# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**76067**

# CHEMISTRY REVIEW(S)

# ANDA FINAL APPROVAL SUMMARY

| ANDA: | CHEMIST: | DATE: |
|---|---|---|
| 76-067 | Gil Kang | February 13, 2002 |

**DRUG PRODUCT:**
Mometasone Furoate Ointment USP

**FIRM:**
Clay-Park Labs, Inc.

| DOSAGE FORM: | STRENGTH: |
|---|---|
| Ointment | 0.1% |

**cGMP:**
EER was found acceptable on 16-NOV-2001

**BIO:**
Bioequivalence was reviewed by C. Chaurasia and found acceptable on 13-JUN-2001.

**VALIDATION - *(Description of dosage form same as firm's):***
Both the drug substance and drug products are USP articles.

**STABILITY:**
The firm has provided 3 months accelerated and 12 months room temperature stability data for Mometasone Furoate Ointment USP, 0.1% stored in 15 g and 45 g laminated tubes with white polypropylene caps. The stability results support an expiration period of 24 months.

**LABELING:**
Labeling was reviewed by A. Payne and found satisfactory on 05-SEP-2001.

**STERILIZATION VALIDATION *(If applicable)*:**
N/A

**SIZE OF BIO BATCH *(Firm's source of NDS ok?)*:**
The size of bio-batch is kg (Lot # RX081).
The drug substance, Mometasone furoate is manufactured by and the DMF was found acceptable on 11-NOV-2001.

**SIZE OF STABILITY BATCHES *(If different from bio batch, were they manufactured via the same process?):***
N/A

**ROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?:**
Proposed production batch: kg
In the event a scale-up batch is required, Clay-Park Labs, Inc. committed to manufacture the scale-up batch based on the FDA guidance for industry (SUPAC-SS) and "Changes to an Approved NDA and ANDA (November 1999)".

| Signature of chemist: | Signature of supervisor: |
|---|---|
| 2/27/02<br>/S/ | 2/27/02 |

Cpl0004.004

1. CHEMISTRY REVIEW NO. 1 2. ANDA # **76-067**

3. NAME AND ADDRESS OF APPLICANT
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Elocon®
(Mometasone furoate ointment) Ointment 0.1%

Innovator Company: Schering Corporation
Application No. 019543

Paragraph III certification: Patent No. 4,472,393
Expiration Date: 18-SEP-01

Exclusivity: None

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Mometasone Furoate Ointment USP, 0.1%

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

9. AMENDMENTS AND OTHER DATES:

| Submission date | Submission type |
|---|---|
| 12/21/00 | original |

10. PHARMACOLOGICAL CATEGORY
Anti-inflammatory: Is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

11. Rx or OTC
Rx

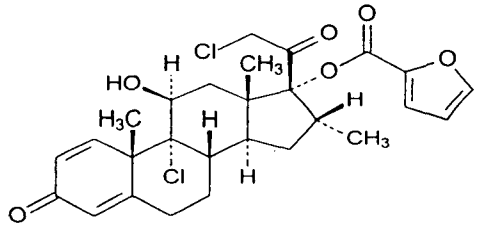
12. RELATED DMFs

| DMF number | DMF type | DMF holder | LOA(s) |
|---|---|---|---|
| | | | 07-NOV-2000 |
| | | | 31-JAN-2000 |

13. DOSAGE FORM
Ointment

14. POTENCY
0.1%

15. CHEMICAL NAME AND STRUCTURE
Mometasone Furoate. Pregna-1,4-diene-3,20-dione, 9,10-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methyl-, (11β,16α)-. $C_{27}H_{30}Cl_2O_6$. 521.43.
CAS number: 83919-23-7.




16. RECORDS AND REPORTS
None

17. COMMENTS
-Review comments are described in the review item No. 38.

-The following sections are not satisfactory:
23. Raw material controls
26. Container
28. Laboratory controls
29. Stability
32. Labeling

-The following sections are pending:
33. EER

18. CONCLUSIONS AND RECOMMENDATIONS
The application is not approvable (Major).

19. REVIEWER:
Gil Kang

DATE COMPLETED:
12-JUN-2001
18-JUN-2001(corrected)

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Chem. Review #1

1. CHEMISTRY REVIEW NO. 2 2. ANDA # **76-067**

3. NAME AND ADDRESS OF APPLICANT
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Elocon®
Mometasone furoate Ointment 0.1%

Innovator Company: Schering Corporation
Application No. 019543

Paragraph III certification: Patent No. 4,472,393
Expiration Date: 18-SEP-01

Exclusivity: None

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Mometasone Furoate Ointment USP, 0.1%

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

9. AMENDMENTS AND OTHER DATES:

| | |
|---|---|
| 21-DEC-2000 | Date of ANDA submission |
| 21-JUN-2001 | Deficiency letter based on review #1 |
| 21-AUG-2001 | Amendment (minor) |
| 31-AUG-2001 | Amendment (informational, 45 g tube testing result and the viscosity testing of the bulk) |
| 06-SEP-2001 | Amendment (informational, retest policy) |

10. PHARMACOLOGICAL CATEGORY
Anti-inflammatory: Is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

11. Rx or OTC
Rx

12. RELATED DMFs

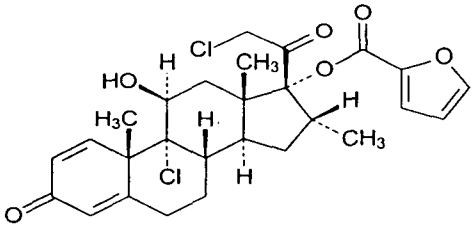
| DMF number | DMF type | DMF holder | LOA(s) |
|---|---|---|---|
| -- | -- | | 07-NOV-2000 |
| | | | 31-JAN-2000 |

13. DOSAGE FORM
Ointment

14. POTENCY
0.1%

15. CHEMICAL NAME AND STRUCTURE
Mometasone Furoate. Pregna-1,4-diene-3,20-dione, 9,10-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methyl-, (11β,16α)-. $C_{27}H_{30}Cl_2O_6$. 521.43.

CAS number: 83919-23-7.




16. RECORDS AND REPORTS
None

17. COMMENTS
-Electronic submission
-Review comments are described in the review item No. 38.

-The following section is not satisfactory:
29. Stability

-The following section is pending:
33. EER

18. CONCLUSIONS AND RECOMMENDATIONS
The application is not approvable (Fax).

19. REVIEWER:
Gil Kang

DATE COMPLETED:
05-NOV-2001

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Chem Review #2

1. CHEMISTRY REVIEW NO. 3 2. ANDA # **76-067**

3. NAME AND ADDRESS OF APPLICANT
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Elocon®
Mometasone furoate Ointment 0.1%

Innovator Company: Schering Corporation
Application No. 019543

Paragraph III certification: Patent No. 4,472,393
Expiration Date: 18-Mar-02

Exclusivity: None

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Mometasone Furoate Ointment USP, 0.1%

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

9. AMENDMENTS AND OTHER DATES:

| | |
|---|---|
| 21-DEC-2000 | Date of ANDA submission |
| 21-JUN-2001 | Deficiency letter based on review #1 |
| 21-AUG-2001 | Amendment (minor) |
| 31-AUG-2001 | Amendment (informational, 45 g tube testing result and the viscosity testing of the bulk) |
| 06-SEP-2001 | Amendment (informational, retest policy) |
| 20-NOV-2001 | Deficiency letter based on review #2 |
| 28-NOV-2001 | Amendment (Fax) |
| 13-DEC-2001 | Telephone conference |
| 14-DEC-2001 | Amendment (Telephone) |

10. PHARMACOLOGICAL CATEGORY
Anti-inflammatory: Is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

11. Rx or OTC
Rx

12. RELATED DMFs

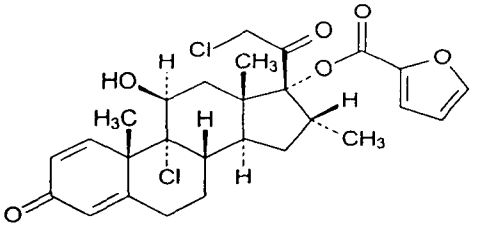
| DMF number | DMF type | DMF holder | LOA(s) |
|---|---|---|---|
| - | - | - | 07-NOV-2000 |
| | | | 31-JAN-2000 |

13. DOSAGE FORM
Ointment

14. POTENCY
0.1%

15. CHEMICAL NAME AND STRUCTURE
Mometasone Furoate. Pregna-1,4-diene-3,20-dione, 9,10-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methyl-, (11β,16α)-. $C_{27}H_{30}Cl_2O_6$. 521.43.

CAS number: 83919-23-7.




16. RECORDS AND REPORTS
None

17. COMMENTS
Electronic submission

18. CONCLUSIONS AND RECOMMENDATIONS
The application is approvable (Tentative Approval).

19. REVIEWER: Gil Kang

DATE COMPLETED: 19-DEC-2001

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Chem. Review #3

1. CHEMISTRY REVIEW NO. 4 2. ANDA # **76-067**

3. NAME AND ADDRESS OF APPLICANT
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Elocon®
Mometasone furoate Ointment 0.1%

Innovator Company: Schering Corporation
Application No. 019543

Paragraph III certification: Patent No. 4,472,393
Expiration Date: 18-MAR-2002

Exclusivity: None

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Mometasone Furoate Ointment USP, 0.1%

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

9. AMENDMENTS AND OTHER DATES:

| | |
|---|---|
| 21-DEC-2000 | Date of ANDA submission |
| 26-JAN-2001 | New Correspondence |
| **-21JUN-2001** | Deficiency letter based on review #1 |
| 21-AUG-2001 | Amendment (minor) |
| 31-AUG-2001 | Amendment (informational, 45 g tube testing result and the viscosity testing of the bulk) |
| 06-SEP-2001 | Amendment (informational, retest policy) |
| **20-NOV-2001** | Deficiency letter based on review #2 |
| 28-NOV-2001 | Amendment (Fax) |
| 13-DEC-2001 | Telephone conference |
| 14-DEC-2001 | Amendment (Telephone) |
| 27-DEC-2001 | Telephone amendment (updated patent certification) |
| **01-FEB-2002** | Tentative approval |
| 07-FEB-2002 | Minor amendment (for full Approval) |

10. PHARMACOLOGICAL CATEGORY
Anti-inflammatory: Is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

11. Rx or OTC
Rx

12. RELATED DMFs

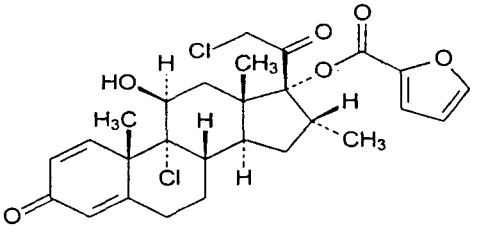
| DMF number | DMF type | DMF holder | LOA(s) |
|---|---|---|---|
| | | | 07-NOV-2000 |
| | | | 31-JAN-2000 |

13. DOSAGE FORM
Ointment

14. POTENCY
0.1%

15. CHEMICAL NAME AND STRUCTURE
Mometasone Furoate. Pregna-1,4-diene-3,20-dione, 9,10-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methyl-, (11β,16α)-. $C_{27}H_{30}Cl_2O_6$. 521.43.

CAS number: 83919-23-7.




16. RECORDS AND REPORTS
None

17. COMMENTS
Electronic submission. In a Minor Amendment submitted on 2/7/02, firm stated that there are no changes under which the drug product was TA on 2/1/02.

18. CONCLUSIONS AND RECOMMENDATIONS
The application is approvable (Final).

19. REVIEWER: Gil Kang

DATE COMPLETED: 13-FEB-2002

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Chem. Review #4

NOV 20 2001

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-067 APPLICANT: Claypark Labs, Inc
DRUG PRODUCT: Mometasone Furoate Ointment USP, 0.1%

The deficiency presented below represents a FAX deficiency.

A. Deficiency:

You have responded that the impurity limits were tightened based on control room temperature stability data, available to date. However, your stability data under room temperature and accelerated conditions do not support your proposed specifications. Please tighten or provide innovator stability data on product near expiration to support your proposed limits.

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

Please provide all available long-term room temperature stability data.

Sincerely yours,

/S/

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

JUN 2 1 2001

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-067 APPLICANT: Claypark Labs, Inc
DRUG PRODUCT: Mometasone Furoate Ointment USP, 0.1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. DMF No. for Mometasone Furoate is inadequate. The DMF holder has been notified. Please do not respond to this letter until you have obtained a letter from the DMF holder stating that they have responded to the DMF deficiencies.

2. Please include the test method and specifications for particle size in the acceptance criteria of the drug substance, and provide test results.

3. Please explain why you did not use NF grade propylene glycol monostearate and include test and set specifications for OVI in your acceptance criteria of this inactive ingredient.

4. Please set the limit for the total amount of phosphoric acid % used for pH adjustment.

5. Please provide the container/closure testing result for body, head and cap of the tubes per USP <661>.

6. You have indicated on page 1809 that 336 tubes were returned to the warehouse after packaging 15 g tubes. Please explain why you have returned these tubes.

7. Please include the resolution between the peaks of mometasone furoate and beclomethasone dipropionate, and also include the tailing factor for mometasone furoate in the method for the determination of Mometasone Furoate in Mometasone Furoate Ointment USP, 0.1% per USP 24.

8. Please tighten the limits for the total related substances for Mometasone Furoate in the finished product release based on the actual data. Also, please classify other individual impurities into known and unknown with proposed limits.

9. Please specify the column used for the assay of residual solvents for the drug substance. Also provide resolution limit between peaks for the system suitability requirement.

10. Please tighten the limits for other individual and the total related substances for Mometasone Furoate in the stability protocol based on the actual data. Also, classify other individual impurities into known and unknown with proposed limits.

11. Your stability protocol indicates that ointment in tubes is tested by sampling at the cap and crimp of the container. Please include a sampling at the middle of the container as well.

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

1. USP methods for the drug substance and product are the regulatory methods and prevail in the event of dispute.

2. Firms referenced in this ANDA should be in compliance with Current Good Manufacturing Practices at the time of approval.

3. Please provide available long-term room temperature stability data.

Sincerely yours,

/S/

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