CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 74-655

CHEMISTRY REVIEW(S)

1. CHEMIST'S REVIEW NO. 4a

2. ANDA # 74-655

3. NAME AND ADDRESS OF APPLICANT
Geneva Pharmaceuticals, Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, Colorado 80038-0446

4. LEGAL BASIS for ANDA SUBMISSION
Ranitidine HCl Capsules, USP 150 mg and 300 mg are the generic version of the listed drug, Zantac®/Gel Dose 150 mg and 300 mg manufactured by Glaxo. Patent Nos. 4,128,658 and 4,521,431 which cover Polymorphic Form I and Form II respectively, will expire on 7/97 and on 2002. Also, patent No. 5,028,432 is referenced for the subject drug product which will expire on July 2, 2008. Paragraph III certifies that upon approval, the applicant will be able to make, use and sell the subject finished drug product as of December 5, 1995 (7/97 after GATT extension is applied).

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Ranitidine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

March 31, 1995--	Original Submission
May 2, 1995--	Acknowledgment receipt
September 21, 1995-	Deficiency letter
January 22, 1996--	Bio. deficiency letter
February 5, 1996--	Amendment
May 10, 1996--	Bio letter
July 11, 1996--	Bio amendment
August 14, 1996--	Deficiency letter
January 16, 1997--	Amendment
January 23, 1997--	Bio review, acceptable.
March 14, 1997--	Deficiency letter (labeling)
March 25, 1997--	Amendment (labeling only)
July 10, 1997--	New Correspondence
July 24 , 1997--	Tentative Approval
July 31, 1997--	Bio letter--acceptable
August 29, 1997--	Minor Amendment
October 1, 1997--	Minor Amendment

10. PHARMACOLOGICAL CATEGORY
H2 Receptor Antagonist

11. Rx or OTC
Rx

12. RELATED DMFs #

Scientific Associates--Contract lab

13. DOSAGE FORM
Capsules

14. POTENCY
150 mg & 300 mg

15. CHEMICAL NAME AND STRUCTURE
N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
The firm has revised their QVI's method to control the five USP listed OVIs and the process solvents used by the drug substance supplier. Also, batch size decreases are proposed for the 150 mg and 300 mg dosage forms. Detailed information can be found written in **bold** under each pertinent section of this review. No other changes are requested.

18. CONCLUSIONS AND RECOMMENDATIONS
Recommend approval letter to issue. Patent litigation issues have been resolved due to a settlement agreement reached between the applicant and Glaxo.

19. REVIEWER:
Edwin Ramos

DATE COMPLETED:
October 6, 1997

Edwin Ramos 10/10/97

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Information and are not

releasable.

Chemistry Review #4a

10/10/97

1. CHEMIST'S REVIEW NO. 4

2. ANDA # 74-655

3. NAME AND ADDRESS OF APPLICANT
Geneva Pharmaceuticals, Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, Colorado 80038-0446

4. LEGAL BASIS for ANDA SUBMISSION
Ranitidine HCl Capsules, USP 150 mg and 300 mg are the generic version of the listed drug, **Zantac®/Gel Dose** 150 mg and 300 mg manufactured by Glaxo. Patent Nos. 4,128,658 and 4,521,431 which cover Polymorphic Form I and Form II respectively, will expire on 12/5/95 and on 2002. Also, patent No. 5,028,432 is referred for the subject drug product which will expire on July 2, 2008. Paragraph III certifies that upon approval, the applicant will be able to make, use and sell the subject finished drug product as of December 5, 1995 (7/97 after GATT extension is applied).

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Ranitidine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

March 31, 1995--	Original Submission
May 2, 1995--	Acknowledgment receipt
September 21, 1995-	Deficiency letter
January 22, 1996--	Bio. deficiency letter
February 5, 1996--	Amendment
April 16, 1996--	Bio Amendment
May 10, 1996--	Bio letter
July 11, 1996--	Bio amendment
August 14, 1996--	Deficiency letter
January 16, 1997--	Amendment
January 23, 1997--	Bio review, acceptable.
March 14, 1997--	Deficiency letter (labeling)
March 25, 1997--	Amendment (labeling only)
June 25, 1997--	Telecom
June 27, 1997--	Amendment

10. PHARMACOLOGICAL CATEGORY
H2 Receptor Antagonist

11. Rx or OTC
Rx

12. RELATED DMFs #

13. DOSAGE FORM
Capsules

14. POTENCY
150 mg/300 mg

15. CHEMICAL NAME AND STRUCTURE
N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
The finished drug product and stability program dissolution specifications were revised from NLT o NLT in compliance with a Division of Bioequivalence recommendation.

18. CONCLUSIONS AND RECOMMENDATIONS
Recommend TA letter to issue.

19. REVIEWER:
Edwin Ramos
/S/

DATE COMPLETED:
June 30, 1997
6/30/97

Page(s) 11

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Chemistry Review #4.

6/30/97

Division Review Summary

ANDA: 74-655 **DRUG PRODUCT:** Ranitidine Hydrochloride I

FIRM: Geneva Pharmaceutical

DOSAGE FORM: Capsules

STRENGTHS: 150 mg & 300 mg

CGMP STATEMENT/EIR UPDATE STATUS:
Acceptable dated 1/23/97.

BIO INFORMATION:
Acceptable dated 1/23/97.

VALIDATION:
N/A

STABILITY:
Accelerated stability data (40°C and 75% RH) on the smallest (30's/150 mg & 60's/300 mg) and largest (500's for both) of the container sizes are included. These data were found to conform to specified limits.

The stability protocol is in conformance with FDA Stability Guidelines. Containers used in the stability studies are the same as those in the container/closure section of the application.

LABELING:
Acceptable, dated 3/25/97.

SIZE OF BIO BATCH:
A batch record for lot No. 6494023/300 mg is appended. A total of tablets were manufactured.

A batch record for lot No. 6494022/150 mg is appended. A total of tablets were manufactured.

DMF , drug substance manufacturer for Ranitidine Hydrochloride (Form I), was reviewed on 8/8/95 and found to be satisfactory. No relevant revisions since last review, as of 4/15/97.

SIZE OF STABILITY BATCHES:
Same as the Bio batch.

PROPOSED PRODUCTION BATCH:

RECOMMENDATION:
Recommend approval of generic drug Ranitidine Hydrochloride

Capsules, 150 mg & 300 mg.

CHEMISTRY REVIEWER:
Edwin Ramos

DATE: April 17, 1997

/S/
4/30/97

(BJ)

1. CHEMIST'S REVIEW NO. 4

2. ANDA # 74-655

3. NAME AND ADDRESS OF APPLICANT
Geneva Pharmaceuticals, Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, Colorado 80038-0446

4. LEGAL BASIS for ANDA SUBMISSION
Ranitidine HCl Capsules, USP 150 mg and 300 mg are the generic version of the listed drug, Zantac®/Gel Dose 150 mg and 300 mg manufactured by Glaxo. Patent Nos. 4,128,658 and 4,521,431 which cover Polymorphic Form I and Form II respectively, will expire on 12/5/95 and on 2002. Also, patent No. 5,028,432 is referred for the subject drug product which will expire on July 2, 2008. Paragraph III certifies that upon approval, the applicant will be able to make, use and sell the subject finished drug product as of December 5, 1995 (7/97 after GATT extension is applied).

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Ranitidine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

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February 5, 1996--	Amendment
April 16, 1996--	Bio Amendment
May 10, 1996--	Bio letter
July 11, 1996--	Bio amendment
August 14, 1996--	Deficiency letter
January 16, 1997--	Amendment
January 23, 1997--	Bio review, acceptable.
March 14, 1997--	Deficiency letter (labeling)
March 25, 1997--	Amendment (labeling only)

10. PHARMACOLOGICAL CATEGORY
H2 Receptor Antagonist

11. Rx or OTC
Rx

12. RELATED DMFs #

13. DOSAGE FORM
Capsules

14. POTENCY
150 mg/300 mg

15. CHEMICAL NAME AND STRUCTURE
N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This application is acceptable from a chemistry standpoint.

18. CONCLUSIONS AND RECOMMENDATIONS
Recommend approval letter to issue. Chemistry review only, no letter will be issued. Awaiting decision from General Counsel.

19. REVIEWER:
Edwin Ramos

DATE COMPLETED:
February 14, 1997

4/30/97

Page(s) 11

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Chemistry Review 4

4/30/97

1. CHEMIST'S REVIEW NO. 3

2. ANDA # 74-655

3. NAME AND ADDRESS OF APPLICANT
Geneva Pharmaceuticals, Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, Colorado 80038-0446

4. LEGAL BASIS for ANDA SUBMISSION
Ranitidine HCl Capsules, USP 150 mg and 300 mg are the generic version of the listed drug, **Zantac®/Gel Dose** 150 mg and 300 mg manufactured by Glaxo. Patent Nos. 4,128,658 and 4,521,431 which cover Polymorphic Form I and Form II respectively, will expire on 12/5/95 and on 2002. Also, patent No. 5,028,432 is referred for the subject drug product which will expire on July 2, 2008. Paragraph III certifies that upon approval, the applicant will be able to make, use and sell the subject finished drug product as of December 5, 1995.

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Ranitidine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

March 31, 1995--	Original Submission
May 2, 1995--	Acknowledgment receipt
September 21, 1995-	Deficiency letter
January 22, 1996--	Bio. deficiency letter
February 5, 1996--	Amendment
May 10, 1996--	Bio letter
July 11, 1996--	Bio amendment
August 14, 1996--	Deficiency letter
January 16, 1997--	Amendment
January 23, 1997--	Bio review, acceptable.

10. PHARMACOLOGICAL CATEGORY
H2 Receptor Antagonist

11. Rx or OTC
Rx

12. RELATED DMFs #

13. DOSAGE FORM
Capsules

14. POTENCY
150 mg/300 mg

15. CHEMICAL NAME AND STRUCTURE
N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This application is acceptable from a chemistry standpoint.

18. CONCLUSIONS AND RECOMMENDATIONS
Recommend facsimile to issue to convey labeling deficiencies and a bio comment.

19. REVIEWER:
Edwin Ramos
/S/

DATE COMPLETED:
February 14, 1997
3/2/97

Page(s) 11

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Chemistry Review #3

3/7/97

1. CHEMIST'S REVIEW NO. 2

2. ANDA # 74-655

3. NAME AND ADDRESS OF APPLICANT
Geneva Pharmaceuticals, Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, Colorado 80038-0446

4. LEGAL BASIS for ANDA SUBMISSION
Ranitidine HCl Capsules, USP 150 mg and 300 mg are the generic versions of the listed drug, Zantac®/Gel Dose 150 mg and 300 mg manufactured by Glaxo. Patent Nos. 4,128,658 and 4,521,431 which covers Polymorphic Form I and Form II respectively, will expire on 12/5/95 and on 2002. Also, patent No. 5,028,432 is referred for the subject drug product which will expire on July 2, 2008. Paragraph III certifies that upon approval, the applicant will be able to make, use and sell the subject finished drug prodcut as of December 5, 1995.

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Ranitidine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

March 31, 1995--	Original Submission
May 2, 1995--	Acknowledgement receipt
September 21, 1995-	Chem. deficiency letter
January 22, 1996--	Bio. deficiency letter
February 5, 1996--	Amendment
April 16, 1996 -	Amendment (bio)

10. PHARMACOLOGICAL CATEGORY
H2 Receptor Antagonist

11. Rx or OTC
Rx

12. RELATED DMFs #

2359-- Scientific Associates--Contract lab

13. DOSAGE FORM
Capsules

14. POTENCY
150 mg/300 mg

15. CHEMICAL NAME AND STRUCTURE
N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
A PAI request will be issued with this review.

18. CONCLUSIONS AND RECOMMENDATIONS
Recommend not approval letter to issue (Minor).

19. REVIEWER:
Edwin Ramos

DATE COMPLETED:
April 12, 1996

/S/

8/2/96

Page(s) 11

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Chemistry Review #2

8/2/96

1. CHEMIST'S REVIEW NO. 1

2. ANDA # 74-655

3. NAME AND ADDRESS OF APPLICANT
Geneva Pharmaceuticals, Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, Colorado 80038-0446

4. LEGAL BASIS for ANDA SUBMISSION
Ranitidine HCl Capsules, USP 150 mg and 300 mg are the generic version of the listed drug, Zantac®/Gel Dose 150 mg and 300 mg manufactured by Glaxo. Patent Nos. 4,128,658 and 4,521,431 which covers Polymorphic Form I and Form II respectively, will expire on 12/5/95 and on 2002. Also, patent No. 5,028,432 is referred for the subject drug product which will expire on July 2, 2008.

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Ranitidine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
March 31, 1995-- Original Submission
May 2, 1995-- Acknowledgement receipt

10. PHARMACOLOGICAL CATEGORY
H2 Receptor Antagonist

11. Rx or OTC
Rx

12. RELATED DMFs #

13. DOSAGE FORM
Capsules

14. POTENCY
150 mg/300 mg

15. CHEMICAL NAME AND STRUCTURE
N[2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl]-N'-methyl-2-nitro-1,1-ethenediamine, hydrochloride.

16. RECORDS AND REPORTS
N/A

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS
Recommend not approval letter to issue.

19. REVIEWER: Edwin Ramos

DATE COMPLETED: July 21, 1995

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Chemistry Review #1

9/20/95