CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74467

CORRESPONDENCE

ANDA 74-467

Geneva Pharmaceuticals, Inc.
Attention: Ms. Beth Brannan
2555 W. Midway Blvd.
P. O. Box 446
Broomfield, Colorado 80038-0446

MAR 17 1995

Dear Ms. Brannan:

This is in reference to your abbreviated new drug application dated February 16, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ranitidine Hydrochloride Tablets, USP, 150 mg and 300 mg.

Reference is also made to your amendment dated November 11, 1994.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies

1. A description of the container configuration to be used to store the dried granulation and the coated tablets should be provided. Also, specify if a desiccant bag will be used. Be aware that the computation of the expiration date should be based from the initial compounding of two ingredients and not from the completion date of the coating process.

2. We recommend that further studies be conducted in order to determine if physical interconversion is occurring during the course of granulating the subject drug product. We propose that a sample of Ranitidine Hydrochloride Form I working standard be diluted in -- evaporated, then test the residues using The spectra obtained should be provided.

3. The coating solution's "total solids" percentage should be provided.

4. Your finished drug product release specifications submitted in attachment 7, of your letter dated 11/11/94, to reflect the revised "Related Compounds" specifications does not harmonize with the proposed specifications submitted in response to deficiency No. 16, page 6, of the subject letter. These specifications should be tightened to reflect the data

obtained for releasing lot Nos. 6494065 and 6494066. Also, your Related Compounds stability specification should be revised according to the data obtained throughout the accelerated stability studies. Please provide revised release and stability specifications for the subject test methods.

5. Your intended marketing container configurations for the subject drug products have been changed. According to the labeling submitted, you are proposing to distribute the 150 mg dosage form in 30's, 100's and 500's rather than the 60's and 1,000's; the 300 mg dosage form in 250's rather than the 1,000's. These are substantially different from the originally proposed container configurations. We recommend that you provide accelerated stability studies data gathered in the smallest/largest of the now proposed container configurations and include a revised "Master Packaging Specification" form. Please be aware that information pertaining to the proposed container/closure systems must be filed in the container section of your application.

B. Labeling Deficiencies

CONTAINER: 30's, 100's, 500's (150 mg) and 30's, 250's (300 mg)

Satisfactory. We acknowledge the change in package sizes.

INSERT:

1. GENERAL COMMENT

   Please increase the readability of the text in your insert. It is difficult to read in some areas.

2. PRECAUTIONS

   Pediatric Use - Revise as follows:

   ...in pediatric patients have...

3. ADVERSE REACTIONS

   Integumentary - Revise as follows:

   ...cases of erythema...

4. OVERDOSAGE

   Paragraph 3, line 1 - Revise so that "mg/kg" appear on the same line.

Please revise your package insert labeling, then prepare and submit final printed insert labeling. Please note that final printed insert labeling is not

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 3/16/95

Frank O. Holcombe, Jr., Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 74-467

Geneva Pharmaceuticals, Inc.
Attention: Beth Brannan
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

MAR 8 1994

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for the following:

NAME OF DRUG: Ranitidine Tablets USP, 150 mg and 300 mg

DATE OF APPLICATION: February 16, 1994

DATE OF RECEIPT: February 17, 1994

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Sincerely yours,

/S/ 3/8/94

Robert W. Pollock
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA#74-467
DUP/Jacket
Division File
Field Copy
HFD-600/Reading File
HFD-82
HFD-615/MBennett

Endorsements:
HFD-615/Gordon Johnston, Chief 3/8/94 /date/
HFD-615/PRickman, CSO date/3/1/94
HFD-615/WRussell, ~~CSO~~ date/3/7/94
HFD-645/BArnwine (BJ 3/8/94
WP File\russell\74-467
F/T by bcw/3-7-94
ANDA Acknowledgement Letter!

1.1

B G

Ranitidine Hydrochloride Tablets, USP
ANDA 74-467

Geneva Pharmaceuticals Inc.
Attention: Ms. Beth Brannan
2555 W. Midway Blvd.
Post Office Box 446
Broomfield, CO 80038-0446

JAN 9

Dear Ms. Brannan:

Reference is made to the *in vivo* bioequivalence study, *in vitro* dissolution data and waiver request submitted February 16, 1994, for Ranitidine Hydrochloride Tablets USP, 300 mg and 150 mg.

The Office of Generic Drugs has reviewed the referenced material and has found the bioequivalence study comparing the test product, ranitidine hydrochloride tablets, 300 mg, lot #6493066, with the reference listed drug, Zantac Tablets, 300 mg, to be incomplete for the following reasons:

1. All of the assayed data was not analyzed statistically.

   The study protocol (No. 930825) states in pertinent part "24 healthy adult male volunteers and 2 alternates will be enrolled. Samples from subjects No. 1-24 will be analyzed if the subjects complete the study." The study report notes that samples from all 26 subjects were assayed by error.

   The use of 24 subjects in the statistical analysis may have been acceptable, before the samples were assayed, however once the samples are assayed, the Office must be assured that there are no biases in selecting 24 of the 26 subjects. Since the samples from all 26 subjects were analyzed, data from all 26 subjects should be statistically analyzed and will be required to satisfy bioequivalence criterion. Please reanalyze the data using all 26 subjects and submit this information for review.

2. The limit of quantification (LOQ) of ng/mL is too low.

   Significant interference was observed for the following subject samples:

The LOQ should be increased in the future.

3. All original values should be reported together with reassayed values which were used in the study and reason for reassaying, and rationale for the used values should be reported and summarized in a table.

   For example the original values for the following samples should be reported:

4. The waiver request for bioequivalence study requirements for the 150 mg product may not be granted at this time. The waiver request should be resubmitted with the amendment.

5. It was stated that samples will be stored frozen until May 25, 1994, and then discarded. The samples were stored less than one year, the clinical study was started on October 8, 1993. In future studies the storage period should be increased to at least one year.

You are required to take an action described under 21 CFR 314.96 which will amend this application.

If you have any questions, please call Jason A. Gross, Pharm.D., at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

/S/

for

Rabindra N. Patnaik, Ph.D.
Acting Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation
and Research

4.1

ANDA 74-467

JUN 18 1997

Geneva Pharmaceuticals, Inc.
Beth Brannan
2655 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ranitidine Tablets USP.

This letter addresses 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) and June 4, 2002, (patent 4,521,431).

The Agency has reviewed the application of the 180-day exclusivity provisions of the Act to the ANDAs submitted for ranitidine. FDA's regulations interpreting these provisions are set out at 21 CFR 314.107(c). The U.S. District Court for the District of Columbia has recently held that the Agency's interpretation of the 180-day exclusivity provisions is inconsistent with the Act, and found invalid the Agency's position that in order to qualify for 180 days of exclusivity the first ANDA applicant with a paragraph IV certification must be sued and prevail in patent infringement litigation. Mova Pharmaceuticals v. Kessler, 955 F. Supp. 128 (D.D.C. 1997). See also Inwood Laboratories, Inc. v. Young, 723 F. Supp. 1523 (D.D.C. 1989), vacated as moot, 43 F.3d 712 (D.C. Cir. 1989). The court determined that the Act requires exclusivity be granted to the first ANDA submitted with a paragraph IV certification to a patent, regardless of whether such certification results in litigation or whether the applicant prevails in the litigation. Until such time as the decision is reversed on appeal, FDA will acquiesce in the Mova decision.

In the case of approval of ANDAs for ranitidine, Mova dictates that Genpharm Inc., the first ANDA applicant with a paragraph IV

certification to the patents listed for the reference drug, receive 180 days of exclusivity. The Act [21 U.S.C. § 355(j)(4)(B)(iv)] provides that a subsequent application shall be made effective not earlier than one hundred and eighty days after:

> (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or
>
> (II) the date of a decision of a court in action described in clause [505(j)(4)(b)(iii)] holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

The Agency interprets this provision as triggering the beginning of the 180 day exclusivity period with a decision of <u>any</u> court in a patent infringement action related to a paragraph IV certification finding the patent invalid or not infringed, whether or not it is the court hearing a patent infringement action resulting from the first paragraph IV certification.

The first decision of a court in an action resulting from a paragraph IV certification to a patent listed for ranitidine holding the patent invalid or not infringed has been rendered. In that case, the District Court for Connecticut granted Boehringer-Ingelheim partial summary judgement on October 7, 1996, finding that the Boehringer-Ingelheim product (Form I) does not infringe the Form II patent (patent 4,521,431). The court ruled on other claims in the case on November 18, 1996. Final judgement was entered on January 31, 1997.

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.

In the case involving Boehringer-Ingelheim, the right to appeal did not lapse until March 3, 1997. Glaxo did not appeal the October 7, 1996 ruling. The 180 day period began on March 3, 1997, and will expire on August 29, 1997. It is important to note that the FDA will not approve an ANDA prior to the expiration of exclusivity notwithstanding a licensing agreement. This is explained in the preamble to the final rule, where the

Agency states that licensees are subject to the 180-day exclusivity period [59 Fed. Reg. 50338, 50346, 50353 (Oct.3, 1994)]. Therefore, final approval cannot be granted until August 29, 1997.

If you have any questions concerning this matter, please feel free to contact Mr. Peter Rickman, Chief, Regulatory Support Branch at (301) 827-5862.

Sincerely yours,

/S/

for 6/18/97

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 74-467

Geneva Pharmaceuticals, Inc.
Attention: Beth Brannan
2655 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ranitidine Tablets USP, 150 mg and 300 mg (present as the hydrochloride).

As you may be aware, the U.S. Food and Drug Administration has recently been involved in litigation with a number of generic pharmaceutical companies over the final approval date for abbreviated new drug applications (ANDAs) for ranitidine hydrochloride tablets (Glaxo's ZANTAC). This letter is intended to provide you with an update on the Office of Generic Drugs' plans for approval of ranitidine hydrochloride ANDAs in light of the litigation.

In mid June, 1997, FDA sent letters to a number of applicants with pending ANDAs for ranitidine hydrochloride, informing them that the agency would acquiesce in Mova Pharmaceuticals v. Kessler, 955 F.Supp. 128 (D.D.C. 1997), and therefore would grant Genpharm, Inc. 180 days of exclusivity as the first ANDA for ranitidine hydrochloride with a paragraph IV certification. Genpharm's exclusivity was calculated to begin on March 3, 1997, and to expire on August 29, 1997. ANDAs for ranitidine hydrochloride could be approved once Genpharm's exclusivity expires.

Granutec Pharmaceuticals, Inc. sued FDA in the U.S. District Court for the Eastern District of North Carolina, claiming that the agency should not acquiesce in the Mova decision, but instead should apply its regulations (21 CFR 314.107(c)) to deny exclusivity to any applicant for generic ranitidine hydrochloride. The district court agreed with Granutec, and on July 3, 1997, entered an order directing FDA to approve the Granutec ANDA on July 10, 1997, pursuant to Granutec's licensing agreement with Glaxo. On July 9, 1997, the United States Court of Appeals for the Fourth Circuit stayed the District Court order.

Because the district court order has been stayed, the agency will proceed as intended prior to the initiation of the litigation.

Under the reasoning of the court in Mova, Genpharm has 180 days of exclusivity, which began on March 3, 1997, and will expire on August 29, 1997.

If you have any questions regarding the effect of this decision on the approval of your application, please contact Kassandra C. Sherrod, Project Manager, at (301) 827-5849 at the Office of Generic Drugs.

Sincerely yours,

/S/

7/15/97

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 74-467

JAN 31 1996

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

Dear Madam:

Reference is made to your abbreviated new drug application dated February 16, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ranitidine Tablets USP, 150 mg and 300 mg. The application contains certifications under section 505(j)(2)(A)(vii)(III) and (IV) of the Act.

Reference is also made to your amendments dated February 27, October 27, November 22, 1995, and January 22, 1996.

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 notice 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 a period of patent protection which expires on July 25, 1997, (patent 4,128,658) and June 4, 2002, (patent 4,521,431). However, litigation is underway in the United States District Court for the District of New Jersey involving a challenge to the patent (Glaxo Inc., Glaxo Group Limited, and Allen & Hanburys Limited v. Geneva Pharmaceuticals Inc., Ciba-Geigy Corporation, Interchem Trading Corporation and Union Quimico Farmaceutica S.A., Civil Action Nos. 94-1921 and 94-4589.) Therefore, final approval 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 [505(j)(4)(B)(iii) (I), (II), or (III)], 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 patent has expired (in this case there are two relevant patents to consider), 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, these drug products 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, Consumer Safety Officer, at (301) 594-1300, for further instructions.

Sincerely yours,

/S/ MD 1/31/96

Charles J. Ganley, M.D.
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

ANDA 74-467
Division File
DUP Jacket
Field Copy
HFD-600/Reading File
HFD-8/P.Savino

Endorsements:

HFD-645/E.Ramos/12/5/95
HFD-645/K.Sherrod/12/7/95
HFD-613/C.Zimmermann 1/3/96
HFD-613/C.Hoppes 1/4/96
HFD-645/B.Arnwine/ 1/31/96

TENTATIVE APPROVAL LETTER

ANDA 74-467

Geneva Pharmaceuticals, Inc.
Attention: Ms. Beth Brannan
2555 W. Midway Blvd.
P. O. Box 446
Broomfield, Colorado 80038-0446

OCT 27 1995

Dear Ms. Brannan:

This is in reference to your abbreviated new drug application dated February 16, 1994, and acceptable for filing on March 8, 1994, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ranitidine Tablets, USP, 150 mg and 300 mg.

Reference is also made to your amendment dated June 8, 1995.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

Chemistry Deficiency

Please revise your 300 mg finished product specification form to reflect the change from to round tablet" shape.

Labeling Deficiencies:

CONTAINER: 1000s (150 mg and 300 mg)

Satisfactory. We acknowledge the change in package size.

INSERT:

1. GENERAL COMMENT

   Due to GATT patent extensions your insert labeling should be revised as indicated below. In addition, you should amend your application as appropriate.

2. CLINICAL PHARMACOLOGY

   Clinical Trials, *Erosive Esophagitis* - Revise the subsubsection heading to appear italicized and not in bold print.

3. INDICATIONS AND USAGE

Revise the sixth indication to read as follows:

Treatment of endoscopically diagnosed erosive esophagitis. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with ranitidine 150 mg qid.

4. ADVERSE REACTIONS

Integumentary - Revise to read:

...cases of erythema multiforme, and rarely, alopecia.

5. DOSAGE AND ADMINISTRATION

a. Active Duodenal Ulcer - Revise paragraph 1 to read:

...daily. An alternative dosage of 300 mg once daily after the evening meal or at bedtime can be used for patients in whom...

b. Maintenance Therapy - Revise this subsection heading to read:

Maintenance of Healing of Duodenal Ulcers

6. HOW SUPPLIED

We encourage you to list the NDC numbers in this section.

Please revise your package insert labeling, then prepare and submit final printed insert labeling. Please note that final printed insert labeling is not required for tentative approval of an application if it is granted with more than 90 days remaining from the date when full approval can be considered. We will accept final "printers proof" for the insert only. Should further information become available relating to the safety and efficacy of this product, you may be asked to further revise your labeling prior to approval.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter

will be considered a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 10/26/95

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Geneva pharmaceuticals, inc.

2555 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

FEDERAL EXPRESS

24Feb95

BIOAVAILABILITY

Acting Director,
Office of Generic Drugs,
Division of Bioequivalence - HFD-650
Centre for Drug Evaluation and Research,
Metro Park North 2,
7500 Standish Place, Room 150
Rockville, MD 20855

DEV CORRESP

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg
Amendment - Bioequivalence Study

Dear Director:

We are submitting an amendment to our unapproved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets, in accord with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to your written communication of January 9, 1995.

1. The data has been reanalyzed to include all 26 subjects and the results are provided in Tables FDA1 and FDA2 of Attachment 1. Ranitidine serum concentrations of subject #'s 25 and 26 are also provided in Attachment 1. The results are similar to those observed for data from 24 subjects. Additional analytical information is provided in Attachment 2. This includes updated tables for quality control samples, back calculated calibration curve standard concentrations, ranitidine concentrations for all 26 subjects, standard curve parameters, repeat analysis and final concentrations, and summary of analyses codes.

2. states that future ranitidine studies will employ a higher LOQ. However, the Cmax values in the current study were greater than 400 times the LOQ and this interference should not effect the results of the bioequivalence comparison (refer to Table FDA2, Attachment 1).

3. Two tables, Tables T5.1 and T6.1, summarize the repeat analyses for this study (Attachment 2). Table T5.1 "The Repeat Analyses and Final Concentrations for Ranitidine in Human Serum" contains all values (originally coded as suspected pharmacokinetic outliers) for which a choice between two evaluable values was made.

RECEIVED

FEB 27 1995

GENERIC DRUGS

If a value was selected as a pharmacokinetic outlier and was repeated in duplicate if possible then the first value along with the repeated value is indicated in this table. If there was only one value available, *i.e.* the original value, this value would not appear in Table T5.1 and the final value would be reported as "NR" in Table T3.1 (Attachment 2). Table T5.1 includes the original value, the reassayed value(s), reason for reassaying, and the rationale for the final value used for the samples:

Table T6.1 "Summary of Analysis Codes for Ranitidine Following a 300 mg Dose" in Attachment 2 lists all repeats from the entire study and the reason for the repeat. The final value for samples listed in this table are also provided in Table T3.1 "Concentrations of Ranitidine in Human Serum Following a 300 mg Dose" (Attachment 2).

Table T5.A (Attachment 3) contains further information on samples that appear in Table T3.1 as "NR" and do not appear in Table T5.1. Table T5.A includes the original value, the reassayed value(s), reason for reassaying and the rationale for the final value use for the samples

4. The waiver request for bioequivalence study requirements for Ranitidine Tablets 150 mg is provided in Attachment 4. A summary of *in-vitro* dissolution data for the test and reference products, a copy of the analytical method, and a copy of the executed batch record for Ranitidine Tablets 300 mg, lot # 6493066, used in the bioequivalence study are also provided in Attachment 4.

5. The samples continue to remain in storage at The statement in the analytical report was incorrect and should indicate that the samples will remain in storage until 25May94 at which time the client will be be contacted regarding further retention of stored samples. This procedure is outlined in the provided in Attachment 5.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

bb/skp
Enclosure

noted 11/6/95
pcs

Geneva pharmaceuticals, inc.

2555 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

FEDERAL EXPRESS

TELEPHONE AMENDMENT

27Oct95

Director,
Office of Generic Drugs,
Division of Bioequivalence - HFD-650
Centre for Drug Evaluation and Research,
Metro Park North 2,
7500 Standish Place, Room 150
Rockville, MD 20855

NEW CORRESP [redacted]

NC

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg
Amendment - Bioequivalence Study

Dear Director:

We are submitting an amendment to our unapproved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets, in accord with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to the telephone conversation between Jason Gross (FDA) and Sue Panesar (Geneva Pharmaceuticals) on October 12, 1995.

The following data is provided in this amendment:

1. The GLM procedures for the statistical reanalysis of all 26 subjects is provided in Attachment 1.

2. A table with a detailed explanation of repeat values, including sample number, original value, repeat value, and reason for repeat is provided in Attachment 2.

This information is provided for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

bb/skp
Enclosure

RECEIVED
OCT 30 1995
GENERIC DRUGS

Geneva pharmaceuticals, inc.

2555 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

FEDERAL EXPRESS

MAJOR AMENDMENT

November 11, 1994

NDA GMC AMENDMENT

Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, Maryland 20855

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg - Form I
Major Amendment-Chemistry, Manufacturing, Controls and Labeling

Dear Director:

We are submitting an amendment to our unapproved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg - Form I in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to your communication dated June 22, 1994. The following is in response to your comments in the order they appeared in your communication.

A. Chemistry Deficiencies

Redacted 5

pages of trade

secret and/or

confidential

commercial

information

Chemistry

B. **Labeling Deficiencies**

In regard to item #B your communication: all of your comments regarding the bottle label have been noted.

Geneva will comply with the Poison Prevention Packaging Act regarding child-resistant closures. We commit our first development batch to be placed on stability with child-resistant closures. Updated Master Packaging Specifications are provided in Attachment 10.

The insert has been revised as requested throughout. Additionally, the HOW SUPPLIED SECTION has been revised to incorporate a change in available bottle sizes.

Final printed bottle labels and draft inserts are provided as requested in Attachment 11.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed and stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

BB/jfo

Geneva pharmaceuticals, inc.

2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

FEDERAL EXPRESS

November 22, 1995

NDA ORIG AMENDMENT

FPL

Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2 Room 150
7500 Standish Place
Rockville, Maryland 20855

MINOR AMENDMENT

RE: ANDA 74-467 Ranitidine Tablets, USP, 150 mg and 300 mg
Minor Amendment - Chemistry, Labeling

We are submitting an amendment to our unapproved Abbreviated new Drug Application for Ranitidine Tablets, USP, 150 mg and 300 mg in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to your communication dated October 27, 1995, which stated our response would be characterized as a minor amendment.

Chemistry Deficiency

The description for the 300 mg strength tablet has been revised to reflect "Round, standard cup" tablet. Revised finished product specification sheet is provided in Attachment 1.

Labeling Deficiencies

Reference is made to item #'s 1 thru 6 of your communication regarding insert labeling. The insert labeling has been revised as requested and is provided in Attachment 2.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-address envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

BB/ap

Enclosures as indicated

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Geneva pharmaceuticals, inc.

2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400

FEDERAL EXPRESS

August 29, 1997

AMENDMENT

Douglas Sporn, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets, 150 mg and 300 mg
Amendment - Patent and Exclusivity Information

Dear Director:

Geneva Pharmaceuticals, Inc. is hereby submitting an amendment to our tentatively approved Abbreviated New Drug Application for ANDA 74-467 Ranitidine Hydrochloride Tablets, 150 mg and 300 mg in accord with Section 505 (j) of the Federal Food, Drug, and Cosmetic Act and with 21 CFR Part 314.96 (a).

Reference is made to calls between Beth Brannan (Geneva) and Peter Rickman (FDA) on 8/28/97.

Per the reference, please find the attached Exclusivity Statement for Ranitidine Hydrochloride Tablets, 150 mg and 300 mg.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

Enclosures

BB/slc

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Geneva pharmaceuticals, inc.

2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400

FEDERAL EXPRESS

August 28, 1997

Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg & 300 mg (Form I)
Amendment - Patent Information Summary

Dear Sir:

Geneva Pharmaceuticals, Inc. is hereby submitting an amendment to our tentatively approved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets USP, 150 mg & 300 mg (Form I) in accord with Section 505 (j) of the Federal Food, Drug, and Cosmetic Act and with 21 CFR Part 314.96 to provide the following information:

Per 21 CFR 314.107(b)(3) Geneva has met the requirement to receive approval of the Ranitidine Tablet ANDA. The court has not reduced nor extended the 30 month period. The issue of extending or reducing the 30 month period has never even been raised.

Please incorporate this information into ANDA 74-467.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

BB:nb

AUG 29 1997

GP097

Geneva pharmaceuticals, inc.
2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446
(303) 466-2400

FEDERAL EXPRESS

August 27, 1997

Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

NEW CORRESP
1C

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg & 300 mg (Form I)
Amendment - Patent Information Summary

Dear Sir:

Geneva Pharmaceuticals, Inc. is hereby submitting an amendment to our tentatively approved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets USP, 150 mg & 300 mg (Form I) in accord with Section 505 (j) of the Federal Food, Drug, and Cosmetic Act and with 21 CFR Part 314.96 to provide the following information:

The certification status of the patents listed in the ***Orange Book*** (current through 17th Edition Supplement 4) for Geneva's Ranitidine Tablets is being provided.

4,880,636 (Expiration 5/13/08) - The '636 patent issued on November 14, 1989, but was not listed in the ***Orange Book*** until the June 1995 supplement. Since the patent was not listed within 30 days of issuance and since Geneva submitted an ANDA which contained the appropriate patent certification on February 16, 1994, prior to the late listing of the '636 patent, Geneva is not required to file a paragraph III or paragraph IV certification {21 CFR 314.97(a)(12)(vi)}.

4,521,431 (Expiration 6/4/02) - A paragraph IV certification was filed in Geneva's original application dated 2/16/94. Notification was sent to Glaxo on March 11, 1994. Glaxo's receipt of notice was dated 3/15/94. Glaxo sued within 45 days (4/28/94) - Civil Action No. 94-1921. Copies of the returned receipt and complaint are provided.

Summary Judgment of non-infringement in Geneva's favor was granted by the court on August 6, 1997. Therefore, it is appropriate to base the 30 months from the date of receipt of the Paragraph IV by the patent holder (September 15, 1996).

4,128,658 (Expiration 7/25/97) - The '658 has expired.

AUG 29 1997

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GP097

Therefore, there are no patent issues preventing the approval of Geneva's Ranitidine application and ANDA approval should be granted upon the conclusion of Genpharm's exclusivity (8/29/97).

Please incorporate this information into ANDA 74-467.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan

Beth Brannan, Director
Drug Regulatory Affairs

BB:nb

Enclosure(s)

Geneva pharmaceuticals, inc.

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FEDERAL EXPRESS

AMENDMENT

MINOR AMENDMENT

April 24, 1997

Douglas Sporn
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, Maryland 20855

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg (Form I) Minor Amendment - Chemistry and Manufacturing Controls, Labeling: Request for Full Approval at Patent Expiration and Updates to ANDA

Dear Director:

We are hereby submitting a minor amendment to our tentatively approved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg (Form I) in accordance with Section 505(j) of the Food, Drug and Cosmetic Act and with 21 CFR Part 314.(6(a).

Reference is made to your communications dated January 31, 1996 and April 3, 1997 (Labeling).

1. Per Section 505(j)(4)B)(iii) and your communication dated January 31, 1996, Geneva requests full approval of ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg (Form I) at the expiration of patent 4,128,658 which expires July 25, 1997.

This request is based upon the 30 month rule allowed for in Section 505(j)(4)(B)(iii). The Certified Return Receipt notifying the patent holder of Geneva's intentions was returned signed March 15, 1994. Based on our paragraph IV certification (certifying that Geneva does not infringe upon Glaxo's patent 4,521,431) and the date the notice was signed (March 15, 1994), we calculate that the 30 month period expired September 14, 1996. Therefore, we request that full approval be granted at the expiration of patent 4,128,658 on July 25, 1997.

2. **UPDATES:**

A. Updates and changes to Specifications and Methods:

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commercial

information

Specs And methods

Revised Master Manufacturing Forms for both 150 mg and 300 mg strengths are provided in Attachment 2.

C. Packaging:

At this time, we would like to take this opportunity to introduce an additional packaging size for the 150 mg strength. Geneva is proposing an intermediate 100 count packaging size which will be bracketed by the 60 count and 1000 count package sizes that have been submitted previously in this application with appropriate supportive data.

The newly proposed 100 count package size will be packaged in the same packaging configuration as the proposed 60 count package size. Because this is a bracketed package size no accelerated stability is being provided. However, the 100 count package size will be incorporated into Geneva's Long Term Room Temperature Stability Program. Since this is the same container/closure system (60cc bottle/PCR /HS/33 mm) utilized in the packaging of the 60 count package size, all supportive data has been provided in our previous amendment. A revised Master Packaging Specification is provided in Attachment 3.

3. **Labeling:**

Per your faxed communication dated April 3, 1997, the insert has been revised to be in accordance with the provided Labeling Guidance (revised February, 1997). In addition the the changes necessitated by the Labeling Guidance, information pertaining to additional package sizes (refer to our March 13, 1997 amendment to this application and #2C of this communication) has been added in the How Supplied section.

Final printed, revised inserts along with final printed container labeling (inclusive of all proposed package sizes) are provided in Attachment 4.
This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed envelope.

Sincerely,
Geneva Pharmaceuticals, Inc.

Beth Brannan, Director
Drug Regulatory
BB/ap
Enclosures as indicated

Geneva pharmaceuticals, inc.

2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

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NEW CORRESPONDENCE

Douglas Sporn
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, Maryland 20855

March 13, 1997

NDA ORIG AMENDMENT
AA

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg (Form I) New Correspondence - Chemistry and Manufacturing Controls: Alternate Package Sizes and Tighter Raw Material Specification (Polymorphism)

Dear Director:

We are hereby submitting New Correspondence to our tentatively approved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets, 150 mg and 300 mg (Form I) in accordance with Section 505(j) of the Food, Drug and Cosmetic Act and with 21 CFR Part 314.96(a).

1. Geneva we would like to take this opportunity add an additional component and packaging counts to our Master Packaging Specifications for both Ranitidine Tablets USP, 150 mg and 300 mg strengths. The following information represents the proposed additions:

Ranitidine Tablets USP 150 mg	**Ranitidine Tablets USP 300 mg**
* Addition of a 60 Count Package Size with a Plastic Child-Resistant Closure (PCR)	* Addition of a 30 Count Package Size with a Plastic Child-Resistant Closure (PCR)
* Addition of a 500 Count Package Size with a Plastic Screw Closure (PSC)	* Addition of a 250 Count Package Size with a Plastic Screw Closure(PSC)

The following data is also provided as support for the proposed additions:

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• Revised Master Packaging Specifications including the additional sizes for both 150 and 300 mg strengths are provided in Attachment 1.

• Twelve week Accelerated and Eighteen month Accumulated Room Temperature Stability for the 150 mg strength are provided in Attachment 2.

• Twelve Accelerated and Thirteen Month Accumulated Room Temperature Stability for the 300 mg strength are provided in Attachment 3.

• The below supportive component information for each bottle size is provided in Attachment 4.

Containers

- For each bottle size:
  - Certificate of analysis for USP testing
  - Diagrammatic representation
  - Moisture permeation testing for each container/closure
  - Geneva's packaging components specifications and methods
  - Geneva's analytical results

Closures

- For each closure size:
  - Manufacturer's specifications and diagrammatic representation
  - Geneva's specifications and methods for packaging components
  - Geneva's analytical results

Manufacturing equipment, processes and formula remain unaffected by the proposed package size additions.

Geneva has also revised its raw material methodology to detect smaller quantities of polymorphic Form II Ranitidine that might be present in the drug substance. Previously, method allowed for a Limit of Quantitation of NMT % and the specification for Polymorphism was set as "No Form II Detected.

The newly proposed active raw material specification for the Form II Polymorph has been has been changed to NMT %.

The revised methodology utilizes an area of ratio method of quantitating Form II material. We believe that the proposed methodology with its new Limit of Quantitation and specification of NMT % is a reliable quality control test based on linearity and reproducibility studies conducted at Geneva.

Also, in a previous amendment dated June 8, 1995 Geneva added a Related Compounds test for Finished Product in response to a deficiency comment. At this time we wish to add Related Compound testing for the Raw Material to ensure the Raw Material meets Finished Product criteria.

As an additional compendial update to the active raw material specification for the Identification test method has been updated to USP, Supplement 3. The revised raw material method and Specification Sheet are provided in Attachment 5.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed envelope.

Sincerely,

Geneva Pharmaceuticals, INC.

Beth Brannan, Director
Drug Regulatory

BB/ap
Enclosures as indicated

Geneva pharmaceuticals, inc.

2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

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TELEPHONE AMENDMENT

Director
Office of Generic Drugs
Centre for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

January 30, 1996

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg
Telephone Amendment - Patent Statements

Dear Sir:

Geneva Pharmaceuticals, Inc. is hereby submitting a Telephone Amendment to our unapproved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg in accord with Section 505 (j) of the Federal Food, Drug, and Cosmetic Act and with 21 CFR Part 314.96.

Reference is made to the telephone conversation between Peter Rickman, Branch Chief of Regulatory Support, (OGD) and Beth Brannan (Geneva Pharmaceuticals) on January 30, 1996.

Per CFR 314.107 (f)(2) the following information and Certification are provided:

NOTIFICATION OF LEGAL ACTION

- ANDA Number: 74-467
- Abbreviated New Drug Name: Ranitidine Hydrochloride Tablets USP, 150 mg and 300 mg
- Established Drug Product Name: Ranitidine Hydrochloride Tablets
- Geneva certifies that it is subject to a lawsuit filed by Glaxo Inc., Glaxo Group Limited, and Allen & Harburys Limited, Civil Action Numbers 94-1921 and 94-4589 (NHP) (Consolidated) in the United States District Court for the District of New Jersey April 28, 1994 for infringement of Patent 4,521,431. This action was filed within the 45 day time clock.

Geneva certifies that the content requirements for notification of the patent owner under CFR 314.95 (b) and (c) were met.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

C. Letue for

Beth Brannan, Director
Drug Regulatory Affairs

Geneva pharmaceuticals, inc.

2655 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

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NEW CORRESP NC

FEDERAL EXPRESS

January 22, 1996

Minor Telephone Amendment

RECEIVED JAN 23 1996 GENE...

Acting Director
Office of Generic Drugs
Centre for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

RE: ANDA 74-467 Ranitidine Hydrochloride Tablets USP, 150 mg, and 300 mg
Amendment - Chemistry

Dear Sir:

Geneva Pharmaceuticals, Inc. is hereby submitting an amendment to our unapproved Abbreviated New Drug Application for Ranitidine Hydrochloride Tablets USP, 150 mg, and 300 mg in accord with Section 505 (j) of the Federal Food, Drug, and Cosmetic Act and with 21 CFR Part 314.96.

Reference is made to the telephone conversation between Edwin Ramos (FDA) and Archie Phillips (Geneva Pharmaceuticals) on January 22, 1996.

The following data is provided in this amendment:

24 Month Room Temperature Stability Results, Lot # 6493065 - 150 mg and Lot # 6493066 300 mg.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan, Director
Drug Regulatory Affairs

Enclosures
BB/slc

ORIGINAL

Geneva pharmaceuticals, inc.

2555 W. Midway Blvd. • P.O. Box 446 • Broomfield, CO 80038-0446

(303) 466-2400 • FAX (303) 466-3717

FEDERAL EXPRESS

AMENDMENT

March 11, 1994

Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, Maryland 20855

RE: ANDA 74-467, Ranitidine Tablets USP, 150 mg and 300 mg
Amendment - Patent Information

Dear Sir:

We are submitting an amendment to our unapproved Abbreviated New Drug Application for Ranitidine Tablets USP, 150 mg and 300 mg in accordance with Section 505(j) of the Federal Food, Drug, and Cosmetic Act.

Geneva wishes to inform you that the Notice to the Patent owner and to the NDA Holder, as required by Section 505(j)(2)(B)(i)(I) and (II) of the Act, has been given upon receipt of an Acceptance Notification from the FDA for the above referenced application. A copy of Geneva's communication is provided in Attachment #1.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan

Beth Brannan
Director
Drug Regulatory Affairs

BB:jh

Attachments

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Geneva pharmaceuticals, inc.

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AMENDMENT

March 2, 1994

Director
Office of Generic Drugs
Center for Drug Evaluation & Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, Maryland 20855

NEW CORRESP
NC

RE: ANDA 74-467, Ranitidine Tablets USP, 150 mg and 300 mg

Dear Sir:

We are submitting an amendment to our unapproved Abbreviated New Drug Application for Ranitidine Tablets USP, 150 mg and 300 mg in accordance with Section 505(j) of the Federal Food, Drug, and Cosmetic Act.

Reference is made to your telephone communication on March 2, 1994.

The Field Copy Certification for this application has been corrected to state that Geneva certifies the field copy of this application is a true copy of the technical section described in 21 CFR 314.94(a)(9). The revised certification is provided in Attachment #1. Additionally, we are providing a fourth copy of our draft labeling, as requested, in Attachment #2. We apologize for any inconvenience this may have caused.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan
Director
Drug Regulatory Affairs

BB:jh

Attachments

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Geneva pharmaceuticals, inc.

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FEDERAL EXPRESS

3/2/94
52582 (2)(E)

February 16, 1994

Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North 2, Room 150
7500 Standish Place
Rockville, MD 20855

RE: Ranitidine Tablets USP, 150 mg and 300 mg - Form I

Dear Director:

Geneva Pharmaceuticals, Inc. is hereby submitting an Abbreviated New Drug Application for Ranitidine Tablets USP, 150 mg and 300 mg as required by Section 505 of the Federal Food, Drug, and Cosmetic Act.

A comprehensive table of contents is provided which shows the volume and page number of our submission's contents, as required by the regulations part 314.94(a)(1).

The blue archival copy contains the complete application. Additionally, the blue archival copy contains a method validation package. Triplicate copies of raw material and finished product specifications have been placed in a plastic sleeve, located just inside the cover.

The red review copy contains labeling and the technical portion of our application. The orange review copy contains bioequivalence information. A bioequivalence study has been completed comparing Geneva's Ranitidine Tablets USP, 300 mg to Zantac® Tablets 300 mg. A full copy of the study and requests for waiver for the 150 mg strength product are provided.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and return it in the self-addressed stamped envelope.

Sincerely,

GENEVA PHARMACEUTICALS, INC.

Beth Brannan

Beth Brannan, Director
Drug Regulatory Affairs

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