

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-101

OTHER ACTION LETTER(s)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-101

AstraZeneca
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) Delayed-Release Granules for Oral Suppression, 10mg.

We acknowledge receipt of your submissions dated November 6, 2006, December 6, 2006, December 19, 2006, January 17, 2007, January 24, 2007, February 1, 2007, March 1, 2007, April 25, 2007, May 16, 2007, and July 25, 2007.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to:

1. Submit draft labeling revised in response to our July 26, 2007 communication.
2. We are in receipt of your final report dated July 25, 2007 to NDA21-153, regarding the potential imbalance of serious cardiac adverse events in two adult studies (SOPRAN and LOTUS). Upon finalizing our reviews of these data, additional changes to the professional labeling for esomeprazole magnesium may be needed.

In addition, please make the following changes to Carton Label (Trade and Physician Label).

- a. De-bold the font used to state the net quantity (e.g. 30 single dose packets).
- b. The color schemes used for the 10 mg packets and 40 mg packets (purple background with white text) are identical, with exception to the background color used for the product strength (red background with white font for 10 mg vs. white background with purple font for 40 mg). A lack of distinct differentiation between the product strengths may lead to product selection errors. We recommend increasing the size of the strength in order to increase it's prominence against the purple background which

overwhelmingly causes the cartons to look similar. Additionally, we request a different background color be used for each strength to avert potential product selection errors.

Also please make the following changes to the Packet Label (Trade and Physician Sample).

The graphic presented in the bottom right corner of the principal display panel is distracting and detracts attention from important information such as the proprietary name, established name, and product strength. Decrease the prominence of the graphic in order to allow for increased prominence of the proprietary and established names.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.
 - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.
4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
7. Provide English translations of current approved foreign labeling not previously submitted.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the

application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with this division to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

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

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

/s/

Joyce Korvick
7/27/2007 11:45:29 AM