DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-001

J&J Pharmaceutical Research & Development, L.L.C.
Attention: Susan Merchant
1125 Trenton-Harbourton Road
P.O. Box 200
Titusville, NJ 08560-0200

Dear Ms. Merchant:

Reference is made to your Proposed Pediatric Study Request submitted on March 28, 2001 for Axert (almotriptan) to NDA 21-001.

To obtain needed pediatric information on almotriptan, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), that you submit information from the following studies:

Types of studies:

Study 1: Adolescent Efficacy Study
Study 2: Adolescent Long-Term Safety Study

Objectives/rationale:

Study 1: To evaluate the efficacy and safety of almotriptan in the treatment of adolescents 12 to 17 years of age with a history of migraine headaches.
Study 2: To evaluate the long-term safety of almotriptan in the treatment of adolescents 12 to 17 years of age with a history of migraine headaches.

Indication(s) to be studied:

The use of almotriptan tablets for the acute treatment of migraine headache in adolescents, ages 12 to 17 years.

Study design

Study 1: Randomized, double-blind, placebo-controlled, parallel group outpatient study in adolescents with a history of migraine headaches. The study must attempt to define the dose-response relationship in this age group, including the identification of a no-effect dose. The protocol must allow the use of appropriate rescue medication after a suitable post-dosing interval. The dose range must be based on the results of the PK study already conducted.

Study 2: Open label, 12-month outpatient study in adolescents with a history of migraine headaches.

Age groups to be studied:

Adolescent patients ages 12 to 17 years, inclusive.

Number of patients to be studied or power of the study to be achieved

Study 1: A sufficient number of adolescent migraine patients to be able to detect a clinically and statistically significant difference between treatment and control on a valid measure of efficacy. There must be similar number of patients in the 12 to 14 and 15 to 17 age groups. The study must be powered to detect an effect size similar to that seen in the adult population.

Study 2: A sufficient number of adolescent migraine patients to be able to characterize the long-term safety of almotriptan when used to treat multiple migraine attacks over one year. Each patient should treat, on average, approximately 1 or more headache(s) per month for six to twelve months. At a minimum, 200 patients, using an effective dose, must be exposed for six months, and 75 patients, using an effective dose, must be exposed for one year. At a minimum, 100 patients, using the highest recommended dose, must be exposed for six months, and 40 patients, using the highest recommended dose, must be exposed for one year. There must be a similar number of patients in the 12 to 14 and 15 to 17 age groups.

Entry criteria (i.e., inclusion/exclusion criteria)

Study 1: Adolescent patients between 12 and 17 years of age, with an average of 1 to 6 International Headache Society (IHS) defined migraine headaches per month.

Study 2: Adolescent patients between 12 and 17 years of age, with an average of 1 to 6 IHS defined migraine headaches per month.

Clinical endpoints

Study 1: The primary endpoint must be a reasonable measure of acute migraine relief in this population, and must be submitted as part of a special protocol for Agency review and concurrence prior to initiating the study. Additional standard secondary migraine efficacy measures and standard measures of safety (clinical- including signs and symptoms, and laboratory) must be included.

Study 2: Appropriately frequent standard measures of safety (clinical-including signs and symptoms, and laboratory).

Study evaluations:

Study 1: Safety and effectiveness data through 24 hours post dose.

Study 2: Safety data as discussed above.

Drug information:

Dosage form: oral tablet
Route of administration: oral
Regimen: To be determined by the development program
Formulation: solid oral dosage form

Statistical information, including:

Study 1: Assessment of the between group difference on the primary endpoint by a statistical methodology appropriate to the data generated.

Study 2: Descriptive analysis of the safety data.

Labeling that may result from these studies:

Appropriate sections of the label may be changed to incorporate the findings of the studies.

***Format of reports to be submitted*:** Full study reports not previously submitted to the Agency addressing the issues outlined in this request with full analysis, assessment, and interpretation. In addition, the reports are to include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the studies should be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander or White. For ethnicity one of the following designations must be used: Hispanic/Latino or Not Hispanic/Latino.

Timeframe for submitting reports of the studies: Reports of the above studies must be submitted to the Agency on or before December 31, 2008. Please keep in mind that pediatric exclusivity attaches only to existing patent protection or exclusivity that has not expired at the time you submit your reports of the studies in response to this Written Request.

Response to Written Request: As per the Best Pharmaceuticals for Children Act, section 4(A), within 180 days of receipt of this Written Request you must notify the Agency as to your intention to act on the Written Request. If you agree to the request then you must indicate when the pediatric studies will be initiated.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission "PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission "PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as a New Drug Application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS - PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED**" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

In accordance with section 9 of the Best Pharmaceuticals for Children Act, *Dissemination of Pediatric Information*, if a pediatric supplement is submitted in response to a Written Request and filed by FDA, FDA will make public a summary of the medical and clinical pharmacology reviews of pediatric

studies conducted. This disclosure, which will occur within 180 days of supplement submission, will apply to all supplements submitted in response to a Written Request and filed by FDA, regardless of the following circumstances:

1. the type of response to the Written Request (complete or partial);
2. the status of the supplement (withdrawn after the supplement has been filed or pending);
3. the action taken (i.e. approval, approvable, not approvable); or
4. the exclusivity determination (i.e. granted or denied).

FDA will post the medical and clinical pharmacology review summaries on the FDA website at http://www.fda.gov/cder/pediatric/Summaryreview.htm and publish in the Federal Register a notification of availability.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "**PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

As required by the Food and Drug Modernization Act and the Best Pharmaceuticals for Children Act, you are also responsible for registering certain clinical trials involving your drug product in the Clinical Trials Data Bank (http://clinicaltrials.gov & http://prsinfo.clinicaltrials.gov/). If your drug is intended for the treatment of a serious or life-threatening disease or condition and you are conducting clinical trials to test its effectiveness, then you must register these trials in the Data Bank. Although not required, we encourage you to register effectiveness trials for non-serious diseases or conditions as well as non-effectiveness trials for all diseases or conditions, whether or not they are serious or life-threatening. Additional information on registering your clinical trials, including the required and optional data elements and the FDA Draft Guidance for Industry, "Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions," is available at the Protocol Registration System (PRS) Information Site http://prsinfo.clinicaltrials.gov/.

If you have any questions, call Lana Chen, Project Manager, at 301-594-5529.

Sincerely,

{See appended electronic signature page}

Robert Temple, M.D.
Office Director
Office of Drug Evaluation I
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/

Robert Temple
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