DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-450/S-005

Lynley K. Thinnes
Director, Regulatory Affairs
Neuroscience Emerging Products
AstraZeneca
1800 Concord Pike
PO Box 8355
Wilmington, DE 19803-8355

Dear Ms. Thinnes:

Please refer to your supplemental new drug application dated December 14, 2007, received December 14, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zomig (zolmitriptan) nasal spray.

We acknowledge receipt of your submissions dated April 3, 2008, August 6, 2008 and September 15, 2008.

This supplemental new drug application provides for the use of Zomig (zolmitriptan) nasal spray **(b) (4)**

We completed our review of this application, as amended.

The pivotal efficacy trial (D1221C00005) in support of adolescent use was a multicenter, double-blind, randomized, placebo-controlled, 2-way crossover study with a single-blind placebo challenge. For each migraine attack, when migraine pain reached moderate-to-severe intensity, all subjects were initially challenged with a placebo nasal spray. Subjects who achieved reduction in headache pain to mild or none within 15 minutes were defined as early placebo responders and did not use randomized treatment for that attack. Subjects who did not respond within 15 minutes used randomized treatment with either zolmitriptan 5-mg nasal spray or placebo. The co-primary efficacy variables were 1-hour headache response and 2-hour sustained headache response.

(b) (4)

(b) (4)

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(b) (4)

[redacted]

(b) (4)

[redacted]

Despite the fact that **(b) (4)** [redacted], the attached, agreed-upon labeling in PLR format, which includes a brief discussion of Study D1221C00005, is approved, effective on the date of this letter, with the minor editorial revisions indicated in the enclosed labeling.

Additionally, we note the following Changes Being Effected (CBE) labeling supplements have been submitted as described below, and have been superseded with the approval of this application. These CBE labeling supplements will be retained in our files.

1. CBE dated July 20, 2006 included prescribing information was revised to include Class Labeling changes as requested by the Agency in correspondence dated May 25, 2006. Changes appear in the **WARNINGS**, **PRECAUTIONS** and **ADVERSE REACTIONS** sections.

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2. CBE dated March 13, 2007 included Class Labeling changes as requested by the Agency in correspondence dated December 20, 2006. These labeling revisions pertain to the risk for serotonin syndrome with the use of triptans. Changes appear in the **WARNINGS**, **PRECAUTIONS** and **PATIENT INFORMATION** sections.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the enclosed labeling (text for the package insert, text for the patient package insert) and submitted labeling (immediate container and carton labels submitted December 14, 2007). These revisions are terms of the approval of this application.

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 supplement NDA 21-450/S-005**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable. We are waiving the pediatric study requirement for ages 0 to 5 years because necessary studies are impossible or highly impracticable. This is because the low prevalence of migraine and migraine presentation in that group would not allow to practically design a study and recruit the needed patient population.

As noted above, (b) (4) you will need to design and conduct an additional study of ZOMIG in adolescents (ages 12-17 years).

In addition, you are required to study ZOMIG for treatment of acute migraine in pediatric patients ages 6-11 years. However, we are deferring submission of this required pediatric study because it should be delayed until additional safety and effectiveness data are available from your study in adolescents.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies under NDA 21-450 N-000 are listed below.

1. Deferred pediatric study under PREA for the acute treatment of migraine in pediatric patients ages 12 to 17 years.

Final Report Submission: October 14, 2011

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2. Deferred pediatric study under PREA for the acute treatment of migraine in pediatric patients ages 6 to 11 years. Upon review of additional safety and effectiveness data in pediatric patients ages 12 to 17 years, we will make a determination as to whether or not pediatric studies are practicable for this age range.

   Final Report Submission: October 14, 2014

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessments**".

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

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

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 Lana Chen, Regulatory Project Manager, at (301) 796-1056.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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

/s/

Russell Katz
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