CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-281

CHEMISTRY REVIEW(S)

NDA 22-281

Zegerid OTC™, Capsule 20 mg

Schering-Plough

Christopher Hough

Review Chemist

Office of New Drug Quality Assessment
Division of Office of New Drug Quality Assessment
Pre-Marketing Division II, Branch III

CMC REVIEW #3

For the Office of Non-Prescription Drugs
(HFD-560)

Table of Contents

CMC Review Data Sheet

1. NDA 22-281

2. REVIEW #: 3

3. REVIEW DATE: 21-Oct-2009

4. REVIEWER: Christopher Hough, Ph.D.

5. PREVIOUS DOCUMENTS:

Original Submission	10-Mar-08
Amendment-New Table of Contents	12-Mar-08
Amendment-Responses to CMC IR requests	27-Jun-08
Amendment-Addition of Executed Batch Records	28-Aug-08

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Resubmission/Class2/Amendment	06-Jun-2009
Labeling/Container-Carton Draft	30-Sep-2009

7. NAME & ADDRESS OF APPLICANT:

Name:	Schering-Plough HealthCare Products
Address:	556 Morris Avenue, Summit, NJ 07901-1330
Representative:	William Cochran, Sr. Manager, Regulatory Affairs
Telephone:	908 473-1858

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Zegerid OTC™ 20 mg capsules
b) Non-Proprietary Name: Omeprazole/Sodium Bicarbonate
c) Code Name/# (ONDQA only): N/A
d) Chem. Type/Submission Priority (ONDQA only):
- Chem. Type: 5
- Submission Priority: Standard

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

10. PHARMACOL. CATEGORY: Antacid

11. DOSAGE FORM: capsule

12. STRENGTH/POTENCY: 20 mg Omeprazole, 1.10 g Sodium Bicarbonate

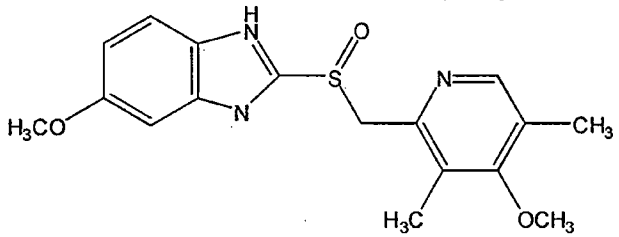
13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx ✓OTC

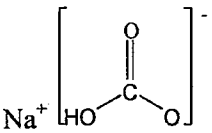
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

___✓___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl] sulfonyl] benzimidazole



$C_{17}H_{19}N_3O_3S$
345.42
Sodium Bicarbonate, Monosodium Carbonate, Monosodium salt of Carbonic Acid



$NaHCO_3$
84.01

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	2		Drug substance	1	Adequate	27-Jul-2007	Chris Hough
	3		Capsule shells	3	Adequate	21-Jan-2003	George Lund
	3		Capsule banding			13-Jun-2003	Arthur Shaw
	3		Printing ink	3	Adequate	19-Jun-2002	Stuart Zimmerman
	3		Containers	3	Adequate	18-Sep-2007	Craig Bertha
	3		Closures	3	Adequate	9-Dec-2004	Rapti Madurawe
	3		Induction seal	3	Adequate	29-Jan-2003	Lyudmila Soldatova,

b(4)

[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		
NDA	21-849 21-636 19-810 21-229	ZegeridRx capsule Zegerid Rx Oral Suspension Prilosec Rx Prilosec OTC

b(4)

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NAI	19-Mar-2008	Mike Welch
EES	Acceptable	22-Dec-2008	Office of Compliance
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A		
DMETS	N/A		
EA	Categorical exclusion is granted	7-Oct-2008	Chris Hough
Microbiology	N/A		

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

In the last review of this application, a recommendation for approval from the CMC perspective could not be made because of an unresolved issue with labeling. This issue has now been resolved. This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. An "Acceptable" recommendation is made from the Office of Compliance for the site inspections. Therefore, from the CMC perspective, this NDA is recommended for approval.

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

N/A

II. Summary of CMC Assessments

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

(1) Drug Substances

See Review #1

(2) Drug Product

See Review #1.

B. Description of How the Drug Product is intended to be used

See Review #1.

C. Basis for Approvability or Not-Approval Recommendation

The sponsor has provided sufficient information on raw material controls, manufacturing processes and process controls, and adequate specification for assuring consistent product quality of the drug substance and drug product. The NDA also has provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product during the expiration dating period.

All facilities have acceptable site recommendations. All labeling issues have been resolved. Therefore, from the CMC perspective, this NDA is recommended for approval.

CMC Assessment

I. Review of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body of Data
See Review #1.

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling: All parties have agreed to the following for the carton and container labels. A mockup container-carton label is shown below at the penultimate state before final agreement was reached. The [redacted] has been removed from the statement of the established names of the active pharmaceutical ingredients (APIs) and the strengths of the APIs have been added after their functions as follows: b(4)

Omeprazole/Acid Reducer 20 mg
Sodium Bicarbonate/Allows Absorption of this Omeprazole Product 1100 mg

[redacted] b(4)

3 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 1

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22281	ORIG-1	SCHERING PLOUGH HEALTHCARE PRODUCTS INC	ZEGERID OTC CAPSULES

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

/s/

CHRISTOPHER J HOUGH
10/22/2009

MOO JHONG RHEE
10/22/2009
Chief, Branch III

NDA 22-281

Zegerid OTC™, Capsule 20 mg

Schering-Plough

Christopher Hough

Review Chemist

Office of New Drug Quality Assessment
Division of Office of New Drug Quality Assessment
Pre-Marketing Division II, Branch III

CMC REVIEW

For the Office of Non-Prescription Drugs
(HFD-560)

Table of Contents

CMC Review Data Sheet

1. NDA 22-281

2. REVIEW #: 2

3. REVIEW DATE: 6-Jan-2009

4. REVIEWER: Christopher Hough, Ph.D.

5. PREVIOUS DOCUMENTS: None

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original Submission	10-Mar-08
Amendment-New Table of Contents	12-Mar-08
Amendment-Responses to CMC IR requests	27-Jun-08
Amendment-Addition of Executed Batch Records	28-Aug-08

7. NAME & ADDRESS OF APPLICANT:

Name:	Schering-Plough HealthCare Products
Address:	556 Morris Avenue, Summit, NJ 07901-1330
Representative:	William Cochran, Sr. Manager, Regulatory Affairs
Telephone:	908 473-1858

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Zegerid OTC™ 20 mg capsules
b) Non-Proprietary Name: Omeprazole/Sodium Bicarbonate 20 mg/1100 mg
c) Code Name/# (ONDQA only): N/A
d) Chem. Type/Submission Priority (ONDQA only):
- Chem. Type: 5
- Submission Priority: Standard

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

10. PHARMACOL. CATEGORY: Antacid

11. DOSAGE FORM: capsule

12. STRENGTH/POTENCY: 20 mg Omeprazole, 1.10 g Sodium Bicarbonate

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx ✓OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
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16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
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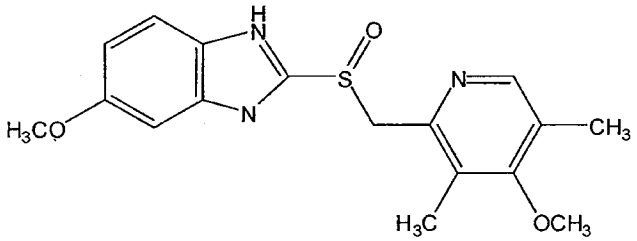

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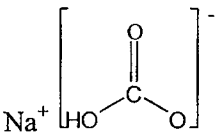

$NaHCO_3$
84.01

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	2		Drug substance	1	Adequate	27-Jul-2007	Chris Hough
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	3		Capsule banding			13-Jun-2003	Arthur Shaw
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	3		Containers	3	Adequate	18-Sep-2007	Craig Bertha
	3		Closures	3	Adequate	9-Dec-2004	Rapti Madurawe
	3		Induction seal	3	Adequate	29-Jan-2003	Lyudmila Soldatova,

b(4)

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B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND		
NDA	21-849 21-636 19-810 21-229	ZegeridRx capsule Zegerid Rx Oral Suspension Prilosec Rx Prilosec OTC

b(4)

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NAI	19-Mar-2008	Mike Welch
EES	Acceptable	22-Dec-2008	Office of Compliance
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A		
DMETS	N/A		
EA	Categorical exclusion is granted	7-Oct-2008	Chris Hough
Microbiology	N/A		

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. An "Acceptable" recommendation is made from the Office of Compliance for the site inspections. However, labeling issues are still pending. Therefore, from the CMC perspective, this NDA is not recommended for approval until labeling issues are resolved.

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

N/A

II. Summary of CMC Assessments

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

(1) Drug Substances

See Review #1

(2) Drug Product

See Review #1.

B. Description of How the Drug Product is intended to be used

See Review #1.

C. Basis for Approvability or Not-Approval Recommendation

The sponsor has provided sufficient information on raw material controls, manufacturing processes and process controls, and adequate specification for assuring consistent product quality of the drug substance and drug product. The NDA also has provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product during the expiration dating period.

All facilities have acceptable site recommendations. However, labeling issues are still pending. Therefore, from the CMC perspective, this NDA is not recommended for approval until all labeling issues are resolved.

CMC Assessment

I. Review of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body of Data
See Review #1.

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling: *Since the clinical division has decided to make sodium bicarbonate an active ingredient in this product, ONDQA recommends that, from the CMC perspective, the established name for the carton and container labels be revised as follows:*

(Omeprazole/Sodium Bicarbonate) Capsules
20 mg/1100 mg

However, ONDQA defers to the clinical division in decisions concerning labeling issues of OTC drugs.

III. Administrative

A. Reviewer's Signature:

(See appended electronic signature page)

Christopher J. Hough, Ph.D.

B. Endorsement Block:

(See appended electronic signature page)

Moo-Jhong Rhee, Branch Chief, Branch III, ONDQA

C. CC Block:

CMC Assessment Section

Attachment:

06-JAN-2009

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 22281/000
Org Code: 560
Priority: 8

Sponsor: SCHERING PLOUGH
56 LIVINGSTON AVE
ROSELAND, NJ 07068

Stamp Date: 10-MAR-2008
PDUFA Date: 10-JAN-2009
Action Goal:
District Goal: 11-NOV-2008

Brand Name : ZEGERID OTC CAPSULES
Estab. Name:
Generic Name: OMEPRAZOLE 20MG SODIUM BICARBONATE 1100M
Dosage Form: (CAPSULE)
Strength: 20 MG AND 1100 MG

FDA Contacts:	E. FORD	Project Manager (HFD-180)	301-796-0193
	C. HOUGH	Review Chemis	301-796-0323
	S. DING	Team Leader	301-796-1349

Overall Recommendation: ACCEPTABLE on 22-DEC-2008
by S. ADAMS (HFD-325) 301-796-3193

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

/s/

Christopher Hough
1/6/2009 03:07:55 PM
CHEMIST

Moo-Jhong Rhee
1/6/2009 03:08:50 PM
CHEMIST
Chief, Branch III

NDA 22-281

Zegerid OTC™, Capsule 20 mg

Schering-Plough

Christopher Hough

Review Chemist

Office of New Drug Quality Assessment
Division of Office of New Drug Quality Assessment
Pre-Marketing Division II, Branch III

CMC REVIEW

For the Office of Non-Prescription Drugs
(HFD-560)

Table of Contents

CMC Review Data Sheet

1. NDA 22-281

2. REVIEW #: 1

3. REVIEW DATE: 7-Oct-2008

4. REVIEWER: Christopher Hough, Ph.D.

5. PREVIOUS DOCUMENTS: None

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original Submission	10-Mar-08
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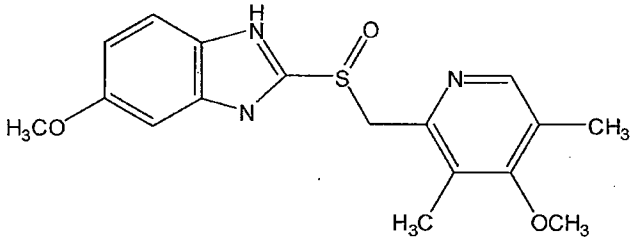

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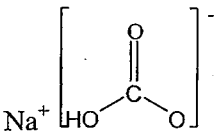

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b(4)

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NAI	19-Mar-2008	Mike Welch
EES	pending		
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A		
DMETS	Pending?		
EA	Categorical exclusion is granted	7-Oct-2008	Chris Hough
Microbiology	N/A		

Executive Summary Section

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. However, labeling issues are still pending and a site recommendation from the Office of Compliance has not been made as of the date of this review. Therefore, from the CMC perspective, this NDA is not recommended for approval until all issues are resolved.

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

N/A

II. Summary of CMC Assessments

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

(1) Drug Substances

Omeprazole:

Schering-Plough HealthCare Products is cooperating with Santarus, Inc. to sponsor this OTC version of approved Zegerid® Capsules, 20 mg (NDA 21-849). The primary active ingredient of Zegerid® is omeprazole, manufactured by

b(4)

. Validations of these latter methods are given in the application and are adequate.

Sodium bicarbonate: In this application, sodium bicarbonate is deemed an active ingredient, though no claim is made by the sponsor for its use in treating the indications listed for Zegerid®.

b(4)

The

Executive Summary Section

stability of sodium bicarbonate is well known and therefore was not tested. Normally, the paucity of information provided for this second active ingredient would be unacceptable. However, the manufacture of sodium bicarbonate, its critical steps and intermediates, process controls, and process validation have long been established and accepted as adequate for the manufacture of food and antacid products. In the final analysis, as long as the USP monograph specification is met - particularly that regarding ——— the substance is considered of adequate quality to be ingested as a drug and should incur no more risk than the ingestion of salt or baking soda. b(4

(2) Drug Product

The application is a 505 (b)(2) application relying on the Agency's finding of safety and efficacy for Prilosec OTC tablets, 20 mg (NDA 21-229). The drug product of this OTC version is identical to the Rx version, Zegerid® 20 mg Capsule (NDA 21-849). Their formulations are identical. Consequently, raw material controls, manufacturing processes and controls, specifications, and stability are identical to those of the approved Rx product (NDA 21-849), which was extensively referenced in this application. The only difference is the tamper-resistant seal added to the capsule. Formerly, the Rx capsule had a blue cap. Now, because the Rx capsule has been changed to all white, the OTC capsule differs from the Rx version only in that it is sealed with a blue, tamper-evident gelatin band. The material controls, manufacture process controls, and specification associated with the banding process are deemed adequate. As with the prescription drug, Zegerid OTC™ is intended to be an immediate release dosage form. Side by side comparisons of dissolution of the prescription and OTC versions showed that during the first 15 minutes, the dissolution of the unbanded capsule exceeded that of the OTC banded capsule. By the 30 minute time point, however, the two capsules provided the same concentrations of dissolved active ingredients. A / overage of omeprazole was used to ensure label claim. The drug product is to be packaged as 5-count and 14-count presentations. The 5-count container is a 30 cc high density polyethylene bottle with a 28 mm opening. The 14-count container is a 40 cc high density polyethylene bottle with a 33 mm opening. In both cases, the closure is a two-piece closure lined with a multilayered material known as C > . These container-closures systems are identical to or differ only in size from those approved for the Rx version of the drug product. The stability data of the approved Rx Zegerid 20 mg Capsule was used to support a 36 month expiration dating period of the OTC product. b(4)

B. Description of How the Drug Product is intended to be used

The 14-capsule drug product represents a 14-day treatment for frequent heartburn. The patient is to take one capsule a day for the full 14 day treatment.

Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

The sponsor has provided sufficient information on raw material controls, manufacturing processes and process controls, and adequate specification for assuring consistent product quality of the drug substance and drug product. The NDA also has provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product during the expiration dating period.

The inspection of all facilities, however, has not been completed, nor have all labeling issues been resolved. Therefore, from the CMC perspective, this NDA is not recommended for approval until all issues are resolved.

III. Administrative

A. Reviewer's Signature:

(See appended electronic signature page)

Christopher J. Hough, Ph.D.

B. Endorsement Block:

(See appended electronic signature page)

Moo-Jhong Rhee, Branch Chief, Branch III, ONDQA

C. CC Block:

53 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 2

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

/s/

Christopher Hough
12/3/2008 01:31:00 PM
CHEMIST

Moo-Jhong Rhee
12/3/2008 01:37:06 PM
CHEMIST
Chief, Branch III

Initial Quality Assessment
Branch III
Pre-Marketing Assessment Division II

OND Division:	Division of Nonprescription Clinical Evaluation
NDA:	22-281
Applicant:.	Schering-Plough HealthCare Products, Inc.
Stamp Date:	Mar. 10, 2008
PDUFA Date	Jan. 10, 2009
Trademark:	Zegerid OTC™
Established Name:	Omeprazole 20 mg/Sodium Bicarbonate 1100 mg
Dosage Form:	Capsule
Route of Administration:	Oral
Indication:	Frequent heartburn
PAL:	Shulin Ding

	YES	NO
ONDQA Fileability:	☒	☐
Comments for 74-Day Letter	☒	☐

Summary and Critical Issues

A. Summary

This NDA is submitted by Schering-Plough HealthCare under section 505(b)(2) of the Federal Food Drug and cosmetic Act in support of the nonprescription marketing of Zegerid OTC™ capsules (omeprazole 20 mg/sodium bicarbonate 1100 mg) for the treatment of frequent heartburn. This is a partial switch of NDA 21-849 Zegerid capsules, which was approved in 2006 for two strengths (20 mg and 40 mg). When comparing with the originally approved Rx product, the OTC product has minor changes in formulation, drug product manufacturing process, and packaging configuration. The drug substance suppliers and specifications, and the drug product specification remain the same as the approved Rx one.

The minor changes in formulation are due to color change in capsule body and cap (all white in OTC version), and the addition of a blue tamper-evident gelatin band around the edge of the capsule body and the cap. The minor changes in drug product manufacturing process are the addition of the banding process and the use of new model of equipment of the same technology.

The applicant references to NDA 21-849 Zegerid capsules for most of CMC information. The following are main pieces of new information added to this OTC switch NDA:

- CMC information and DMF reference for tamper-evident band
- Manufacturing process for banding operation
- Information for the new packaging size, 14 counts
- Justification for referencing stability data to NDA 21-849

- Batch analysis and executed batch records for those batches used in the two bioequivalence studies supporting this OTC NDA.

Zegerid OTC™ 20 mg capsules are size 00 hard gelatin capsules with white cap, white body, and a blue tamper-evident band around the edge of the body and the cap. A blue logo, ZEG-20, is printed on the white capsule body. Two packaging configurations are proposed for the OTC marketing: 5 counts in 30 cc white high-density-polyethylene bottle, and 14 counts in 40 cc white high-density-polyethylene bottle. Both configurations are equipped with a child-resistant closure.

The stability data supporting the proposed 36 month expiry period at the storage of 20-25°C are referenced to NDA 21-849. A categorical exclusion from the requirement to prepare an Environmental Assessment is claimed for this NDA.

B. Critical issues for review

With exception of the issue described in the paragraph below there are no other critical review issues identified for this NDA. This is because (1) all important CMC aspects of this NDA (including sodium bicarbonate drug substance supplied by have been reviewed and approved under NDA 21-849, (2) the formulation/manufacturing changes caused by capsule color change and banding are considered to be minor, and (3) the reference to NDA 21-849 for stability data was concurred by the FDA in the pre-NDA meeting. b(4)

The outstanding issue is regarding the use of Rx Zegrid capsules in the pivotal comparative bioavailability study. One of the conditions required by the Agency for agreeing with such a use is that the OTC product needs to meet the currently approved dissolution specification and shows a dissolution profile which is similar to that of the marketed Rx product. Although the batch analysis provided in the NDA shows the OTC product batches made to-date can meet the currently approved dissolution specification, the information about the dissolution profile is not provided. A request should be made to the applicant to provide the comparative dissolution profile information.

C. Comments for 74-Day Letter

The NDA applicant should provide a proper letter of authorization with a correct applicant name for DMF

b(4)

The NDA applicant should provide a comparative dissolution profile of the proposed OTC product and the approved Rx product.

D. Comments/Recommendation

This NDA is **fileable** from chemistry, manufacturing and controls (CMC) perspective. There are no major review issues.

GMP inspections have been requested. The omeprazole drug substance manufacturing site is in Spain. The sodium bicarbonate drug substance and the drug product manufacturing sites are in the U.S.

Shulin Ding
Pharmaceutical Assessment Lead, Branch III

Moo-Jhong Rhee
Chief, Branch III

Filing Checklists

A. Administrative Checklists

YES	NO		Comments
x		On its face, is the section organized adequately?	
x		Is the section indexed and paginated adequately?	
x		On its face, is the section legible?	
x		Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	
x		Has an environmental assessment report or categorical exclusion been provided?	

B. Technical Checklists

1. Drug Substance: Omeprazole USP referenced to DMF 11551

	x	Does the section contain synthetic scheme with in-process parameters?	
	x	Does the section contain structural elucidation data?	
x		Does the section contain specifications?	
	x	Does the section contain information on impurities?	
x		Does the section contain validation data for analytical methods?	
	x	Does the section contain container and closure information?	
	x	Does the section contain stability data?	

Drug Substance: Sodium Bicarbonate USP

x		Does the section contain synthetic scheme with in-process parameters?	
	x	Does the section contain structural elucidation data?	Not applicable
x		Does the section contain specifications?	
	x	Does the section contain information on impurities?	Compendial material
	x	Does the section contain validation data for analytical methods?	Compendail method
x		Does the section contain container and closure information?	The applicant states that it is stored in the original sealed container.
	x	Does the section contain stability data?	The applicant states that the stability data can be obtained from the supplier.

2. Drug Product

x		Does the section contain manufacturing process with in-process controls?	
x		Does the section contain quality controls of excipients?	
x		Does the section contain information on composition?	
x		Does the section contain specifications?	
	x	Does the section contain information on degradation products?	Reference to NDA 21-849.

x		Does the section contain validation data for analytical methods?	
x		Does the section contain information on container and closure systems?	
x		Does the section contain stability data with a proposed expiration date?	Referenced to NDA 21-849 for stability data with justification.
x		Does the section contain information on labels of container and cartons?	
x		Does the section contain tradename and established name?	

C. Review Issues

x		Has all information requested during the IND phases, and at the pre-NDA meetings been included?	
	x	Is a team review recommended?	
x		Are DMFs adequately referenced?	The LOA for DMF [redacted] is addressed to Schering Corporation not Schering Plough.

b(4)

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
4/29/2008 03:26:49 PM
CHEMIST

Moo-Jhong Rhee
4/29/2008 04:17:24 PM
CHEMIST
Chief, Branch III

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application:	NDA 22281/000	**Sponsor:**	SCHERING PLOUGH
Type Code:	560		56 LIVINGSTON AVE
Priority:	8		ROSELAND, NJ 07068
Stamp Date:	10-MAR-2008	**Brand Name:**	ZEGERID OTC CAPSULES
PDUFA Date:	08-DEC-2009	**Estab. Name:**	
Action Goal:		**Generic Name:**	OMEPRAZOLE 20MG SODIUM BICARBONATE 1100M
District Goal:	09-OCT-2009	**Product Number; Dosage Form; Ingredient; Strengths**	001; CAPSULE, HARD GELATIN; OMEPRAZOLE; 20.4MG 001; CAPSULE, HARD GELATIN; SODIUM BICARBONATE; 1100MG

FDA Contacts:	E. FORD	Project Manager	(HFD-180)	301-796-0193
	C. HOUGH	Review Chemist		301-796-0323
	S. DING	Team Leader		301-796-1349

Overall Recommendation: ACCEPTABLE on 22-DEC-2008 by S. ADAMS () 301-827-2443

Establishment: **CFN:** — **FEI:** —

DMF No: /

AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile: NON-STERILE BULK BY —

OAI Status: NONE

Last Milestone: SUBMITTED TO DO

Milestone Date: 01-JUL-2009

b(4)

Establishment: **CFN:** — **FEI:** —

DMF No: /

AADA: N 021849

Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE OTHER TESTER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER

Profile: CAPSULES, PROMPT RELEASE

OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 02-MAY-2008

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

b(4)

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Establishment: **CFN:** **FEI:**

DMF No: **AADA:**

Responsibilities: FINISHED DOSAGE OTHER TESTER

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 30-APR-2008

Decision: ACCEPTABLE

Reason: BASED ON PROFILE

b(4)

Establishment: **CFN:** **FEI:**

DMF No: **AADA:** N 021849

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Profile: NON-STERILE BULK BY **OAI Status:** NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 22-DEC-2008

Decision: ACCEPTABLE

Reason: DISTRICT RECOMMENDATION

b(4)

There was no review performed for this application.

Mary R. Vienna, Regulatory Project Manager

Date: 11/30/09

There was no Microbiology Review for this application.

Mary R. Vienna

Mary R. Vienna, Regulatory Project Manager

Date: 11/30/09

Refer to CMC review for Environmental Assessment Review.

Mary R. Vienna, Regulatory Project Manager

Date: 12/08/08