



NDA 206353

**NDA APPROVAL**

Bristol-Myers Squibb Company  
Attention: Lisa Percival  
Director, Global Regulatory Strategy  
5 Research Parkway, Mailstop 2CW-506  
Wallingford, CT 06492

Dear Ms. Percival:

Please refer to your New Drug Application (NDA) dated and received April 4, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for EVOTAZ<sup>®</sup> (atazanavir and cobicistat) tablet, 300 mg and 150 mg.

We acknowledge receipt of your amendments dated:

April 24, 2014  
April 28, 2014  
June 10, 2014  
July 2, 2014  
July 22, 2014  
September 19, 2014  
December 9, 2014  
December 26, 2014  
January 22, 2015  
January 26, 2015  
January 28, 2015

This new drug application provides for the use of EVOTAZ<sup>®</sup> (atazanavir and cobicistat) tablet for patients 18 years and older for the treatment of HIV-1 infection.

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 text.

**WAIVER OF HIGHLIGHTS SECTION**

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

## **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). 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*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

## **CARTON AND IMMEDIATE CONTAINER LABELS**

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 206353.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages < 3 months of age because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group due to risk of kernicterus.

We are deferring submission of your pediatric studies for ages 3 months to 18 years 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 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)(3)(C) of the FDCA. These required studies are listed below.

- 2850-1 Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of atazanavir and cobicistat fixed-dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 3 months to less than 3 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 3 months to less than 3 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.

Final Protocol Submission: 03/2018  
Study Completion: 08/2018  
Final Report Submission: 02/2019

- 2850-2 Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of atazanavir and cobicistat fixed-dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 3 years to less than 6 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 3 years to less than 6 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.

Final Protocol Submission: 03/2018  
Study Completion: 08/2018  
Final Report Submission: 02/2019

- 2850-3 Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of atazanavir and cobicistat fixed-dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 6 years to less than 12 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 6 years to less than 12 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.

Final Protocol Submission: 03/2018  
Study Completion: 08/2018  
Final Report Submission: 02/2019

- 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.

Final Protocol Submission: 03/2018  
Study Completion: 08/2018  
Final Report Submission: 02/2019

Submit the protocols to your IND 117131, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (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. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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>.

## **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 Sammie Beam RPh, Regulatory Project Manager, at (301) 796-0080.

Sincerely,

*{See appended electronic signature page}*

Debra Birnkrant, MD  
Director  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosures:

Content of Labeling  
Carton and Container Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JEFFREY S MURRAY  
01/29/2015