

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 74-489

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 74-489

3. NAME AND ADDRESS OF APPLICANT

Copley Pharmaceutical Inc.
25 John Rd
Canton, MA 02021

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge that there are no patents listed for this drug product.
Exclusivity has not been granted to hydrocortisone valerate cream 0.2%, manufactured by

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Hydrocortisone Valerate

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

N/A

9. AMENDMENTS AND OTHER DATES:

Original 3/28/94
Amendment 10/3/94
Amendment 1/23/95
Amendment 10/26/95
Amendment 12/15/95
Amendment 10/31/97
Amendment 3/16/98
Amendment 7/9/98

10. PHARMACOLOGICAL CATEGORY

Anti-inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM 14. POTENCY

Cream

0.2%

15. CHEMICAL NAME AND STRUCTURE

Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17-[(1-oxopentyl)oxy]-, (11)

16. RECORDS AND REPORTS

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER:

DATE COMPLETED:

Nashed E. Nashed, Ph.D.

7/17/98

Supervisor: Paul Schwartz, Ph.D.

7/17/98

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Chemistry Review #3

MAR 02 1998

38. Chemistry Comments to be Provided to the Applicant:

ANDA: 74-489

APPLICANT: Copley Pharmaceutical Inc.

DRUG PRODUCT: Hydrocortisone Valerate Cream USP, 0.2%

The deficiencies presented below represent FACSIMILE deficiencies.

A. Deficiencies:

- B. In addition to the above deficiencies, please note that firms referenced in your application must be in compliance with CGMP at the time of approval.

Sincerely yours,



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

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 74-489

3. NAME AND ADDRESS OF APPLICANT

Copley Pharmaceutical Inc.
25 John Rd
Canton, MA 02021

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge that there are no patents listed for this drug product.

Exclusivity has not been granted to hydrocortisone valerate cream 0.2%, manufactured by

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME FOR:

Hydrocortisone Valerate

8. SUPPLEMENT(s) PROVIDE(s)

N/A

9. AMENDMENTS AND OTHER DATES:

Original 3/28/94
Amendment 10/3/94
Amendment 1/23/95
Amendment 10/26/95
Amendment 12/15/95
Amendment 10/31/97

10. PHARMACOLOGICAL CATEGORY

Anti-inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM

14. POTENCY

Cream 0.2%

15. CHEMICAL NAME AND STRUCTURE

Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17-[(1-oxopentyl)oxy]-, (11)

16. RECORDS AND REPORTS

17. COMMENTS

The firm will be asked to provide upper limit for the viscosity.

The firm will be asked to tighten the limit for based on their data.

The firm will be asked to explain the wide variation seen in the analysis of the active . Such variation is not seen in the corresponding assay of the active

The firm will be informed that Matrix approach should be submitted as supplement post approval.

The firm will be informed that the lengthening time intervals of stability testing in subsequent years should be submitted as supplement post approval.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER:

DATE COMPLETED:

Nashed E. Nashed, Ph.D.

1/20/98

Supervisor: Paul Schwartz, Ph.D.

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Chemistry Review 2

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 74-489

3. NAME AND ADDRESS OF APPLICANT

Copley Pharmaceutical Inc.
25 John Rd
Canton, MA 02021

4. LEGAL BASIS FOR SUBMISSION

The firm certifies that to the best of their knowledge that their are no patents listed for this drug product. Exclusivity has not been granted to hydrocortisone valerate cream 0.2%, manufactured by Westwood Pharmaceuticals.

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Hydrocortisone Valerate

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

N/A

9. AMENDMENTS AND OTHER DATES:

Original 3/28/94
Amendment 10/3/94
Amendment 1/23/95
Amendment 10/26/95
Amendment 12/15/95

10. PHARMACOLOGICAL CATEGORY

Anti-inflammatory

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM

Cream

14. POTENCY

0.2%

15. CHEMICAL NAME AND STRUCTURE

Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17-[(1-oxopentyl)oxy]-, (11)

16. RECORDS AND REPORTS

17. COMMENTS

The firm will be asked to revise their specification for the drug substance to include limits and specifications for and other related substances and total impurities and related substances and organic residual solvents and water. The tests results should be submitted.

The firm will be asked to provide a revised certificate of analysis from the manufacturer of the drug substance to include limits and specifications for other individual related substances and total impurities and related substance.

The firm will be asked to provide certificates of analysis from their suppliers of the inactive ingredients.

The firm will be asked to revise their specifications for the finished drug product to include limits and specifications for other individual related substances and total impurities and related substances.

The firm will be asked to revise their specification for finished drug product to indicate that the assay will be conducted by sampling at the surface, middle and bottom of the tube. In addition, tubes should be sampled at the crimp.

The firm will be asked to revise their specifications for the stability samples to include limits and specifications for other individual related substances and total impurities, related substances and degradation products.

The firm will be asked to provide the stability data for 18 and 24 months at room temperature.

The firm will be asked to revise their specifications for the release and stability of the drug product to include limits and specifications for pH and viscosity.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER:

DATE COMPLETED:

Nashed E. Nashed, Ph.D.

3/13/96

Supervisor: Paul Schwartz, Ph.D.

5/8/96

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Amnesty Review #1

74-489
Copley

COMPOSITION OF HYDROCORTISONE VALERATE CREAM USP, 0.2%

| <u>INGREDIENTS</u> | <u>GMS/KG</u> |
|--|---------------|
| HYDROCORTISONE VALERATE, USP | *2.10 gm |
| WHITE PETROLATUM, | |
| STEARYL ALCOHOL, | |
| AMPHOTERIC-9 | |
| SODIUM LAURYL SULFATE, | |
| CARBOMER 940, | |
| SORBIC ACID, | |
| PROPYLENE GLYCOL, | |
| DIBASIC SODIUM PHOSPHATE, ANHYDROUS, USP | |
| PURIFIED WATER, | 10 |
| ** (approx) | 5 |

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