CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

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

Administrative Documents

PATENT INFORMATION

pursuant to 21 C.F.R. § 314.53
for

AGENERASE® (amprenavir) Capsules
sNDA 21-007

The following is provided in accord with the Drug Price Competition and Patent Term Restoration Act of 1984:

Trade Name:	Agenerase®
Active Ingredient(s):	amprenavir
Strength(s):	50 mg and 150 mg
Dosage Form:	Capsule

Applicable Patent Numbers and Expiration Dates:

Patent No.	5,585,397
Expires:	December 17, 2013
Owner:	Vertex Pharmaceuticals Inc. Licensed to Glaxo Wellcome Inc.
Type:	Drug Substance Drug Product Composition Formulation

Patent No.	5,723,490
Expires:	March 3, 2015
Owner:	Vertex Pharmaceuticals Inc. Licensed to Glaxo Wellcome Inc.
Type:	Method of Use (treatment of HIV)

Patent No.	5,646,180
Expires:	July 8, 2014
Owner:	Vertex Pharmaceuticals Inc. Licensed to Glaxo Wellcome Inc.
Type:	Method of Use (treatment of HIV)

The undersigned declares that U.S. Patent 5,585,397 covers the composition, formulation and/or method of use of AGENERASE® (amprenavir) Capsules. This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

The undersigned declares that U.S. Patent 5,723,490 covers the composition, formulation and/or method of use of AGENERASE® (amprenavir) Capsules. This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

The undersigned declares that U.S. Patent 5,646,180 covers the composition, formulation and/or method of use of AGENERASE® (amprenavir) Capsules. This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

Please address all communications to:

David J. Levy, Ph.D.
Patent Counsel
Glaxo Wellcome Inc.
Intellectual Property Department
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709
(919)483-2723

Respectfully submitted,

May 15, 2000
Date

Karen L. Prus
Karen L. Prus, Ph.D.
Registered Patent Attorney
Glaxo Wellcome Inc.

PATENT INFORMATION

pursuant to 21 C.F.R. § 314.53
for

AGENERASE® (amprenavir) Oral Solution
sNDA 21-039

The following is provided in accord with the Drug Price Competition and Patent Term Restoration Act of 1984:

Trade Name:	Agenerase®
Active Ingredient(s):	amprenavir
Strength(s):	15 mg/mL
Dosage Form:	Oral Solution

Applicable Patent Numbers and Expiration Dates:

Patent No.	5,585,397
Expires:	December 17, 2013
Owner:	Vertex Pharmaceuticals Inc. Licensed to Glaxo Wellcome Inc.
Type:	Drug Substance Drug Product Composition Formulation

Patent No.	5,723,490
Expires:	March 3, 2015
Owner:	Vertex Pharmaceuticals Inc. Licensed to Glaxo Wellcome Inc.
Type:	Method of Use (treatment of HIV)

Patent No.	5,646,180
Expires:	July 8, 2014
Owner:	Vertex Pharmaceuticals Inc. Licensed to Glaxo Wellcome Inc.
Type:	Method of Use (treatment of HIV)

The undersigned declares that U.S. Patent 5,585,397 covers the composition, formulation and/or method of use of AGENERASE® (amprenavir) Oral Solution. This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

The undersigned declares that U.S. Patent 5,723,490 covers the composition, formulation and/or method of use of AGENERASE® (amprenavir) Oral Solution. This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

The undersigned declares that U.S. Patent 5,646,180 covers the composition, formulation and/or method of use of AGENERASE® (amprenavir) Oral Solution . This product is currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

Please address all communications to:

David J. Levy, Ph.D.
Patent Counsel
Glaxo Wellcome Inc.
Intellectual Property Department
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709
(919)483-2723

Respectfully submitted,

May 15, 2000
Date

Karen L. Prus, Ph.D.
Registered Patent Attorney
Glaxo Wellcome Inc.

EXCLUSIVITY SUMMARY for NDA #21-007 SUPPL # 006

Trade Name Agenerase® Capsules **Generic Name** amprenavir

Applicant Name GlaxoSmithKline **HFD-** 530

Approval Date _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/___/ NO /_X__/

   b) Is it an effectiveness supplement? YES /_X_/ NO /___/

      If yes, what type(SE1, SE2, etc.)? SE7

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /__X_/ NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      _____

      _____

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical

data:

d) Did the applicant request exclusivity?

YES /___/ NO /_X__/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

NA

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /__X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No - Please indicate as such).

YES /__X_/ NO /___/

If yes, NDA # 21-007 Drug Name Agenerase Capsules

Explanation: This supplement is for traditional approval of a product approved under the accelerated approval (Subpart H) regulations. This was a review of 48-week data from two studies PROAB3001 and PROAB3006 that were submitted with the original NDA. The active ingredients, dosage form, strength, route of administration, and dosing schedule remain the same.

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE

SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application,

answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

   For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

   (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

   YES /___/ NO /___/

   If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # _____ YES /___/ NO /___/ Explain: _____

_____

_____

Investigation #2

IND # _____ YES /___/ NO /___/ Explain: _____

_____

_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

/S/

_____ 5-1-01

Signature of Preparer Date

Title: Project Manager

/S/

_____

Signature of Office or Division Director Date

Debbie -

This Form will also be ENTERED in DFS For Sign-off.

/S/

cc:
Archival NDA
HFD- /Division

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA Number: N 021039
Trade Name: AGENERASE (AMPRENAVIR)15MG/ML ORAL SOLUTI
Generic Name: AMPRENAVIR
Supplement Number: 006 **Supplement Type:** SE7
Dosage Form:
Regulatory Action: OP **Action Date:** 7/14/00
COMIS Indication: TREATMENT OF HIV INFECTION

Indication #1: Agenerase is indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection.
Label Adequacy: Adequate for some pediatric age groups
Formulation Needed: Other
Comments (if any) 5/1/01 The current oral formulation of Agenerase is contraindicated in children less than 4 years of age because of the large amount of the excipient propylene glycol used in the manufacture of this product. Therefore, a new formulation would be needed to treat children < 4 years of age. At this time, the sponsor has not indicated if they have plans for a new formulation.

Lower Range	Upper Range	Status	Date
4 years	17 years	Completed	4/15/99
0 months	4 years	Deferred	4/15/99

Comments: This SE7 application does not trigger the Pediatric Rule.

This page was last edited on 5/2/01

Signature

5-2-01
Date

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA Number: N 021007
Trade Name: AGENERASE (AMPRENAVIR) CAPS 50MG/150MG
Generic Name: AMPRENAVIR
Supplement Number: 006 **Supplement Type**: SE7
Dosage Form:
Regulatory Action: OP **Action Date**: 7/14/00
COMIS Indication: TREATMENT OF HIV-1 INFECTION

Indication #1: Agenerase is indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection.
Label Adequacy: Adequate for some pediatric age groups
Formulation Needed: Other
Comments (if any) 5/1/01. The capsule formulation is labeled down to 4 years of age. The current oral formulation of Agenerase is contraindicated in children less than 4 years of age because of the large amount of the excipient propylene glycol used in the manufacture of this product. Therefore, a new formulation would be needed to treat children < 4 years of age. At this time, the sponsor has not indicated if they have plans for a new formulation.

Lower Range	Upper Range	Status	Date
4 years	17 years	Completed	4/15/99
0 months	4 years	Deferred	4/15/99

Comments: This SE7 application does not trigger the Pediatric Rule.

This page was last edited on 5/2/01

Signature

5-2-01
Date

NDA 21-007 AGENERASE® (amprenavir) Capsules
NDA 21-039 AGENERASE® (amprenavir) Oral Solution

Supplemental New Drug Application
for Traditional Approval

DEBARMENT CERTIFICATION

Glaxo Wellcome hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

27 June 2000

Charles E. Mueller
Head, North American Clinical Compliance
World Wide Compliance

Date

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical estigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	AGENERASE® (amprenavir) Capsules NDA 21-007	See Attached Listings
	AGENERASE® (amprenavir) Oral Solution NDA 21-039	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Lucy G. Martindale	Vice President and Director, R&D Finance
FIRM / ORGANIZATION: Glaxo Wellcome Inc.	
SIGNATURE: Lucy G Martindale	DATE: May 24, 2000

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

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pages of trade

secret and/or

confidential

commercial

information

Group Leader Memorandum

NDA:	**21-007 (capsules)** **21-039 (oral solution)**
Drug:	**Amprenavir (Agenerase™)**
Indication:	**Treatment of HIV infection**
Dose:	**1200 mg BID (adults)** **20 mg/kg BID (pediatrics)**
Application:	**Glaxo Wellcome Inc.**
Submission received:	**July 13, 2000**
Date of memorandum:	**May 3, 2001**

In this NDA submission the applicant requests traditional approval of amprenavir, a protease inhibitor of human immunodeficiency virus (HIV). Amprenavir was granted accelerated approval in April, 1999, based upon the 24 week safety and efficacy results from two phase 3 well-controlled studies. In support of the request for traditional approval, the applicant has submitted the 48 week results from the same studies. In both studies the primary efficacy measure was the proportion of subjects whose viral load was < 400 c/mL. CD4 count changes were evaluated as a secondary endpoint.

Study PROAB 3001 was a randomized, double-blind, placebo-controlled, multicenter study conducted in 232 treatment-naïve adults. The triple-drug combination amprenavir/ZDV/3TC was compared to combination therapy with ZDV/3TC/placebo. Study PROAB 3006 wan an open-label, active-controlled, multicenter study conducted in 504 protease inhibitor-naïve adults. In this equivalence-design study the combination of amprenavir/ZDV/3TC was compared to indinavir/ZDV/3TC.

I concur with Mr. Fleischer, the primary-clinical reviewer, that this application should be approved.

Issues of note at the time of this regulatory approval include 1) utility of amprenavir in protease inhibitor-experienced patients, and 2) outstanding post-marketing commitments 3) update on propylene glycol related adverse events.

1) The results of a clinical study conducted with amprenavir in protease inhibitor-naïve subjects led to modification of the INDICATIONS section of the label

that describes the inferior antiviral activity of this agent when compared to indinavir. Though not included in the label, the 48 week results of this study show that amprenavir in combination with two nucleosides appears to be less efficacious than most combination therapies that are currently available to treatment- or PI-naïve patients. No studies of PI-experienced patients were conducted. Treatment with amprenavir is associated with GI adverse events, which, while but mild or moderate in severity, frequently lead to discontinuation of amprenavir within the first 12 weeks of treatment. Amprenavir therapy requires twice daily ingestion of eight large capsules formulated with large amounts of both Vitamin E and propylene glycol. For these reasons, it is unlikely that an amprenavir-containing regimen would be initiated in treatment-naïve or PI-naïve patients, and that it will be prescribed when all other treatment options have been exhausted. There are no data to support such use, and, it appears that an amprenavir-containing regimen in this population would be of very limited efficacy. However, because the applicant has an [redacted] it is doubtful that further studies of amprenavir will be undertaken. Therefore, this will likely remain an unresolved issue until further development [redacted] takes place.

2) Outstanding post-marketing commitments at the time of traditional approval include evaluation of the clinical implications of the sulfonamide-like chemical structure of amprenavir and evaluation of Vitamin E levels and the potential for Vitamin E-related toxicities. The approval letter will remind the applicant of these commitments, and we will request an update of activities related to these commitments.
3) No information on propylene glycol-related adverse events was included in this NDA submission. Continued availability of the oral solution containing potentially toxic amounts of propylene glycol allows for potential exposure of susceptible populations. We will request an update on adverse events that could potentially be associated with propylene glycol toxicity.

/S/

5/7/01

Therese Cvetkovich, M.D.
Medical Team Leader, DAVDP

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Antiviral Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: May 8, 2001

To: Robert Watson
Glaxo Wellcome Inc.

From: Melissa M. Truffa, R.Ph., DAVDP

Through: Therese Cvetkovich, M.D., Medical Officer 5-8-01

NDAs: 21-039 Agenerase ™ (amprenavir) Oral Solution

Subject: Post-Marketing commitment

Comment:

- 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 amprenavir oral solution. These data will include adverse events reported from clinical trials and from post-marketing reports, as well as the propylene glycol concentration data as outlined in your May 8, 2000 correspondence.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Antiviral Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: March 30, 2001

To: Robert Watson
Glaxo Wellcome Inc.

From: Melissa M. Truffa, R.Ph., DAVDP

NDAs: 21-007 and 21-039 Agenerase ™ (amprenavir) Capsules and Oral Solution

Subject: Request for Case Report Forms (CFR).

Comment:

Please provide the case report forms for the attached list of subjects from Study PROAB3006 by April 6, 2001. We would prefer that you provide them electronically, if possible.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Antiviral Drug Products
Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF TELEPHONE FACSIMILE CORRESPONDENCE

Date: December 14, 2000

To: Robert Watson
Glaxo Wellcome Inc.

From: Melissa M. Truffa, R.Ph., DAVDP

Through: Rafia Bhore, Ph.D., Statistical Reviewer eso 12-11-00
Greg Soon, Ph.D., Acting Statistical Team Leader eso 12-12-00

NDAs: 21-007 and 21-039 Agenerase ™ (amprenavir) Capsules and Oral Solution

Subject: Traditional Approval Supplement: Statistical Request.
Comments:

Dr. Bhore would like to make the following data request regarding NDA 21-007/S-006 and NDA 21-039/S-006.

1. DEMOGRAPHICS Dataset(s)
   - Raw data

2. EFFICACY Dataset(s)
   - Raw data containing efficacy measurements and laboratory measurements (if any).
   - Programs transforming raw data into intermediate analysis datasets.
   - Programs, algorithms, and macros (if any) using intermediate analysis datasets to get efficacy results.
   - Please provide efficacy data beyond week 48, if available.

3. SAFETY Dataset(s)
   - Raw data containing safety variables.
   - Programs for obtaining results on safety parameters.

4. DOCUMENTATION
   - Clear and concise documentation of variables.
   - Comments will need to be included in programs and algorithms to make them readable and understandable

5. SAS TRANSPORT FILES
   - One dataset per SAS Transport file is preferred. If one SAS Transport file can be (un)compressed into individual SAS datasets through a short SAS code, then a single SAS Transport file will be acceptable.

6. ELECTRONIC MEDIA
   - SAS Transport files and other electronic files on CD-ROM and/or ZIP disk.

7. COMPATIBILITY
   - All programs, datasets, and other files must be compatible with Windows 95 and PC SAS Version 6.12.

We are providing the above information via telephone facsimile for your convenience. **THIS MATERIAL SHOULD BE VIEWED AS UNOFFICIAL CORRESPONDENCE.** Please feel free to contact me if you have any questions regarding the contents of this transmission.