

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-015

CHEMISTRY REVIEW(S)



NDA 22-015

**MiraLAX™
(polyethylene glycol 3350) powder for solution**

Braintree Laboratories, Inc.

Shulin Ding, Ph.D.

**Office of New Drug Quality Assessment
Division of Pre-Marketing Assessment II**



Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	3
The Executive Summary	7
I. Recommendations.....	7
A. Recommendation and Conclusion on Approvability.....	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable.....	7
II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used.....	8
C. Basis for Approvability or Not-Approval Recommendation.....	8
III. Administrative.....	8
A. Reviewer's Signature.....	8
B. Endorsement Block.....	8
C. CC Block	8
Chemistry Assessment.....	9
I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data.....	9
S DRUG SUBSTANCE [Name, Manufacturer].....	9
P DRUG PRODUCT [Name, Dosage form].....	13
A APPENDICES	24
R REGIONAL INFORMATION	24
II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1	24
A. Labeling & Package Insert	24
B. Environmental Assessment Or Claim Of Categorical Exclusion	24
III. List Of Deficiencies To Be Communicated.....	24
IV. Establishment Inspection	25



Chemistry Review Data Sheet

1. NDA 22-015
2. REVIEW #: 1
3. REVIEW DATE: 25-Aug-2006
4. REVIEWER: Shulin Ding, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous DocumentsDocument Date

N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) ReviewedDocument Date

Original

6-Dec-2005

Amendment¹

15-Mar-2006

Amendment²

15-Aug-2006

¹The 3/15/06 amendment provides for a response to the information request outlined in the filing letter.²The 8/15/06 amendment provides for a response to the CMC IR letter dated Aug. 8, 2006.

7. NAME & ADDRESS OF APPLICANT:

Name: Braintree Laboratories, Inc.

Address: 60 Columbian Street
P.O. Box 850929
Braintree, MA 02185Representative: Vivian A. Caballero, Director of Regulatory Affairs
Braintree Laboratories, Inc.
P.O. Box 850929
Braintree, MA 02185Telephone: 781-843-2202
781-843-7932 (fax)



CHEMISTRY REVIEW



Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: MiraLAX OTC
b) Non-Proprietary Name (USAN): Polyethylene glycol 3350, NF
c) Code Name/# (ONDC only): None
d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type: 8a
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(1)

10. PHARMACOL. CATEGORY: Laxative

11. DOSAGE FORM: Powder for solution

12. STRENGTH/POTENCY: 17 g per dose

13. ROUTE OF ADMINISTRATION: Oral

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:

- USAN NAME: Polyethylene glycol 3350, NF
CHEMICAL NAME: Poly(oxy-1,2-ethanediyl), α -hydro- ω -hydroxy-
CAS NUMBER: CAS-25322-68-3
MOLECULAR WEIGHT: Average molecular weight 3000-3700
CHEMICAL FORMULA: $H(OCH_2CH_2)_nOH$ (n=68-84)



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS	DATE REVIEW COMPLETED	COMMENTS ³
[REDACTED]	II	[REDACTED]	[REDACTED]	3	Adequate	May 10, 2006	Reviewed by David Skanchy.
[REDACTED]	III	[REDACTED]	[REDACTED]	2	N/A	N/A	A review is not conducted because this is a facility DMF.
[REDACTED]	III	[REDACTED]	[REDACTED]	4	Adequate	N/A	Information provided in the NDA is adequate.
[REDACTED]	III	[REDACTED]	[REDACTED]	4	Adequate	N/A	Information provided in the NDA is adequate.
[REDACTED]	III	[REDACTED]	[REDACTED]	3	Adequate	Nov. 14, 2005	Reviewed by Raymond Frankewich
[REDACTED]	III	[REDACTED]	[REDACTED]	3	Adequate	August 25, 2006	Reviewed by Shulin Ding.

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")

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
None		

C. Related Documents:

DOCUMENT	APPLICATION NUMBER	OWNER	DESCRIPTION/COMMENT
NDA	20-698	Braintree Laboratories	Approved prescription use of MiraLax



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. CONSULTS/CMC-RELATED REVIEWS:

CONSULTS	RECOMMENDATION	DATE	REVIEWER	COMMENTS
Biometrics	N/A			
EES	Acceptable	April 24, 2006	Shulin Ding	
Pharm/Tox	Approval	July 7, 2006	Tamal K. Chakraborti	
Biopharm	Acceptable	Aug. 17, 2006	Tien Mien Chen	
DMETS	N/A			
Division of Nonprescription Products	Acceptable with the recommended changes	Aug. 25, 2006	Reynold Tan	OTC comments on labeling and labels.
Methods Validation	N/A	---	N/A	No consult needed.
EA (Environmental assessment)	Acceptable	---	Shulin Ding	The applicant requests a categorical exclusion pursuant to 21 CFR 25.31(a).
Microbiology	N/A	---	N/A	No consult needed

19. ORDER OF REVIEW (OGD Only): N/A

**Appears This Way
On Original**



The Chemistry Review for NDA 22-015

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is recommended for APPROVAL (AP) from a CMC standpoint.

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

No recommendations at this time.

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

1) Drug Product

The proposed drug product, MiraLAX™ (polyethylene glycol 3350) powder for solution, is an OTC switch of the prescription product MiraLax™ owned by Braintree Laboratories, Inc. The prescription MiraLax (NDA 20-698) was approved on Feb. 18, 1999 for the indication of adult occasional constipation. The NDA holder, Braintree Laboratories, is now seeking OTC marketing of the product for the adult indication of occasional constipation.

MiraLAX™ (polyethylene glycol 3350) powder for solution contains no excipients. It is composed of only the active ingredient, polyethylene glycol 3350, NF. The product is packaged in white, _____ bottles at three sizes (119 g, 238 g, and 527 g), and also in unit dose foil pouch at the size of 17 g. The bottle and unit dose pouch configurations have been approved for the prescription NDA. The supplier of the bottles and closures for the OTC marketing, however, is different from that approved for the prescription NDA. The OTC NDA proposes to source bottles and closures from _____) whereas the approved source for the prescription NDA is _____

The recommended expiry period for the MiraLAX OTC is 24 months when stored at 25°C (77°F) with excursions permitted to 15-30°C (59-86°F), which is the approved expiry period/storage condition for the prescription MiraLax. Because the Division of Nonprescription Products prefers only a temperature range to be given in the OTC label/labeling for storage instruction, the recommendation is modified and becomes "24 months when stored at 20°-25°C". The temperature range of 20°-25°C is preferred over 15°-25°C because the former is consistent with USP definition of "controlled room temperature," and supported by the long term stability data provided in the NDA. The temperature range of 15°-25°C is also acceptable to this reviewer but its support would require an extraordinary extrapolation of the accelerated 4°C stability data.

The recommended expiry period and storage condition is supported by the stability data provided in the OTC NDA under review, which include accelerated (6 months at 4°C and 40°C) and long term (25°C, 12 months for bottles and 24 months for pouch) stability data from one drug product batch for each packaging configuration. The submitted data show the OTC product well meets the product specification throughout

**Chemistry Assessment Section**

the study period. The limited stability data (i.e. only one batch) is acceptable since all packaging configurations have been approved under the prescription NDA and the only difference between the two NDAs is the bottle/closure supplier.

2) Drug Substance

NDA 22-015 contains one active ingredient, polyethylene glycol 3350, whose pharmacological class is osmotic laxative. Unlike other osmotic laxatives such as lactulose, phosphates, sulfates or magnesium salts, polyethylene glycol 3350 is virtually non-absorbed, and metabolism is not required for its action. It works by retaining water with the stool.

The NDA applicant references _____ for polyethylene glycol 3350 drug substance. _____ has recently been reviewed and concluded to be adequate to support _____ (DMF Chemistry Review #5 by David Skanchy, May 10, 2006), _____

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

The drug product is intended to be used for the treatment of occasional constipation in adults. The average dose is 17 g per day in 4-8 ounces of water, juice, soda, coffee or tea. It should always be taken by mouth.

The drug product is packaged in the following configurations: bottles (119 g, 238 g, and 527 g), and unit dose foil pouch (17 g).

C. Basis for Approvability or Not-Approval Recommendation

The application is recommended for approval (AP) based on the following:

- Satisfactory cGMP status of the manufacturing/testing sites.
- Same CMC information which has been approved for prescription MiraLax NDA (NDA 20-698) with the exception of bottle/closure information.
- Adequate stability and container/closure information to support the new bottles and closure.
- Confirmed comparability to the prescription MiraLax in drug product stability.

III. Administrative**A. Reviewer's Signature**

Shulin Ding, Ph.D.

B. Endorsement Block: in DFS**C. CC Block: in DFS**

19 Page(s) Withheld

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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/

Shulin Ding
8/28/2006 05:06:03 PM
CHEMIST

Moo-Jhong Rhee
8/28/2006 05:54:36 PM
CHEMIST
Chief, Branch III