CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-007/SE7-006
21-039/SE7-006

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-007/S-006

GlaxoSmithKline
Attention: Robert Watson
Antiviral Group, Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Watson:

Please refer to your supplemental new drug application dated July 13, 2000, received July 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Agenerase® (amprenavir) Capsules.

We acknowledge receipt of your submissions dated: December 14, 2000, January 12, 2001, March 7, 2001, March 8, 2001, March 23, 2001, April 11, 2001, and May 3, 2001.

This NDA was approved under 21 CFR 314.510, the regulation for accelerated approval of new drugs for serious or life-threatening illnesses. This supplemental new drug application provides information to fulfill the accelerated approval commitments as required under 21 CFR 314.510. Specifically, this supplemental application provides for the use of Agenerase® in combination with other antiretroviral agents for the treatment of HIV-1 infection.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon label text dated May 9, 2001. Accordingly, this application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert), and must be formatted in accordance with the requirements of 21 CFR 201.66. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please mount individually ten of the copies on heavy weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format-NDAs (January 1999).* For administrative purposes this submission should be designated "FPL for approved supplement NDA 21-007/S-006. Approval of this submission by FDA is not required before the labeling is used.

We remind you of the following outstanding postmarketing study commitments as specified in your submission dated April 13, 1999 and the approval letter dated April 15, 1999:

1. The applicant agrees to propose and conduct a study of a) the tolerability of amprenavir in patients with a known sulfonamide allergy, and b) the tolerability of sulfonamide therapy after patients have been treated with amprenavir.

2. The applicant agrees to propose and conduct an evaluation of the safety of chronic, high-dose Vitamin E administration in adults and pediatric patients receiving amprenavir, including the evaluation of vitamin E levels.

3. The applicant agrees to submit reports of completed carcinogenicity studies in a timely manner.

A separate letter that addresses all the postmarketing study commitments outlined in the April 15, 1999 approval letter will be sent at a later date.

If a letter communicating important information about the drug product (i.e., a "Dear Health Care Practitioner" 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:

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

Finally, 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 Leslie Stephens, Regulatory Project Manager, at 301-827-2335.

Sincerely,

{See appended electronic signature page}

5/11/01

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

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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NDA 21-039/S-006

GlaxoSmithKline
Attention: Robert Watson
Antiviral Group, Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Watson:

Please refer to your supplemental new drug application dated July 13, 2000, received July 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Agenerase® (amprenavir) Oral Solution.

We acknowledge receipt of your submissions dated: December 14, 2000, January 12, 2001, March 7, 2001, March 8, 2001, March 23, 2001, April 11, 2001, and May 3, 2001.

This NDA was approved under 21 CFR 314.510, the regulation for accelerated approval of new drugs for serious or life-threatening illnesses. This supplemental application provides information to fulfill the accelerated approval commitments as required under 21 CFR 314.510. Specifically, this supplemental new drug application provides for the use of Agenerase® in combination with other antiretroviral agents for the treatment of HIV-1 infection.

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We remind you of your postmarketing study commitment in your submission dated May 9, 2001.

This commitment is listed below:

- The applicant will commit to the submission of data that will address concerns about the potential for toxicity related to the high propylene glycol content of Agenerase® (amprenavir) oral solution. These data will include propylene glycol concentration data and adverse events reported from clinical trials and from postmarketing reports, as outlined in the correspondence of May 8, 2000.

  Final Report Submission: Within 60 days of the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 21 CFR 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and for clinical studies, number of patients entered in each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

In addition, we remind you of the following outstanding postmarketing study commitments as specified in your submission dated April 13, 1999 and the approval letter dated April 15, 1999:

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Debra Birnkrant, M.D.
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