

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

40374

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 1
2. ANDA # 40-374
3. NAME AND ADDRESS OF APPLICANT

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

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge, the reference listed drug has no unexpired patent and not entitled to a period of marketing exclusivity.

5. SUPPLEMENT(s) Original 6/7/99
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

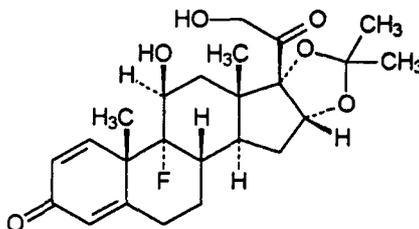
10. PHARMACOLOGICAL CATEGORY Anti inflammatory steroid
11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM Ointment
14. POTENCY 0.025%

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 β ,16 α)-.C₂₄H₃₁FO₆. 434.51. 76-25-5. Glucocorticoid.



16. RECORDS AND REPORTS

17. COMMENTS

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 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 test and specification for with RSD.

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

The firm will be requested to provide limit of quantitation and limit of detection for their method validation

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

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

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.

DMF () is deficient.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 8/30/99

Supervisor: Paul Schwartz, Ph.D.

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Chem Review #1

Verified 6/5/2001
awb

**ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT**

Application: **ANDA 40374/000**
Stamp: **07-JUN-1999** Regulatory Due:
Applicant: **THAMES PHARMA**
2100 5TH AVE
RONKONKOMA, NY 11779

Priority:
Action Goal:
Brand Name:
Established Name: **TRIAMCINOLONE ACETONIDE**
Generic Name:
Dosage Form: **ONT (OINTMENT)**
Strength: **0.025%**

Org Code: **600**
District Goal: **07-MAY-2000**

FDA Contacts: **E. HU (HFD-615) 301-827-5862 , Project Manager**
N. NASHED (HFD-629) 301-827-5848 , Review Chemist
P. SCHWARTZ (HFD-629) 301-827-5848 , Team Leader

Overall Recommendation:

ACCEPTABLE on 16-MAY-2001 by S. FERGUSON (HFD-324) 301-827-0062
WITHHOLD on 10-MAY-2001 by J. D AMBROGIO (HFD-324) 301-827-0062
WITHHOLD on 12-DEC-2000 by M. GARCIA (HFD-322) 301-594-0095
WITHHOLD on 30-MAR-2000 by B. URATANI (HFD-322) 301-827-7267
WITHHOLD on 29-MAR-2000 by B. URATANI (HFD-322) 301-827-7267

Establishment:

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **29-JUL-1999**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE RELEASE
TESTER
DRUG SUBSTANCE STERILITY
TESTER
FINISHED DOSAGE RELEASE
TESTER
~~FINISHED DOSAGE STERILITY
TESTER~~**

Establishment:

DMF No:
AADA No:

Profile: **CRU** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **12-DEC-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE MICRONIZER**

Establishment:

DMF No:
AADA No:

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

KALAMAZOO, MI 49001

Profile: **CSN** OAI Status: **NONE**
 Last Milestone: **OC RECOMMENDATION**
 Milestone Date: **29-JUL-1999**
 Decision: **ACCEPTABLE**
 Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE
MANUFACTURER**

Establishment: 1

DMF No:
AADA No: 1

Profile: **CSN** OAI Status: **NONE**
 Last Milestone: **OC RECOMMENDATION**
 Milestone Date: **29-JUL-1999**
 Decision: **ACCEPTABLE**
 Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE
MANUFACTURER**

Establishment: 1

DMF No:
AADA No:

Profile: **OIN** OAI Status: **NONE**
 Last Milestone: **OC RECOMMENDATION**
 Milestone Date: **10-MAY-2001**
 Decision: **ACCEPTABLE**
 Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE LABELER
FINISHED DOSAGE
MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE
TESTER
FINISHED DOSAGE STABILITY
TESTER
FINISHED DOSAGE STERILITY
TESTER**

1. CHEMISTRY REVIEW NO. 2
2. ANDA # 40-374
3. NAME AND ADDRESS OF APPLICANT

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

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge, the reference listed drug has no unexpired patent and not entitled to a period of marketing exclusivity.

5. SUPPLEMENT(s) Original 6/7/99
6. PROPRIETARY NAME N/A
7. NONPROPRIETARY NAME Triamcinolone Acetonide
8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Amendment 6/19/00

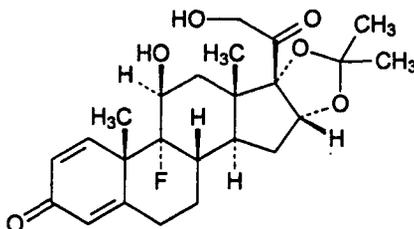
10. PHARMACOLOGICAL CATEGORY Anti inflammatory steroid
11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM Ointment
14. POTENCY 0.025%

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 β ,16 α)-.C₂₄H₃₁FO₆. 434.51. 76-25-5. Glucocorticoid.



16. RECORDS AND REPORTS

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Chem Review # 2

38. Chemistry Comments to be provided to the Applicant.

ANDA: 40-374

APPLICANT: Thames Pharmacal Co., Inc.

DRUG PRODUCT: Triamcinolone Acetonide Ointment USP, 0.025%

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.
 2. Please revise your bulk product specifications to include test and specification for blend uniformity with RSD.
 3. Please revise your finished drug product specifications to include limits and specifications for viscosity, and related substance and impurities.
 4. Please provide limit of quantitation and limit of detection for your method validation.
 5. Please provide full term room temperature stability data.
 6. Please revise your stability specifications to include tests and specifications for viscosity, and related substances and impurities.
 7. Please revise your stability specifications to indicate that the assay test will be conducted at the top, middle, and bottom of the tubes to show uniformity. It is not acceptable to mix the contents from the entire tube.
 8. DMF is deficient. The DMF holder has been notified. Please do not respond to this amendment until you have been notified by the DMF holder that the DMF deficiencies have been addressed.
- 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.

Sincerely yours,

/S/

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

ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: ANDA 40374/000
 Stamp: 07-JUN-1999
 Regulatory Due:
 Applicant: THAMES PHARMA
 2100 5TH AVE
 RONKONKOMA, NY 11779

Action Goal:
 District Goal: 07-MAY-2000
 Brand Name:
 Estab. Name: TRIAMCINOLONE ACETONIDE
 Generic Name:

Priority:
 Org Code: 600

Dosage Form: (OINTMENT)
 Strength: 0.025%

Application Comment:

FDA Contacts: J. BUCCINE (HFD-623) 301-827-5848 , Project Manager
 P. SCHWARTZ (HFD-629) 301-827-5848 , Team Leader

Overall Recommendation:

Establishment: ✓

DMF No:

AADA: ✓

Responsibilities: DRUG SUBSTANCE RELEASE TESTER
 DRUG SUBSTANCE STERILITY TESTER
 FINISHED DOSAGE RELEASE TESTER
 FINISHED DOSAGE STERILITY TESTER

Profile: CTL

OAI Status: NONE

Estab. Comment: ✓

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	29-JUL-1999				MAHMUDN

Establishment: ✓

DMF No:

AADA: ✓

Responsibilities: DRUG SUBSTANCE RELEASE TESTER
 DRUG SUBSTANCE STERILITY TESTER
 FINISHED DOSAGE RELEASE TESTER
 FINISHED DOSAGE STERILITY TESTER

Profile: CTL

OAI Status: OAI ALERT

Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	29-JUL-1999				MAHMUDN

Establishment: ✓

DMF No:

AADA: ✓

Responsibilities: DRUG SUBSTANCE STERILITY TESTER
 FINISHED DOSAGE STERILITY TESTER

Profile: CTL

OAI Status: OAI ALERT

Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
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ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

SUBMITTED TO OC 29-JUL-1999

MAHMUDN

Establishment: {

DMF No: 8821

AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile: CSN

OAI Status: NONE

Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	29-JUL-1999				MAHMUDN

Establishment: {

DMF No: 4712

AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile: CSN

OAI Status: NONE

Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	29-JUL-1999				MAHMUDN

Establishment: 2432447

THAMES PHARMACAL CO INC
2100 5TH AVE
RONKONKOMA, NY 11779

DMF No:

AADA:

Responsibilities: FINISHED DOSAGE LABELER
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER
FINISHED DOSAGE STERILITY TESTER

Profile: OIN

OAI Status: NONE

Estab. Comment:

Milestone Name	Date	Req. Type	Insp. Date	Decision & Reason	Creator
SUBMITTED TO OC	29-JUL-1999				MAHMUDN

APPROVAL PACKAGE SUMMARY FOR 40-374

ANDA: 40-374

FIRM: Thames Pharmacal Co., Inc.

DRUG: Triamcinolone Acetonide

DOSAG: Ointment

STRENGTH: 0.025%

CGMP STATEMENT/EIR UPDATE STATUS: EER acceptable 5/16/2001

BIO STUDY/BIOEQUIVALENCE STATUS: Bio waiver was granted 5/23/01

METHODS VALIDATION: The drug product is compendial

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

LABELING REVIEW STATUS: Labeling is satisfactory 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 #M299, _____ kg) using _____ drug substance and lot #349, _____ kg) using _____ drug substance. The firm will be using the same drug substance suppliers, same equipment, and same process.

COMMENTS: The application is Approvable ~~Pending acceptable EER.~~

REVIEWER: Nashed E. Nashed, Ph.D.

DATE: 4/23/01

SUPERVISOR: Paul Schwartz, Ph.D.

DATE: 4/26/01

PS 5/2/01

1. CHEMISTRY REVIEW NO. 3
2. ANDA # 40-374
3. NAME AND ADDRESS OF APPLICANT

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

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge, the reference listed drug has no unexpired patent and not entitled to a period of marketing exclusivity.

- | | |
|-------------------------------|-----------------------------------------|
| 5. <u>SUPPLEMENT(s)</u> | 6. <u>PROPRIETARY NAME</u> |
| Original 6/7/99 | N/A |
| 7. <u>NONPROPRIETARY NAME</u> | 8. <u>SUPPLEMENT(s) PROVIDE(s) FOR:</u> |
| Triamcinolone Acetonide | N/A |

9. AMENDMENTS AND OTHER DATES:

Amendment 6/19/00
 Amendments 3/9/01, 4/12/01, 5/8/01, 5/31/01, 6/1/01

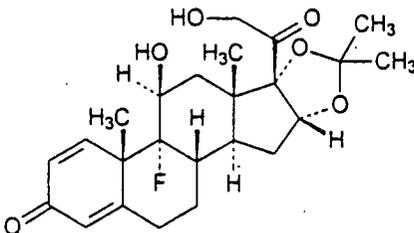
- | | |
|-------------------------------------|----------------------|
| 10. <u>PHARMACOLOGICAL CATEGORY</u> | 11. <u>Rx or OTC</u> |
| Anti inflammatory steroid | Rx |

12. RELATED IND/NDA/DMF(s)

- | | |
|------------------------|--------------------|
| 13. <u>DOSAGE FORM</u> | 14. <u>POTENCY</u> |
| Ointment | 0.025% |

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 β ,16 α)-.C₂₄H₃₁FO₆. 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 40-374
Dup
Division File

Endorsements:

HFD-623/NNashed/

HFD-623/PSchwartz/

nn 6/4/01
ps 6/4/01

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Chem Review #3

DEC 21 1990

38. Chemistry Comments to be provided to the Applicant.

ANDA: 40-374

APPLICANT: Thames Pharmacal Co., Inc.

DRUG PRODUCT: Triamcinolone Acetonide Ointment USP, 0.025%

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:

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