

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
22-056

OTHER ACTION LETTER(s)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-056

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 December 20, 2006, received December 20, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec (omeprazole magnesium) Delayed-Release Granules for Oral Suspension, 10 mg.

We acknowledge receipt of your submissions dated February 8, March 15, April 18, May 1, May 2, May 8, July 3, July 11, July 25, July 31, August 29, September 24, September 27, and October 4, 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 October 18, 2007 communication.
2. We are in receipt of your final report dated July 25, 2007 to NDA 19-810, 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.

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 Brian Strongin, R.Ph., M.B.A., Regulatory Project Manager, at (301) 796-1008.

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
10/19/2007 01:41:51 PM