CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-930

CHEMISTRY REVIEW(S)

NDA 21-930

Tradename
(Fluocinolone Acetonide 0.01% Topical Oil)

Hill Dermaceuticals, Inc.

Yong-de Lu, Ph.D.

Division of Anti-Infective and Ophthalmology Drug Products

HFD-520

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-930

2. REVIEW #: 1

3. REVIEW DATE: 07-Sep-2005

4. REVIEWER: Yong-de Lu, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
N/A	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	04-May-2001
Amendment (BC)	20-Jun-2005
Amendment (BC)	27-Jun-2005
Amendment (BC)	06-Jul-2005

7. NAME & ADDRESS OF APPLICANT:

Name:	Hill Dermaceuticals, Inc.
Address:	2650 South Mellonville Avenue Sanford, FL 32773
Representative:	Rosario G. Ramirez, Director of Medical/Regulatory Affairs
Telephone:	407-323-1887

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: [redacted]

Chemistry Review Data Sheet

b) Non-Proprietary Name (USAN): Fluocinolone Acetonide
c) Code Name/#: N/A
d) Chem. Type/Submission Priority:
- Chem. Type: 6
- Submission Priority: SP

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: anti-inflammatory agent

11. DOSAGE FORM: liquid

12. STRENGTH/POTENCY: 0.01%

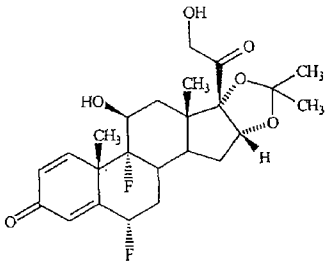
13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: _X_ Rx ___ OTC

15. _____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



6α,9-difluoro-11β,17,21-tetrahydroxypregna-1,4-diene-3,12-dione cyclic 16,17-acetal with acetone
$C_{24}H_{30}F_2O_6$, MW: 452.50, CAS#: 67-32-2

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	[redacted]	3	Current & adequate	12-Jan-2005	No need to review

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the NDA application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	33,448	Derma/Smoothe/FS for dermatitis /eczema
NDA	19,452	Derma/Smoothe/FS for dermatitis /eczema
IND	62,200	[redacted] for chronic eczematous external otitis

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	2 sites accepted	9/30/2005	Yong-de Lu
Pharm/Tox	Same as NDA19-452		
LNC			
Methods Validation	Same as NDA19-452		

Chemistry Review Data Sheet

OPDRA			
EA	Categorical exclusion		Yong-de Lu
Microbiology	Approval	01-Sep-2005	Suzanne Berkman

Appears This Way
On Original

Appears This Way
On Original

The Chemistry Review for NDA 21-930

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the chemistry, manufacturing and controls standpoint, the NDA is recommended for **approval**.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Fluocinolone Acetonide topical oil has been approved for the indication of atopic dermatitis/eczema since 1988 under the IND 33,448 and NDA 19-452 at Division of Dermatologic and Dental Products (HFD-540). Later, an amendment was filed to the original IND for Derma-Smoothe/FS (IND 33,448) to conduct clinical studies for a new indication, chronic eczematous external otitis. However, FDA assigned a new IND 62,200 to be filed with Division of Anti-inflammatory, Analgesic, and Ophthalmic Drug Product (HFD-550) to cover this new clinical studies.

Due to no changes in symptom treatment, active moiety, dosage form, formulation and manufacturing processes, applicant originally submitted an efficacy supplement to NDA 19-452 as an addition of new indication to previously approved product. However, FDA assigned this submission as a new type 6 NDA (NDA 21-930), because this drug product duplicates a drug product already approved or marketed in the United states by the same applicant, except that it is intended for a new indication or claim.

The drug substance, fluocinolone acetonide, is one of the typical corticosteroids which has been used for humans for over 50 years. The manufacturer of the drug substance is [redacted]. The detailed manufacturing and control information are located in [redacted] DMF [redacted] which was current and fully reviewed by Su Tso, Ph.D. in January 2005 and found adequate in support of the ophthalmic applications. The Letter of Authorization issued by [redacted] to authorize FDA to reference this DMF was attached in the NDA. It is justified that DMF [redacted] will also support this NDA.

The manufacturing process of Tradename for the indication of chronic eczematous external otitis is no different than that of [redacted] for the indication of adult scalp psoriasis or atopic dermatitis/eczema. There has been no change to the Chemistry, Manufacturing, and Control for Derma-Smoothe/FS.

Drug product information may be referred to the approved original NDA 19-452 for Derma-Smoothe/FS (0.01% fluocinolone acetonide) and Supplement #003 (approved on 6/27/1989), Supplement #004 (approved on 1/10/1990), and Supplement #013 (approved 4/26/1996) of NDA 19-452.

The only change is the size of the container which is changed from 4 oz used in NDA 19-452 to 1 oz being used in the NDA 21-930.

The proposed expiry date is 6 months.

B. Description of How the Drug Product is Intended to be Used

Tradename is a low to medium potency corticosteroid used for the treatment of chronic eczematous external otitis. Each gram of Tradename contains approximately 0.11 mg of fluocinolone acetonide in a blend of oils. See the packaging insert for the details.
Tradename is supplied in the [redacted] bottles containing 1 fluid ounce with the droppers (NDC 28105-XXX-XXX).

The drug product is granted for 6 months expiration dating period.

The product should be stored at 25°C (77°F); excursion permitted to 15° – 30°C (59°-86°F).

The drug product should be avoided to contact the eyes. In case of contact, wash eyes with water.

C. Basis for Approvability or Not-Approval Recommendation

Tradename duplicates drug product Derma-Smoothe/FS that has already been marketed in the United States by the same applicant in the approved NDA 19-452, except that it is intended for a new indication of chronic eczematous external otitis. It has been verified that there are no changes to Chemistry, Manufacturing, and Control sections for Derma-Smoothe/FS in NDA 19-452.

The cGMP inspection for the manufacturing and testing facilities were completed. An acceptable overall recommendation was issued by the Office of Compliance on September 9, 2005.

Actually, there is no approvability issues in the CMC section of this submission. Only container/closure system was evaluated due to the physical size change. In addition, the stability data were evaluated and the expiry date was re-assessed.

III. Administrative

A. Reviewer's Signature

Signed electronically in DFS

B. Endorsement Block

Signed electronically by Chemistry Team Leader in DFS

C. CC Block

Original NDA [redacted]
HFD-520/Chem Team Leader/LNg
HFD-830/NSchmuff
HFD-520/MED/JHarris
HFD-520/Chem Reviewer/YLu
HFD-520/CSO/MPuglisi
HFD-520/MED/WChambers

8 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry- 1

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Yong-De Lu
10/4/2005 03:37:05 PM
CHEMIST

Linda Ng
10/4/2005 07:39:18 PM
CHEMIST