DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21-450/S-008

SUPPLEMENT APPROVAL

FULFILLMENT OF POSTMARKETING REQUIREMENTS

RELEASE OF POSTMARKETING REQUIREMENT

NEW POSTMARKETING REQUIREMENTS

AstraZeneca Pharmaceuticals LP
Attention: Mr. Robert Griffin
Regulatory Affairs Director
One MedImmune Way
Gaithersburg, MD 21878

Dear Mr. Griffin:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 14, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zomig (zolmitriptan) nasal spray 0.5mg, 2.5mg, and 5mg.

We acknowledge receipt of your amendments dated the following:

December 17, 2014	May 19, 2015
March 9, 2015	June 4, 2015
April 14, 2015	June 5, 2015

This Prior Approval supplemental new drug application proposes zolmitriptan for the acute treatment of migraine with or without aura in adolescents 12 to 17 years old.

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.

LABELING

Submit final printed labeling, as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the enclosed labeling (package insert,) and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted 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 (June 2008)." 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 Labeling for approved NDA 21-450/S-008**." Approval of this submission by FDA is not required before the labeling is used.

DRUG REGISTRATION AND LISTING

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. In addition, representative container or carton labeling, whichever includes Drug Facts, (where differences exist only in the quantity of contents statement) should be submitted as a JPG file.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We refer to the deferred pediatric study noted in our S-005 approval letter dated October 14, 2008:

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

We have reviewed your supplemental application (S-008) and conclude that the above requirement was fulfilled.

RELEASE OF POSTMARKETING REQUIREMENTS

We refer to the deferred pediatric study noted in our S-005 approval letter dated October 14, 2008:

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.

Based on our review of the safety and efficacy data for zolmitriptan nasal spray for the treatment of migraine in children ages 12 years to 17 years that you have submitted in supplement S-008, and our review of other information, we have determined that pediatric studies to evaluate the safety and efficacy of zolmitriptan nasal spray in children ages 6 years to 11 years with migraine are practicable. Therefore, the above requirement is being released and replaced with PMR 2921-2 below.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We have waived the pediatric requirement for ages 0 months to up to 6 years because necessary studies are impossible or highly impracticable in that age group.

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 FDCA. These required studies are listed below.

PMR 2921-1 Conduct a juvenile rat toxicology study to identify the unexpected serious risk of adverse effects of zolmitriptan on postnatal growth and development. The study should utilize animals of an age range and stage(s) of development that are comparable to the intended pediatric population; the duration of dosing should cover the intended length of treatment in the pediatric population. In addition to the usual toxicological parameters, this study must evaluate effects of zolmitriptan on growth, reproductive development, and neurological and neurobehavioral development.

Final Protocol Submission: November 2016
Study Completion: November 2017
Final Report Submission: May 2018

PMR 2921-2: Conduct a controlled efficacy and pharmacokinetics (PK) study in children ages ≥6 years to 11 years with migraine that includes sparse PK samples throughout the efficacy study. Conduct a long-term open-label safety study in pediatric patients with migraine ages ≥6 years to 11 years. The long-term safety study must provide a descriptive analysis of safety data in at least 50 pediatric patients

exposed for at least 6 months, treating on average at least one migraine attack per month, at doses evaluated in the efficacy study.

Final Protocol Submission: February 2016
Study Completion: November 2020
Final Report Submission: May 2021

Submit the protocols to your IND 53,848, with a cross-reference letter to this NDA 21-450.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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

Sincerely,

{See appended electronic signature page}

Eric Bastings, M.D.
Deputy Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Labeling

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

/s/

ERIC P BASTINGS
06/12/2015