2019 submission, we note (b) (4)

PRESCRIBING INFORMATION

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CARTON AND CONTAINER LABELING

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Sincerely,

{See appended electronic signature page}

John Farley, MD, MPH
Director (Acting)
Office of Infectious Diseases
Center for Drug Evaluation and Research

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/

JOHN J FARLEY
12/19/2019 05:17:22 PM