



NDA 021797/S-023  
NDA 021798/S-024

## SUPPLEMENT APPROVAL

Bristol-Myers Squibb Company  
Attention: Maria Fradlina-Svirid  
TA Lead Mature Products, Global Labeling & Mature Products Strategy  
P.O. Box 4000  
Princeton, NJ 08543

Dear Ms. Fradlina-Svirid:

Please refer to your supplemental new drug applications (sNDA) dated and received on May 7, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for BARACLUDE<sup>®</sup> (entecavir) tablets and BARACLUDE<sup>®</sup> (entecavir) oral solution.

These Prior Approval supplemental new drug applications provide for the following changes to the Prescribing Information:

- **ADVERSE REACTIONS, Postmarketing Experience**, updated with a new subheader entitled "Data from Long-Term Observational Study" which follows with new information from the clinical trial AI463080, a randomized, global, observational, open-label Phase 4 study to assess long-term risks and benefits of BARACLUDE (0.5 mg/day or 1 mg/day) as compared to other standard-of-care HBV nucleos(t)ide analogues in subjects with chronic HBV infection. This includes the addition of the new Table 6, entitled "Principal Analyses of Time to Adjudicated Events - Randomized Treated Subjects".
- **ADVERSE REACTIONS, Postmarketing Experience**, updated with a new subheading entitled Adverse Reactions from Postmarketing Spontaneous Reports.
- **HOW SUPPLIED/STORAGE AND HANDLING** updated with removal of the reference to the 90-tablet quantity of the 0.5 mg film-coated tablet as this quantity is no longer marketed.

### **APPROVAL & LABELING**

We have completed our review of these applications, as amended. They are 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](http://FDA.gov).<sup>1</sup> 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*.<sup>2</sup>

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> 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>.

## **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 Suzanne Strayhorn, Regulatory Project Manager, at (240) 402-4247.

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

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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.**  
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/s/  
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