CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 74-655

Approval Letter

ANDA 74-655

OCT 22 1997

Geneva Pharmaceuticals, Inc.
Attention: Beth Brannan
2555 W. Midway Blvd.
Broomfield, CO 80038-0446

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated March 31, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ranitidine Capsules, 150 mg and 300 mg (present as the hydrochloride).

Reference is also made to your correspondence dated July 10, 1997, and to your amendments dated August 29 and October 1, 1997.

The listed drug product referenced in your application is subject to periods of patent protection which expire on June 4, 2002, (patent 4,521,431) and February 22, 2010 (patent 5,028,432). Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of ranitidine hydrochloride will not infringe on the patent or that the patent is otherwise invalid. You further informed the Agency that Glaxo, Inc. initiated a patent infringement suit against you in the United States District Court for the District of New Jersey (Glaxo Wellcome Inc., Glaxo Group Limited and Allen and Hanbury's Limited v. Novartis Corporation, Geneva Pharmaceuticals Inc., Interchem Trading Corporation, and Union Quimico Farmaceutica S.A., Civil Action No. 94-1921, 94-4589 and 96-3849). You also have notified the Agency, that on October 1, 1997, the District Court hearing the patent case issued a Stipulated Dismissal pursuant to Rule 41(a)(1)(ii). This order states:

> [T]he Dismissal will have the full force and effect of a decision of non-infringement of United States Patent Nos. 4,521,431, 4,128,658, 4,672,133 from which no appeal can be taken; and pursuant to 21 USC 355(j)(4)(B)(iii), the thirty (30) month stay of approval of Geneva Pharmaceutical Inc.'s ANDA 74-655 is dissolved and the Food and Drug Administration may approve ANDA 74-655 immediately.

The Agency has reviewed the application of the 180-day exclusivity provisions of the Act to this ANDA submitted for Ranitidine Capsules. FDA's regulations interpreting these provisions are set out at 21 CFR 314.107(c). The Agency has concluded that Geneva Pharmaceuticals is entitled to 180 days for marketing exclusivity for Ranitidine Capsules.

FDA regulations describe that the 180-day period will begin running from "the date of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed." 21 CFR 314.107(c)(1)(ii). The relevant date of final decision of a court on patent issues is defined in 21 CFR 314.107(e)(2)(I) as follows:

> If the district court enters a decision that the patent is invalid, unenforceable, or not infringed, and the decision is not appealed, the date on which the right to appeal lapses.

As stated above, the right to appeal lapsed on October 1, 1997. The 180 day period began on October 1, 1997, and will expire on March 29, 1998. It is important to note that FDA will not approve an ANDA for ranitidine capsules prior to the expiration of exclusivity notwithstanding a licensing agreement.

If you have any questions concerning this matter, please feel free to contact Jerry Phillips; Director, Division of Labeling and Program Support at (301) 827-5846.

Sincerely yours,

/S/ 10/30/97

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 74-655

Geneva Pharmaceuticals, Inc.
Attention: Beth Brannan
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80020-0446

JUL 24 1997

Dear Madam:

This is in reference to your abbreviated new drug application dated March 31, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ranitidine Capsules, 150 mg and 300 mg (present as the hydrochloride). The application contains patent certifications under section 505(j)(2)(A)(vii)(III and IV) of the Act.

Reference is also made to your amendments dated April 16 and July 11, 1996, January 16, March 25, June 13 and 27, 1997.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time, which includes information in your application and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug products. Therefore, this determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(4)(B)(iv) of the Act.

The listed drug product referenced in your application is subject to periods of patent protection which expire on July 25, 1997 (patent 4,128,658), June 4, 2002 (patent 4, 521,431), and February 22, 2010 (patent 5,028,432). However, you have informed us that litigation is underway in the United States District Court for the District of New Jersey, involving a challenge only to patent 4,521,431 (Glaxo Wellcome, Inc. And Glaxo Group Limited v. Geneva Pharmaceuticals Inc., Civil Action No. 96-3849(NHP).

Final approval of your application cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(4)(B)(iii) since the date of receipt of the 45-day notice required under section 505(j)(2)(B)(i), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or,

   b. the date of court decision finding the patent invalid or not infringed, [505(j)(4)(B)(iii)(I)], which has been interpreted by the Agency to mean the date of the final order or judgement of that court from which no appeal can be or has been taken, or,

   c. the latest expiring patent has expired, and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

Because the Agency is granting a tentative approval for this application, when you believe that your application may be considered for final approval, you must amend your application to notify the Agency whether circumstances have or have not arisen that may affect the effective date of final approval. Your amendment must provide:

1. a copy of a final order or judgement from which no appeal may be taken (which might not be the one from the district court), or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information, and

2. a. updated information related to labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this abbreviated application, or

   b. a statement that no such changes have been made to the application since the date of tentative approval.

Any changes in the conditions outlined in this abbreviated application and the status of the manufacturing and testing facilities' compliance with current good manufacturing procedures are subject to Agency review before final approval of the application will be made.

In addition to, or instead of, the amendments referred to above, the Agency may, at any time prior to the final date of approval, request that you submit amendments containing the information requested above.

Failure to submit either or both amendments may result in rescission of this tentative approval determination, or delay in issuance of the final approval letter.

The drug product that is the subject of this abbreviated application may not be marketed without final Agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug before the effective final approval date is prohibited under section 501 of the Act. Also, until the Agency issues the final approval letter, this drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list.

The amendment should be designated as a MINOR AMENDMENT in your cover letter. Before you submit the amendment, please contact Ms. Kassandra C. Sherrod, Project Manager, at (301) 827-5849, for further instructions.

Sincerely yours,

/S/ 7/22/97

Roger L. Williams, M.D.
Deputy Center Director for Pharmaceutical Science
Center for Drug Evaluation and Research