CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 21153/S-045

Trade Name: **NEXIUM**

Generic Name: **Esomeprazole Magnesium**

Sponsor: **AstraZeneca LP**

Approval Date: 06/17/2013

Indications: NEXIUM is a proton pump inhibitor indicated for the following:

- Treatment of gastroesophageal reflux disease (GERD)
- Risk reduction of NSAID-associated gastric ulcer
- H. pylori eradication to reduce the risk of duodenal ulcer recurrence
- Pathological hypersecretory conditions, including Zollinger-Ellison syndrome

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APPLICATION NUMBER:

NDA 21153/S-045

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21153/S-045

APPROVAL LETTER

AstraZeneca LP
Attention: Judy W. Firor
Regulatory Affairs Director
1800 Concord Pike, PO Box 8355
Wilmington, DE 19803

Dear Ms. Firor:

Please refer to your Supplemental New Drug Application (sNDA) dated December 18, 2012, received December 18, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nexium® (esomeprazole magnesium) Delayed-Release Capsules.

This "Changes Being Effected in 30 days" supplemental new drug application provides for updating the drug product method and specification information to allow adoption of the USP monograph for the drug product.

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Cathy Tran-Zwanetz, Regulatory Project Manager, at (301) 796-3877.

Sincerely,

{See appended electronic signature page}

Thomas F. Oliver, Ph.D.
Branch Chief, Branch VI
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

CATHERINE A TRAN-ZWANETZ
06/17/2013

DAVID B LEWIS
06/17/2013
Concur, APPROVAL is recommended. Signing for T. Oliver.

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APPLICATION NUMBER:

NDA 21153/S-045

CHEMISTRY REVIEW(S)

Initial Quality Assessment and Triage

ONDQA Branch VI

OND Division: HFD-180 (DGIEP)
NDA: 21-153
Supplement: S-045
DARRTS Document Number: SDN2504
Applicant: AstraZeneca
Letter Date: 12-18-2012
Stamp Date: 12-18-2012
ONDQA Receipt Date: delivered to CMC lead on 1-09-2013
ONDQA CMC Lead triage date: 1-16-2013
Application Type: electronic
Proprietary Name: NEXIUM® (esomeprazole magnesium) Delayed-release capsules
Established Name: esomeprazole magnesium Delayed-release capsules
Dosage Form: Delayed-release capsules
Route of Administration: oral
Submission Type: Changes Being Effected in 30 Days (CBE-30)
Recommended submission type: CBE-30

Moderate to minor changes in DP specs to comply with new USP monograph

This electronic CBE-30 supplement provides a change in the drug product specification to correspond with the newly-implemented USP monograph for esomeprazole magnesium delayed-release capsules.

The proposed specification includes the following tests, methods, and acceptance criteria:

- **Appearance**: via visual description, described the appearance of the dosage unit (color, material of composition [hard gelatin capsule], shape, and printing)
- **Identity**: positive for esomeprazole and for magnesium
- **Content**: use assay method, requires 90.0% to 110.0%
- **Content uniformity**: meets the requirements in USP <905>
- **Dissolution**: meets the requirements in USP "Dissolution - delayed-release dosage forms, buffer stage". After 30 minutes not less than 75% (Q) of stated amount.
- **Organic impurities**: NMT 2% in total, NMT 0.5% of omeprazole sulfone, and NMT 0.2% of any other individual impurity

The new tests are for omeprazole sulfone, and the "any other individual impurity". (b) (4).

The applicant provides batch records (20 mg and 40 mg product), indicating that they comply with the new compendial requirements. It is noted that additional non-compendial testing is retained for the product.

From examining a batch record from a previous quality (CMC) supplement, it appears that the changes are minimal to moderate; no previously-approved tests were eliminated.

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/s/

DAVID B LEWIS
02/08/2013
IQA, CBE-30 acceptable

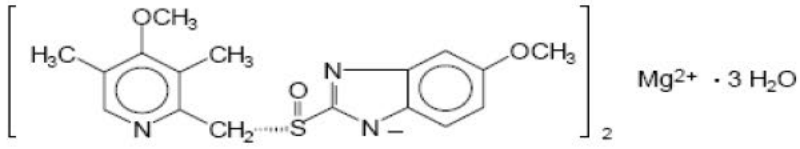
THOMAS F OLIVER
02/13/2013

Chemistry Review: # 1	**1. Division:** HFD-180	**2. NDA Number:** **21-153**

3. Name and Address of Applicant:	**4. Supplement(s):**
AstraZeneca LP 1800 Concord Pike P.O. Box 8355 Wilmington, DE 19803-8355	**Number: S-045; CBE-30** **Date(s):** December 18, 2012 **Stamp Date:** December 18, 2012 **Due Date:** June 18, 2013
5. Name of Drug: NEXIUM®	**6. Nonproprietary name:** Esomeprazole magnesium

7. CBE-30 Supplement Provides for: the update of the drug product method and specification information to allow adoption of the USP monograph for esomeprazole magnesium delayed-release capsules		**8. Amendment(s):**None
9. Pharmacological Category: Acute healing of erosive esophagitis, and symptomatic gastroesophageal reflux disease.	**10. How Dispensed:** R_x	**11. Related Documents:** None.
12. Dosage Form: Delayed-Release Capsules.	**13. Potency:** Esomeprasol magnesium, 20 and 40 mg	

14. Chemical Name and Structure: bis(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1*H*-benzimidazole-1-yl), magnesium trihydrate . $(C_{17}H_{18}N_3SO_3)_2MgX_3H_2O$. M.W [redacted] (b) (4)



15. Comments: This supplement requests approval for updating of the current Specification Sheet to conform with the most recently implemented USP 35-NF30 monograph for esomeprazole magnesium delayed-release capsules.

All the analytical procedures will remain as currently approved and comply with the USP monograph.

The proposed change includes mainly updated terminology. The current names for the test `**Appearance**`. `**Identity**` and `**Content**` are replaced with `**Description**` `**Identification**` **and** ` **Assay**` respectively in the updated Specification Sheet.

The acceptance criterion for **Assay** is changed from [redacted] (b) (4) to 90.0 -110.0%.

Under `**Organic Impurities**`, the acceptance criterion for [redacted] (b) (4) is changed to **"Not more than 0.5% Omeprazole sulfone"** and the criterion for [redacted] (b) (4) is changed to " **"Not more than 0.2% of any other individual impurity"**.

See side by side comparison of the current and proposed Specification sheet and justification for specifications in the Chemistry Review Section below.

Additional support for the proposed change is included in the form of Batch Analyses for the drug product, 20 mg and 40 mg, according to present and USP monograph specification. See Chemistry Review Notes Section below.

16. Conclusions and Recommendations: The information, rationale and data provided in support of the proposed change demonstrates that updating the current Specification sheet for this drug product to the current Specification for the USP monograph for esomeprazole magnesium delayed-release capsules does not have any adverse effect on the final quality of the drug product. For this reason, from the point of view of CMC, this supplemental application is recommended for **Approval.**		
17. Name: **Libaniel Rodriguez Ph.D., Chemist**	**Signature:**	**Date:**
18. Concurrence: **Thomas Oliver, Ph.D.,** **Branch chief/ONDQA/ONDQII/Branch VI**	**Signature:**	**Date:**

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/s/

LIBANIEL RODRIGUEZ
06/11/2013

THOMAS F OLIVER
06/11/2013

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21153/S-045

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21153/S-045

CBE SUPPLEMENT – ACKNOWLEDGEMENT

AstraZeneca LP
Attention: Judy W. Firor
Regulatory Affairs Director
1800 Concord Pike, PO Box 8355
Wilmington, DE 19803

Dear Ms. Firor:

We have received your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA NUMBER: 21153

SUPPLEMENT NUMBER: 045

PRODUCT NAME: Nexium® (esomeprazole magnesium) Delayed Release Capsules

DATE OF SUBMISSION: December 18, 2012

DATE OF RECEIPT: December 18, 2012

This supplemental application, submitted as a "Changes Being Effected in 30 days" supplement, proposes the following change: the update of the drug product method and specification information to allow adoption of the USP monograph for the drug product.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 16, 2013 in accordance with 21 CFR 314.101(a).

If the application is filed, the user fee goal date will be June 18, 2013.

Cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology Drug Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have questions, call me, at (301) 796-3877.

Sincerely,

{See appended electronic signature page}

Cathy Tran-Zwanetz
Regulatory Project Manager
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

CATHERINE A TRAN-ZWANETZ
01/23/2013