

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-844

CHEMISTRY REVIEW(S)



NDA 21-844

Desonate™ (desonide gel), 0.05%

Skin Medica

Division of Dermatological and Dental Drug Products

Ernest G. Pappas

**Branch III, Premarketing Assessment Division II
Office of New Drug Quality**



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Chemistry Review Data Sheet

1. NDA 21-844
2. REVIEW # 1
3. REVIEW DATE: 9/11 /06
4. REVIEWER: Ernest G. Pappas

5. PREVIOUS DOCUMENTS:

Previous Documents

N.A.

Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Original

Amendment

Amendment

Document Date

12/19/05

8/16/06

8/18/06

7. NAME & ADDRESS OF APPLICANT:

Name: Skin Medica

Address: 5909 Sea Lion Place, Suite
Carlsbad, CA 92008

Representative: Barry M. Cavarese, VP Regulatory & Clinical
Affairs



CHEMISTRY REVIEW



Chemistry Review Data Sheet

Telephone: (707) 793-2600

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name:
- b) Non-Proprietary Name (USAN): Desonide
- c) Code Name/# (ONDC only): CAS # 638-94-8
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 3
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b) (2)

10. PHARMACOL. CATEGORY: Atopic Dermatitis

11. DOSAGE FORM: Gel

12. STRENGTH/POTENCY: 0.05%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: Rx OTC

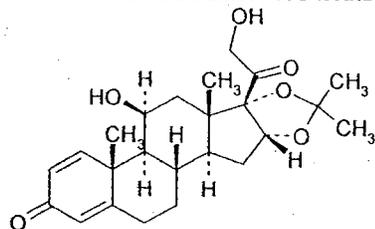
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product -- Form Completed

Not a SPOTS product

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

Figure 2.3.S.1.2.1 Chemical Structure of Desonide



Molecular Formula: $C_{24}H_{32}O_6$

Molecular Weight: 416.52

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

| DMF # | TYPE | HOLDER | ITEM REFERENCED | CODE ¹ | STATUS ² | DATE REVIEW COMPLETED | COMMENTS |
|-------|------|--------|-----------------|-------------------|---------------------|-----------------------|----------|
| — | II | — | — | 1 | Adequate | 1/30/06 | Holbert |
| — | III | — | — | 4 | Adequate | 5/15/06 | N.A. |

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)



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Chemistry Review Data Sheet

18. STATUS:

ONDC:

| CONSULTS/ CMC RELATED REVIEWS | RECOMMENDATION | DATE | REVIEWER |
|--|-----------------------|-------------|-----------------|
| EES | Acceptable | 8/30/06 | Ambrogio |
| DMETS | Acceptable | 8/8/06 | Arnwine |

**APPEARS THIS WAY
ON ORIGINAL**



The Chemistry Review for NDA 21-844

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA can be approved from a Chemistry standpoint.

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

None

II. Summary of Chemistry Assessments

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

(1) Drug Product:

The drug product, Desonate™ (desonide gel) 0.05% is a topical aqueous gel packaged in 1-g, 15-g, 30-g and 60-g tubes.

Desonate™ (desonide gel) 0.05 % was developed for the topical treatment of atopic dermatitis. In addition, desonide in an aqueous gel has anti-inflammatory, and antipruritic properties.

The firm indicated that the properties relevant to the performance of Desonate Gel 0.05% are, for example

Desonide drug substance is compatible with all of the excipients in Desonate Gel 0.05%. Each gram of Desonate Gel, 0.05% contains 0.5 mg of desonide in an aqueous gel base of purified water, glycerin, propylene glycol, edetate disodium dihydrate, methylparaben, propylparaben, sodium hydroxide, and Carbopol® 981.

This product is manufactured with components that have a history in the pharmaceutical and cosmetic applications. These components have been shown to be compatible through appropriate testing with each other and primary packages.



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Chemical testing of the product during stability has demonstrated that there are no adverse interactions between Desonide and the excipients.

The key property of Desonide drug product is the drug substance's _____

Stability data were submitted for the three (3) primary stability batches in support of the container/closure system proposed for the marketplace. Up to 18 months of stability data and statistical analysis support an expiration date of 24 months.

The Tradename, Desonate™, is currently under review by DMETS and DDMAC, and it is to be determined later by the OND Division. The labeling was reviewed and found acceptable from a technical standpoint. The storage condition is Store at 25 ° C (77 ° F); excursions permitted to 15°- 30 ° (59-86 ° F).

Establishment Inspections: All facilities as indicated in the NDA are found acceptable for CGMPs. An overall recommendation of acceptability has not been received to date from the Office of Compliance as of 8/30/06..

Environmental Assessment: The applicant's claim of categorical exclusion under regulation 21 CFR 25.31 (b) is acceptable since the EIC projection was found to be at a level well below 1ppb.

(2) Drug Substance:

The drug substance, desonide, is manufactured and supplied to by Dow Pharmaceutical Sciences, Inc. (DPSI) and Bristol-Myers Squibb - Buffalo Technical Operations (BMS-BTO) by _____. The desonide drug substance is currently marketed for NDAs 17-010 and 17-426 for Tridesilon® (Desonide 0.05%) Topical Cream and Ointment, respectively; NDA 19-048 and ANDA 72-354 for DesOwen® (Desonide 0.05%) Topical Cream and Lotion, respectively. The details of the method of

Chemistry Assessment Section

manufacture, controls, and packaging of the drug substance have been described in these NDAs and ANDAs.

The applicant cross-referenced DMF [redacted] for all CMC information as it relates to Desonide drug substance. DMF [redacted] was reviewed and found acceptable (see Chemist's Review dated 1/30/06). In this regard, information as to the description, characterization/proof of structure, synthesis, process controls, reference standard, purity profile, container/closure and stability of the desonide drug substance can be found in this DMF. A letter of authorization was given by [redacted], to allow FDA reference to DMF [redacted] in behalf of Dow Pharmaceutical Sciences, Inc. (DPSI) and Bristol-Myers Squibb - Buffalo Technical Operations (BMS-BTO).

The NDA contained the HPLC method and Validation for the determination of Desonide and related substances. The acceptance criteria and results were reported in the NDA.

The impurity profile was established for desonide and is consistent throughout its manufacturing (see DMF [redacted]). The following potential impurities have been determined: [redacted]

[redacted] Only impurity, [redacted] has been consistently found in the previously approved marketed drug products and this NDA. The acceptance criteria for related substances are the same for both specifications and comply with ICH Q3A limits. Qualification of the impurity, [redacted] has been demonstrated in the previously approved marketed drug products.

Stability data for Desonide drug substance were included in the DMF [redacted]. The drug substance has demonstrated stability for up to [redacted] under controlled room temperature conditions, and to [redacted] under accelerated conditions.

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

Desonate Gel, 0.05% is a low-to-medium potency corticosteroid indicated for the topical treatment of atopic dermatitis. Desonate Gel, 0.05% may be used in adults and in pediatric patients 3 months of age or older, although the safety and efficacy of drug use for longer than 4 weeks have not been established (see INFORMATION FOR PATIENTS- Pediatric use). Since safety and efficacy of Desonate Gel, 0.05% have not been established in pediatric patients below 3 months of age, its use in this age group is not recommended.



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C. Basis for Approvability or Not-Approval Recommendation

The NDA is recommended for approval because the information submitted in this NDA ensures the Agency's Quality Standards; i.e., identity, strength, quality and purity. In addition, the establishment inspections for all of the facilities in the NDA are found acceptable. The labeling was found acceptable from a technical standpoint.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

ChemistName/Date: Same date as draft review
ChemistryTeamLeaderName/Date
ProjectManagerName/Date

C. CC Block

Chemistry Assessment

**I. Review of Common Technical Document-Quality (Ctd-Q) Module 3.2:
Body of Data**

S DRUG SUBSTANCE [Desonide, _____]

Desonide was first approved for the treatment of steroid responsive dermatoses in the United States in the 1970s and is currently available in topical ointment, cream, and lotion formulations with indications for short-term dermal treatment. The desonide drug substance is currently marketed for NDAs 17-010 and 17-426 for Tridesilon® (Desonide 0.05%) Topical Cream and Ointment, respectively; NDA 19-048 and ANDA 72-354 for DesOwen® (Desonide 0.05%) Topical Cream and Lotion, respectively.

The applicant cross-referenced DMF _____ for all CMC information as it relates to Desonide drug substance. DMF _____ was reviewed and found acceptable (see Chemist's Review dated 1/30/06). In this regard, information as to the description, characterization/proof of structure,

75 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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

/s/

Ernest G. Pappas
9/13/2006 04:23:43 PM
CHEMIST

My chemistry review is ready for signature. I recommend
approval of the NDA.

Moo-Jhong Rhee
9/13/2006 04:45:11 PM
CHEMIST
Chief, Branch III