

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-789

CHEMISTRY REVIEW(S)



NDA 21-789

METROGEL® (metronidazole gel), 1%

Dow Pharmaceutical Sciences

Joel Steven Hathaway, Ph.D.

Division of Dermatologic and Dental Drug Products

HFD-540

Review #1

17-JUNE-2005



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Chemistry Review Data Sheet

1. NDA 21-789
2. REVIEW #1
3. REVIEW DATE 17-JUN-2005
4. REVIEWER: Joel S. Hathaway, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous Documents

Document Date

Not Applicable

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

NDA 21-789 / N-000

27-AUG-2004

NDA 21-789 / N-000 (BZ)

03-SEP-2004

NDA 21-789 / N-000 (BZ)

11-NOV-2004

NDA 21-789 / N-000 (BC)

14-FEB-2005

NDA 21-789 / N-000 (BL)

08-MAR-2005

NDA 21-789 / N-000 (BZ)

12-APR-2005

NDA 21-789 / N-000 (BC)

13-JUN-2005

7. NAME & ADDRESS OF APPLICANT:

Name: Dow Pharmaceutical Sciences, Inc.

Address: 1330A Redwood Way
Petaluma CA, 94954-1169

Representative: Barry M. Calvarese, M.S.
Vice President, Regulatory and Clinical Affairs

Telephone: (707) 793-2600

8. DRUG PRODUCT NAME/CODE/TYPE:

- | | |
|--|-------------------|
| a) Proprietary Name: | METROGEL® |
| b) Non-Proprietary Name (USAN): | metronidazole gel |
| c) Code Name/# (ONDC only): | N/A |
| d) Chem. Type/Submission Priority (ONDC only): | |
| • Chem. Type: | 3 |

Chemistry Review Data Sheet

• Submission Priority: S

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

10. PHARMACOL. CATEGORY:

11. DOSAGE FORM: Gel (aqueous)

12. STRENGTH/POTENCY: 1% (w/w)

13. ROUTE OF ADMINISTRATION: Topical

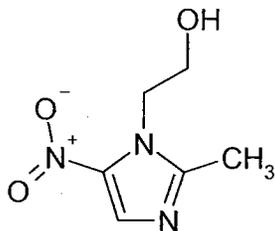
14. Rx/OTC DISPENSED: Rx OTC

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:



Appearance: White to pale yellow crystalline powder

Solubility: Metronidazole solubility at 20°C:

Solubility (Literature): Water 10.0 mg/mL

Melting Range:

pH: 5.8 (saturated aqueous solution)



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
				3	Adequate	27-SEP-2004	Reviewed for ANDA 77-197
				3			

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: N/A

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	02-JUN-2005	J. D'Ambrogio
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A		
ODS/DMETS	Acceptable		
EA	Acceptable	26-MAY-2005	J. S. Hathaway, Ph.D. (HFD-540)
Microbiology	N/A		

The Chemistry Review for NDA 21-789

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The recommendation for this NDA for the chemistry, manufacturing and controls (CMC), as submitted in the application and supporting documents, is for APPROVAL.

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)

The drug product, METROGEL®, 1%, contains the active ingredient (drug substance) metronidazole. The drug product has been developed by the Sponsor, Dow Pharmaceutical Sciences, Petaluma, California. The drug product is a topical gel with 1% w/w of the drug substance. METROGEL®, 1%, is applied topically to skin for the treatment of rosacea.

Metronidazole is an antimicrobial agent used in several approved prescription products indicated for the treatment of rosacea. These products include MetroGel® (metronidazole), 0.75%, MetroCream® (metronidazole), 0.75%, MetroLotion® (metronidazole), 0.75%, and Noritate® Cream, (metronidazole), 1%.

Chemically, metronidazole is 2-methyl-5-nitro-1 H -imidazole-1-ethanol. The molecular formula for metronidazole is C₆H₉N₃O₃. Metronidazole is an imidazole anti-bacterial agent and is also classified as an anti-protozoal. Metronidazole has also been shown to possess anti-inflammatory activity.

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

The proposed product in this 505(b)(2) application, Metronidazole Gel 1%, has been developed for the topical treatment of rosacea. This product will provide a non-alcoholic gel dosage form (often preferred by patients with rosacea) in a 1% metronidazole strength. In addition to topical products, oral and intravenous dosage forms of metronidazole are currently marketed for treatment of a variety of infectious diseases.



C. Basis for Approvability or Not-Approval Recommendation

Not applicable.

III. Administrative

A. Reviewer's Signature

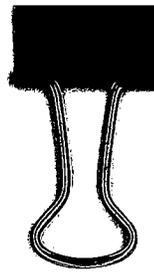
(See attached electronic signature page)

Joel S. Hathaway, Ph.D.
Review Chemist

B. Endorsement Block

JSHathaway/Date: 03-JUN-2005
ChemistryTeamLeader/RSood/
ProjectManager/KBhatt/Date:

C. CC Block



54 Page(s) Withheld

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

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

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

/s/

Steve Hathaway
6/17/05 10:54:24 AM
CHEMIST
AP recommended for CMC
Final revision for your concurrence

Ramesh Sood
6/17/05 11:05:13 AM
CHEMIST