CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-835

CHEMISTRY REVIEW(S)

NDA 21-835

Clobex® (clobetasol propionate) Spray, 0.05%

Dow Pharmaceutical Sciences

Hossein S. Khorshidi
Division of Anti-Infective and Ophthalmology Product
HFD-520

Table of Contents

Chemistry Review Data Sheet

1. NDA # **21-835**

2. REVIEW # 1

3. REVIEW DATE:

4. REVIEWER: Hossein S. Khorshidi

5. PREVIOUS DOCUMENTS:

None

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Date
Original	11/22/05
Amendment	8/15/05
Amendment	8/29/05
Amendment	9/26/05
Amendment	10/5/05

7. NAME & ADDRESS OF APPLICANT:

Name:	Dow Pharmaceutical Sciences
Address:	1330A Redwood Way Petaluma, CA 94954-1169
Representative:	Barry M. Calvarese, MS
Telephone:	(707) 793-2600, # 610

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Clobex®
b) Non Proprietary Name (USAN): Clobetasol propionate
c) Code Name #: N/A
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: Treatment of plaque psoriasis

11. DOSAGE FORM: Spray

12. STRENGTH/POTENCY: 0.05%

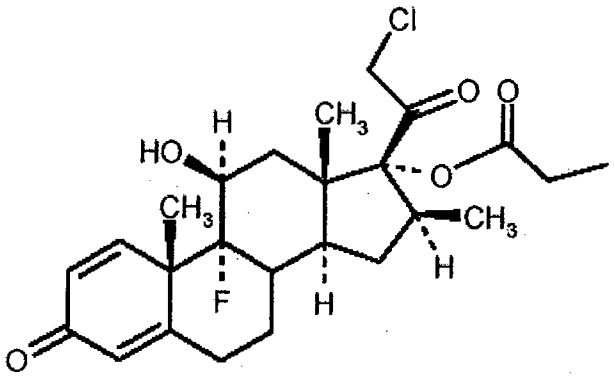
13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__X___Not a SPOTS product

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



Clobetasol Propionate
Molecular Weight: 466.97
Molecular Formula: $C_{25}H_{32}ClFO_5$
CAS # 25122-46-7

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENT
	II			3	Adequate	1/28/05	
	III			1	Adequate	9/15/05	
	III			1	Adequate	9/15/05	
	III			3	Adequate	9/15/05	

[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 application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	62,543	Clobetasol propionate spray, 0.05%

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	Acceptable by OC	9/30/05	Dr. Hossein Khorshidi
Pharm/Tox			
Biopharm			
LNC			
Methods Validation	Acceptable	9/30/05	Dr. Hossein Khorshidi
OPDRA			
EA	Acceptable	9/30/05	Dr. Hossein Khorshidi
Microbiology			

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From CMC standpoint, this NDA application is recommended for Approval.

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

Not at this time.

II. Summary of Chemistry Assessments

This is a 505(b)(1) submission which is being submitted entirely electronically on one CD-ROM. An IND was submitted under IND 62,543 which was reviewed by Dr. Saleh A. Turujman, HFD-540 on 3/7/2002. Reference is also made to pre-IND meeting on 12/19/2000 and pre NDA meeting on 10/5/04. According to the applicant, all manufacturing and testing facilities are ready for the pre approval inspection.

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

Drug Substance:

Clobetasol propionate is a white (or almost white), odorless and crystalline powder. [redacted]. The drug substance, Clobetasol Propionate, USP is manufactured and tested by [redacted] under DMF # [redacted] Adequate drug substance specification is provided. Specific [redacted] assay, impurity are among the critical parameters for establishing the identity and quality of this drug substance. Analytical procedures and the validation data are described in details. Adequate stability protocols and supporting data are submitted. Up to [redacted] of long term stability data [redacted] and up to [redacted] of accelerated stability data [redacted] are submitted in the corresponding DMF which supports the retest period of [redacted] for this drug substance.

Drug product:

The drug product is a clear, colorless alcoholic solution (spray) for topical use to treat psoriasis. It contains clobetasol propionate, USP, at the strength of 0.05% (0.5 mg/ml).

The manufacturing process consists of [redacted]

Adequate drug product specification is provided. Certain test parameters such as assay, ethanol content, and impurities are among the critical parameters for establishing the identity and quality of this product. Analytical procedures and the validation data are described in details. Three (3) primary batches (Lot Numbers 669, 670 and 671) of Clobex™ (clobetasol propionate) spray, 0.05%, and a pilot-scale Clobex™ (clobetasol propionate) spray vehicle batch (Lot Number 672) have been manufactured and submitted as primary stability batches. These batches have been incorporated in the stability program at Dow Pharmaceutical Sciences as registration batches in accordance with the ICH guidelines, including long-term ([redacted]), intermediate ([redacted]) and accelerated ([redacted]) stability conditions.

[redacted]

However, storage of this product for [redacted] under ICH intermediate stability condition (30°C/60%RH) resulted in no physical change to the container/closure system. Based on stability data, an expiration dating period of 24 months under USP controlled temperature of 20°C-25°C (68°F-77°F) with excursions between 15°C and 30°C (59°F and 86°F) is proposed for this drug product.

The drug product is filled into a 2-oz high density polyethylene (HDPE) bottle with a polypropylene cap. All related DMFs were reviewed and found to be adequate in support of NDA 21-835.

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

The drug product is a non sterile solution which is filled into a 2-oz high density polyethylene (HDPE) bottle with a polypropylene cap. The product will be dispensed from the bottle using a non-aerosol spray pump. A dose of approximately 0.14 ml per actuation (116 mg of solution containing [redacted] of clobetasol propionate is delivered from the non-aerosol spray pump. As I discussed above, the proposed container/closure system seems to be sensitive to high temperature and humidity, therefore, it is recommended that the product be not stored above 30°C.

C. Basis for Approvability or Not-Approval Recommendation

N/A to this review. The application is approved.

III. Adminstrative

A. Reviewer's Signature

Hossein S. Khorshidi, Ph.D. (signed electronically in DFS).

B. Endorsement Block

Ramesh Sood, Ph.D./Chemistry Team Leader (singed electronically in DFS).

37 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/

Hossein Khorshidih
10/24/2005 01:48:40 PM
CHEMIST

Ramesh Sood
10/24/2005 02:14:44 PM
CHEMIST