CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-881

CHEMISTRY REVIEW(S)

NDA 21-881

MoviPrep® (PEG 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid) Powder for Oral Solution

Norgine B.V.

Sharon L. Kelly, Ph.D.
Division of Post-Marketing Assessment

Table of Contents

Chemistry Review Data Sheet

1. NDA 28-881

2. REVIEW #: 1

3. REVIEW DATE: April 05, 2006

4. REVIEWER: Sharon Kelly, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
None	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original Amendment	07-JUN-2005
Amendment 000 BC	29-DEC-2005
Amendment 000 BC	03-JAN-2006
Amendment 000 BC	01-MAR-2006
Amendment 000 BC	15-MAR-2006
Amendment 000 BC	20-MAR-2006
Amendment 000 BC	23-MAR-2006
e-mail from Sponsor (labeling)	04-April-2006

7. NAME & ADDRESS OF APPLICANT:

Name: Norgine B.V.

Address: Keaton House, Widewater Place, Moorhall Road, Harefield, Uxbridge, Middlesex, UB9 6NS, United Kingdom

Representative: Ramona Krailler, Ph.D., Regulatory Affairs
Norgine International Ltd. ALSO
Marilyn R. Carlson, D.M.D., M.D., RAC
entreMeDica, Inc., 1229 Caminito Graciela,
Encinitas, California 92024

Telephone: +44 7795 005 484 ALSO
(858) 759 - 8265

8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: MoviPrep®
   b) Non-Proprietary Name (USAN): Polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid powder for oral solution
   c) Code Name/# : NRL994; "Low Dose Bowel Prep"
   d) Chem. Type/Submission Priority
      - Chem. Type: 5
      - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 21 USC Sec. 505 (b)(2)

10. PHARMACOL. CATEGORY: Bowel cleansing prior to colonoscopy,

11. DOSAGE FORM: Powder for reconstitution

12. STRENGTH/POTENCY: Polyethylene glycol 3350 NF 100g, sodium sulfate USP 7.500g, sodium chloride USP 2.691g, potassium chloride USP 1.015g, sodium ascorbate USP 5.900g and ascorbic acid USP 4.700g per Pouch (A or B)

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: XX 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:

Polyethylene glycol 3350 NF $H(C_2H_4O)_nOH$ Average MW= 3350 (n=76)

sodium sulfate USP	Na_2SO_4 MW= 142.06
sodium chloride USP	NaCl MW=58.44
potassium chloride USP	KCl MW=74.55
sodium ascorbate USP	$C_6H_7NaO_6$ MW=198.11
ascorbic acid USP	$C_6H_8O_6$ MW=176.12

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	[redacted]	4	N/A		Letter of Authorization in NDA submission
[redacted]	II	[redacted]	[redacted]	4	N/A		As above
[redacted]	II	[redacted]	[redacted]	4	N/A		As above

[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

Original application	IND 63,268 (MOVIPREP)	Provided CMC information for the drug substance and product
FAX Communication of April 8th , 2005 (Letter to Sponsor dated April 7, 2005)	IND 63,268	Agency response providing specific guidance for Module 3 information requirements

18. STATUS:

CONSULTS/CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	**Withhold**	**April 5, 2006**	**S. Adams**
DMETS	**Moviprep Acceptable as a proprietary name; see Review for further CMC recommendations**	**17-AUG-2005**	**Nora Roselle, PharmD, Safety Evaluator**

The Chemistry Review for NDA 21-881

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From a Chemistry, Manufacturing, and Controls perspective, this NDA application is approvable pending satisfactory CGMP inspections on the manufacturing facilities.

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)

The drug product, Moviprep powder for oral solution, is formulated from compendial pharmaceutical ingredients which have been used in FDA-approve products, or in the food or vitamin industry, and is packaged in four individual pouches (2xPouch A and 2xPouch B) containing different active ingredients. Pouch A contains polyethylene glycol 3350, NF; sodium sulfate _____, USP; sodium chloride, USP and potassium chloride, USP with sweetening and flavoring excipients. Pouch B contains sodium ascorbate, USP and ascorbic acid, USP. The ingredients have adequate specifications to ensure the safety and efficacy of the drug product. The manufacturing procedure is sufficiently controlled to produce a drug product that meets the dosage claim on the package insert. The pouches are made of the same _____

The powders in the individual pouches are reconstituted, together, in water to a volume of 1 liter, in a supplied _____ container or in a container of the patient's choosing.

Each active ingredient is a known chemical entity that has been adequately characterized in the literature with regards to its physical and chemical properties and is controlled by a United States Pharmacopeia (USP) or National Formulary (NF) monograph.

The Sponsor provides 24 months real time stability data that supports a 36 month expiration dating period when labeled with the following uniform storage statement:
Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]

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

Moviprep is administered orally as a gastrointestinal lavage. It is indicated for bowel cleansing prior to colonoscopy _____ Since treatment

is generally limited to annual use, the patient has limited exposure to the drug product formulation.

A course of treatment consists of 2 liters of MoviPrep, i.e. , 1 x pouch A and 1 x pouch B dissolved together in 1 liter of water, followed by a second pouch A and a second pouch B dissolved together in a further 1 liter of water.

The reconstituted solution should be refrigerated and used within 24 hours.

C. Basis for Approvability or Not-Approval Recommendation

All CMC information requests to the Sponsor have been satisfactorily addressed.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Sharon Kelly, Ph.D. /
Moo-Jhong Rhee, Ph.D. /
Project Manager /

C. CC Block

115 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/

Sharon Kelly
4/6/2006 04:35:25 PM
CHEMIST

Moo-Jhong Rhee
4/6/2006 05:34:12 PM
CHEMIST
Chief, Branch III

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On Original

NDA 21-881

MoviPrep® (PEG 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid) Powder for Oral Solution

Norgine B.V.
Division of Gastroenterology Drug Products

Sharon L. Kelly, Ph.D.
Division of Post-Marketing Assessment

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Chemistry Review Data Sheet

1. NDA 28-881

2. REVIEW #: 2

3. REVIEW DATE: July 20, 2006

4. REVIEWER: Sharon Kelly, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents:	Document Date
Original Amendment	07-JUN-2005
Amendment 000 BC	29-DEC-2005
Amendment 000 BC	03-JAN-2006
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e-mail from Sponsor (labeling)	04-APR-2006

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	02-JUN-2006

7. NAME & ADDRESS OF APPLICANT:

Name:	Norgine B.V.
Address:	Keaton House, Widewater Place, Moorhall Road, Harefield, Uxbridge, Middlesex, UB9 6NS, United Kingdom
Representative:	Ramona Krailler, Ph.D., Regulatory Affairs Norgine International Ltd. ALSO Marilyn R. Carlson, D.M.D., M.D., RAC entreMeDica, Inc., 1229 Caminito Graciela, Encinitas, California 92024
Telephone:	+44 7795 005 484 ALSO (858) 759 - 8265

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: MoviPrep®

b) Non-Proprietary Name (USAN): Polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid powder for oral solution

c) Code Name/# : NRL994; "Low Dose Bowel Prep"

d) Chem. Type/Submission Priority:

- Chem. Type: 5
- Submission Priority: S

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18. STATUS:

CONSULTS/CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Acceptable	11-JUL-2006	S. Adams
DMETS	Moviprep Acceptable as a proprietary name; see Review for further CMC recommendations	17-AUG-2005	Nora Roselle, PharmD, Safety Evaluator

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Each active ingredient is a known chemical entity that has been adequately characterized in the literature with regards to its physical and chemical properties and is controlled by a United States Pharmacopeia (USP) or National Formulary (NF) monograph.

The Sponsor provides 24 months real time stability data that supports a 36 month expiration dating period when labeled with the following uniform storage statement: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]

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The prepared solution should be refrigerated and used within 24 hours.

C. Basis for Approvability or Not-Approval Recommendation

All CMC information requests to the Sponsor have been satisfactorily addressed.

III. Administrative

A. Reviewer's Signature

Sharon Kelly, Ph.D. /

B. Endorsement Block

Moo-Jhong Rhee, Ph.D. /
Project Manager /

C. CC Block

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_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Sharon Kelly
7/25/2006 01:58:35 PM
CHEMIST

Moo-Jhong Rhee
7/25/2006 02:17:57 PM
CHEMIST
Chief, Branch III

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