



NDA 021797 / S-019
NDA 021798 / S-021

SUPPLEMENT APPROVAL

Bristol-Myers Squibb Company
Attention: Maria Wagner, Ph.D.
Director, Global Regulatory, Safety & Biometrics
P.O. Box 5326
Princeton, NJ 08543

Dear Dr. Wagner:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received on March 23, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Baraclude® (entecavir), 0.05 mg/mL oral solution, and for Baraclude® (entecavir), 0.5 mg and 1.0 mg tablets.

These Prior Approval supplemental new drug applications provide for the following updates to the BARACLUDE® (entecavir), US prescribing information (USPI):

- **SECTION 12, CLINICAL PHARMACOLOGY (Subsection 12.4 Microbiology):**
Updated to include information related to the identified hepatitis B virus substitution, rtA181C, that confers resistance to entecavir.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 prescribing information, text for the patient package insert), with the addition of any labeling changes in pending "Changes Being Effectuated" (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 titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. 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 provide appropriate annotations, including supplement number(s) and annual report date(s).

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, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

POONAM MISHRA
06/22/2018
on behalf of Debra Birnkrant, MD