DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-957

AstraZeneca LLP
George A. Kummeth
Director Regulatory Affairs
1800 Concord Pike, P.O. Box 8355
Wilmington, Delaware 19803-8355

Dear Mr. Kummeth:

Please refer to your new drug application (NDA) dated December 22, 2005, received December 22, 2005, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for NEXIUM® for Delayed Release Oral Suspension, 20 and 40 mgs.

We acknowledge receipt of your submissions dated December 22, 2005; and April 17, 2006; April 20, 2006; July 11, 2006; July 13, 2006; August 23, 2006; September 6, 2006; September 7, 2006; October 10, 2006; October 13, 2006; and October 17, 2006.

This new drug application provides for the use of NEXIUM® for Delayed Release Oral Suspension for treatment of Gastroesophageal Reflux Disease (GERD): Healing of Erosive Esophagitis, Maintenance of Healing of Erosive Esophagitis, Symptomatic Gastroesophageal Reflux Disease; Risk Reduction of NSAID-Associated Gastric Ulcer; *H. pylori* Eradication to Reduce the Risk of Duodenal Ulcer Recurrence; and Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome.

We completed our review of this application as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

Submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and labeling for immediate container and carton labels submitted on December 22, 2005. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-957**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for the following indications in this application: Risk reduction of NSAID- Associated Gastric Ulcer; *H. pylori* Eradication to Reduce the Risk of Duodenal Ulcer Recurrence; and Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome.

We are deferring pediatric studies (Birth – 11 years) for Gastroesophageal Reflux Disease (GERD): Healing of Erosive Esophagitis, Maintenance of Healing of Erosive Esophagitis, Symptomatic Gastroesophageal Reflux Disease for this application. Pediatric studies (ages 12 – 17) for this indication have been already completed.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Gastroenterology Products and two copies of both the promotional materials and the package insert directly to:

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

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Marlène G. Swider, Regulatory Project Manager, at (301) 796-2104.

Sincerely,

{See appended electronic signature page}

Joyce A. Korvick, M.D., M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE

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

/s/

Brian Harvey
10/24/2006 05:10:20 PM
For Dr. Joyce Korvick

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

NDA APPROVAL

AstraZeneca LP
Attention: George Kummeth
Global Director, Regulatory Affairs
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803

Dear Mr. Kummeth:

Please refer to your new drug application (NDA) dated September 27, 2006, received September 27, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nexium (esomeprazole magnesium) For Delayed-Release Oral Suspension, 10 mg.

We acknowledge receipt of your submission dated November 21, 2007, December 27, 2007, February 19, 2008, and February 26, 2008.

The December 27, 2007, submission constituted a complete response to our July 27, 2007, action letter.

This new drug application provides for the use of Nexium (esomeprazole magnesium) For Delayed-Release Oral Suspension, 10 mg for short-term treatment of GERD and healing of erosive esophagitis in pediatric patients aged 1-11 years. In addition, it provides a new dosing schedule for pediatric patients.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions indicated in the enclosed labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling. These revisions are terms of the NDA approval. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "SPL for approved NDA 22-101."

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your December 27, 2007, submission containing final printed carton and container labels and have the following recommendations for this approval:

1. The prominence of the bubble graphic on the foil pouch should be deleted or at a minimum decreased.
2. The color and location of the font on the physician sample foil pouch needs to be changed, in efforts to make the statement, "Physician's Sample Not for Sale" more prominent.

Submit final printed carton and container labels that are identical to the submitted carton and immediate container labels, except with the revisions listed above, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22-101**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PEDIATRIC RESEARCH EQUITY ACT (PREA)

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 0 to < 1 year until December 31, 2008.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of GERD and healing of erosive esophagitis in pediatric patients ages 0 to <1 year.

   Final Report Submission: December 31, 2008

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Chantal Phillips, Regulatory Project Manager, at (301) 796-2259.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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/s/

Joyce Korvick
2/27/2008 05:51:17 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21153-S53
NDA 22101-S17
NDA 21957-S20

SUPPLEMENTS APPROVAL

AstraZeneca Pharmaceuticals LP
Attention: Emery V. Gigger
Regulatory Affairs Director
One MedImmune Way
Gaithersburg, MD 20878

Dear Ms. Gigger:

Please refer to your Supplemental New Drug Applications (sNDAs) dated May 24, 2018, received and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for NEXIUM (esomeprazole magnesium) delayed-release capsules and NEXIUM (esomeprazole magnesium) for delayed-release oral suspension.

We also refer to our letter dated January 24, 2018, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for PPIs. This information pertains to the risk of Fundic Gland Polyps (FGPs) among patients using PPIs for more than one year.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with minor editorial revisions listed below:

- Updated revision dates to the current date
- Added a line of white space between the Highlights limitation statement and the Product Title line.

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Mimi Phan, Regulatory Project Manager, at (301) 796-5408.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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/s/

JOYCE A KORVICK
06/07/2018

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21153-S53
NDA 22101-S17
NDA 21957-S20

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AstraZeneca Pharmaceuticals LP
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Regulatory Affairs Director
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Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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/s/

JOYCE A KORVICK
06/07/2018