NDA 206353/S-7

SUPPLEMENT APPROVAL

Bristol-Myers Squibb Company
Attention: Maria Wagner, PhD
Director, Global Regulatory, Safety & Biometrics
PO Box 5326
Princeton, NJ 08543-5326

Dear Dr. Wagner:

Please refer to your supplemental new drug application (sNDA) dated and received December 6, 2019 and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Evotaz (atazanavir and cobicistat) tablets.

This Prior Approval supplemental new drug application provides for the following changes to the Evotaz US Prescribing Information (USPI):

1. INDICATIONS AND USAGE and DOSAGE AND ADMINISTRATION are updated to include use in the pediatric population weighing at least 35 kg
2. WARNINGS AND PRECAUTIONS, Immune Reconstitution Syndrome section is updated with autoimmune hepatitis
3. ADVERSE REACTIONS, is updated with a separate section on clinical trial experience in pediatric subjects
4. USE IN SPECIFIC POPULATIONS, Pediatric Use section is updated with information regarding Evotaz use from trial GS-US-216-0128 which evaluated components of Evotaz in pediatric subjects with HIV-1 infection aged 12 to less than 18 years
5. CLINICAL PHARMACOLGY
    a. Pharmacokinetics, Specific Populations/Pediatric section is updated with addition of relevant pharmacokinetic data following coadministration of atazanavir and cobicistat
    b. Microbiology section is updated with a new subsection titled “Clinical Study of Pediatric Subjects Receiving Atazanavir Coadministered with Cobicistat” containing resistance analysis information from study GS-US-216-0128
6. CLINICAL STUDIES is updated with a new section containing trial results from study GS-US-216-0128 in pediatric subjects
7. The Patient Information has been updated to reflect changes in the USPI

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 (text for the 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

[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.

the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have fulfilled the pediatric study requirement for ages 12 years to less than 18 years and weighing at least 35 kg for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated December 6, 2019, containing the final report for the following postmarketing requirement listed in the January 29, 2015 approval letter.

2850-4	Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of atazanavir and cobicistat fixed-dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 12 years to less than 18 years of age. The safety and antiviral activity (efficacy) of atazanavir and cobicistat FDC age-appropriate formulation in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children 12 years to less than 18 years of age may not be required if the dosing recommendation for the FDC age-appropriate formulation can be supported by pediatric trials already conducted with the individual drug products and if the age-appropriate FDC produces similar exposures as the individual components.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there are postmarketing requirements listed in the January 29, 2015 approval letter that are still open.

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.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication

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

[21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

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 labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

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 Nina Mani, Senior Regulatory Project Manager, at 301-796-1500.

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 or Medication Guide

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] 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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