DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-412/S-017, S-018
NDA 20-413/S-008, S-009

Bristol-Myers Squibb Company
Attention: Marie-Laure Papi
Associate Director, Worldwide Regulatory Affairs
5 Research Parkway
Wallingford, CT 06492

Dear Ms. Papi:

Please refer to your supplemental new drug applications dated August 16, 2001, received August 20, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZERIT® (stavudine) Capsules and Pediatric Oral Solution (POS).

We acknowledge receipt of your submissions dated November 12, 2001 and February 7, 2002.

These supplemental new drug applications provide for changes in the **WARNINGS**, **PRECAUTIONS**, **ADVERSE REACTIONS,** and **PATIENT INFORMATION** sections of the ZERIT® label. These revisions describe the occurrence of lactic acidosis and neuromuscular toxicity in patients using stavudine.

Please also refer to your supplemental new drug applications dated November 30, 2001, received December 3, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZERIT® (stavudine) Capsules and Pediatric Oral Solution (POS).

These supplemental new drug applications provide for the inclusion of information regarding fat redistribution (lipodistrophy) associated with the use of combination antiretroviral therapy in the **PRECAUTIONS**, **ADVERSE REACTIONS,** and **PATIENT INFORMATION** sections of the ZERIT® label.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted February 7, 2002, patient package insert submitted February 7, 2002).

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL

for approved supplement NDA 20-412/S-017, S-018, 20-413/S-008, S-009." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Destry M. Sillivan, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

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

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

/s/

Debra Birnkrant
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NDA 20-413, 20-412