CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40386

CHEMISTRY REVIEW(S)

APPROVAL PACKAGE SUMMARY 40-386

ANDA: 40-386

FIRM: Thames Pharmacal Co., Inc.

DRUG: Triamcinolone Acetonide

DOSAGE: Ointment

STRENGTH: 0.5%

CGMP STATEMENT/EIR UPDATE STATUS: EER acceptable 5/16/01

BIO STUDY/BIEQUIVALENCE STATUS: Bio waiver granted 9/18/00

METHODS VALIDATION: The drug is compendial

STABILITY: The firm has provided 24 months room temperature at 25-30°C and ambient humidity. The stability data conducted on 15 g, 1 oz, 80 g, and 16 oz for both lots.

LABELING REVIEW STATUS: 3/27/01

STERILIZATION VALIDATION: N/A

BATCH SIZES: The firm proposes production batch sizes are kg, kg, kg, and kg. The firm has provided copies of the executed batch records lot #300 kg) using drug substance and lot #350 kg) using drug substance. The firm Will be using the same drug substance supplier', same equipment, and same process.

COMMENTS: The application is Approvable.

REVIEWER: Nashed E. Nashed, Ph.D. DATE: 4/23/01

SUPERVISOR: Paul Schwartz, Ph.D. DATE: 4/26/01

PS 5/25/01

0N

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 40-386

3. NAME AND ADDRESS OF APPLICANT

Thames Pharmacal Co, Inc.
2100 Fifth Ave.
Ronkonkoma, NY 11779

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge this application shall entitle "paragraph II certification" that is, the reference listed drug Aristocort A Ointment 0.5% has no unexpired patent and not entitled to a period of marketing exclusivity.

5. SUPPLEMENT(s)

Original 8/3/99

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Triamcinolone Acetonide

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

N/A

10. PHARMACOLOGICAL CATEGORY

Anti inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF's

13. DOSAGE FORM

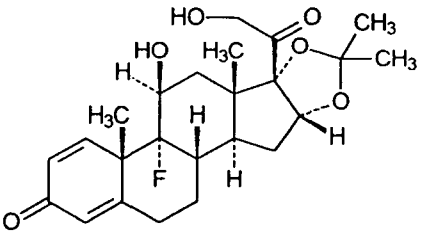
Topical Ointment

14. POTENCY

0.5%

15. CHEMICAL NAME AND STRUCTURE

Triamcinolone Acetonide. Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, $(11\beta,16\alpha)$-. $C_{24}H_{31}FO_6$. 434.51. 76-25-5. Glucocorticoid.



16. RECORDS AND REPORTS

17. COMMENTS

The firm will be asked to revise their specifications for the drug substance to include test and specifications for chromatographic purity, residual solvents, and organic volatile impurities

The firm will be asked to revise their bulk product specifications to include assay, and specification for blend uniformity with RSD.

The firm will be asked to revise their finished drug product specifications to include limits and specifications for viscosity, and related substance and impurities

The firm will be asked to provide full term room temperature Stability data.

The firm will be asked to provide cycle study data.

The firm will be asked to revise their stability specifications to include test and specification for viscosity, and related substance.

The firm will be asked to revise their stability specifications to indicate that the assay test will be conducted at the top, middle and bottom of the tubes.

The firm will be asked to provide information on the container liner.

What tests you will perform on your containers?

The firm will be asked to provide a categorical exclusion Request under 21 CFR 25.31 (a) and certifies that they are In compliance with all applicable local, state and federal environmental regulations.

The firm will be asked to provide the supplier of the drug substance on the stability report p.1140-1147.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER:	DATE COMPLETED:
Nashed E. Nashed, Ph.D.	2/3/00
Supervisor: Paul Schwartz, Ph.D.	2/7/00

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Chem. Review #1

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 40-386

3. NAME AND ADDRESS OF APPLICANT

Thames Pharmacal Co, Inc.
2100 Fifth Ave.
Ronkonkoma, NY 11779

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge this application shall entitle "paragraph II certification" that is, the reference listed drug Aristocort A Ointment 0.5% has no unexpired patent and not entitled to a period of marketing exclusivity.

5. SUPPLEMENT(s)

Original 8/3/99

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Triamcinolone Acetonide

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

2/25/00 Bio-Amendment
6/20/00 Amendment
8/31/00 Bio-Amendment

10. PHARMACOLOGICAL CATEGORY

Anti inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF's

13. DOSAGE FORM

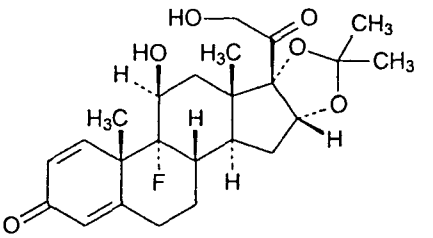
Topical Ointment

14. POTENCY

0.5%

15. CHEMICAL NAME AND STRUCTURE

Triamcinolone Acetonide. Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11β,16α)-.$C_{24}H_{31}FO_6$. 434.51. 76-25-5. Glucocorticoid.



16. RECORDS AND REPORTS

17. COMMENTS

The firm will be informed that they cannot rely on the certificate of analysis provided by the drug substance manufacturer until the validated the manufacturer. Please revise your specifications for the drug substance to include test and specifications for residual solvents, and organic volatile impurities.

The firm will be asked to tighten their limits for individual and total degradants for the finished drug product.

The firm will be asked to provide a categorical exclusion Request under 21 CFR 25.31 (a) and certifies that they are In compliance with all applicable local, state and federal environmental regulations.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 11/27/00

Supervisor: Paul Schwartz, Ph.D. 12/4/00

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Chem. Review #2

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 40-386

3. NAME AND ADDRESS OF APPLICANT

Thames Pharmacal Co, Inc.
2100 Fifth Ave.
Ronkonkoma, NY 11779

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge this application shall entitle "paragraph II certification" that is, the reference listed drug Aristocort A Ointment 0.5% has no unexpired patent and not entitled to a period of marketing exclusivity.

5. SUPPLEMENT(s)

Original 8/3/99

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Triamcinolone Acetonide

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

2/25/00 Bio-Amendment
6/20/00 Amendment
8/31/00 Bio-Amendment
Amendments 3/9/01, 4/12/01, 5/8,01, 5/31/01, 6/01/01

10. PHARMACOLOGICAL CATEGORY

Anti inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF's

13. DOSAGE FORM

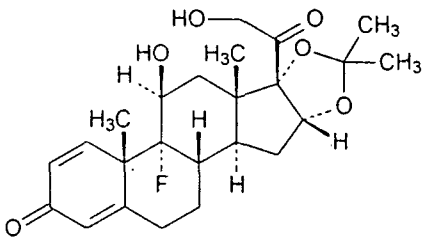
Topical Ointment

14. POTENCY

0.5%

15. CHEMICAL NAME AND STRUCTURE

Triamcinolone Acetonide. Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, $(11\beta,16\alpha)$-.$C_{24}H_{31}FO_6$. 434.51. 76-25-5. Glucocorticoid.



16. RECORDS AND REPORTS

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 6/01/01

Supervisor: Paul Schwartz, Ph.D. 6/01/01

cc: ANDA 40-386
Dup
Division File

Endorsements:

HFD-623/NNashed/ NN 6/4/01
HFD-623/PSchwartz/ PS 6/4/01

20. COMPONENTS AND COMPOSITION Satisfactory

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Chem Review #3

DEC 21 2000

38. Chemistry Comments to be provided to the Applicant.

ANDA: 40-386 APPLICANT: Thames Pharmacal Co., Inc.

DRUG PRODUCT: Triamcinolone Acetonide Ointment USP, 0.5%

The deficiencies presented below represent FAX deficiencies.

A. Deficiencies:

1. Please be informed that you cannot rely on the certificate of analysis provided by the drug substance manufacturer until you validated the manufacturer. Please revise your specifications for the drug substance to include test and specifications for residual solvents and organic volatile impurities.

2. Please tighten your limits for individual and total degradants for the finished drug product.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please provide a categorical exclusion request under 21 CFR 25.31 (a) and certify that you are in compliance with all applicable local, state and federal environmental regulations.

Sincerely yours

/S/

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

38. Chemistry Comments to be provided to the Applicant.

ANDA: 40-386 APPLICANT: Thames Pharmacal Co., Inc.

DRUG PRODUCT: Triamcinolone Acetonide Ointment USP, 0.5%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. Please revise your specifications for the drug substance to include test and specifications for chromatographic purity, residual solvents, and organic volatile impurities. Provide a revised COA with the results of those tests.

2. Please revise your bulk product specifications to include assay and specification for with RSD.

3. Please revise your finished drug product specifications to include limits and specifications for viscosity, and related substance and impurities and provide the result.

4. Please provide full term room temperature stability data.

5. Please provide cycle study data.

6. Please revise your stability specifications to include test and specification for viscosity, and related substances (individual and total). Provide the results with your additional stability data.

7. Please revise your stability specifications to indicate that the assay test will be conducted at the top, middle and bottom of the tubes.

8. Please provide information on the container liner.

9. What tests do you perform on your containers? Provide the results of such tests.

10. Please provide the supplier of the drug substance on the stability report on pages 1140 through 1147.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of the approval.

2. Please provide a categorical exclusion request under 21 CFR 25.31 (a) and certify that you are in compliance with all applicable local, state and federal environmental regulations.

3. USP methods are the regulatory methods and will prevail in the event of dispute.

4. We are waiting for your response to the letter from the Division of Bioequivalence dated November 19, 1999.

5. Please update your list of outside laboratories that will be used.

Sincerely yours,

/S/

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Chemistry I
Center for Drug Evaluation and Research