



NDA 21-016

Pfizer Inc.  
Regulatory Affairs  
Attention: Casilda Luck Barnes, Pharm.D.  
235 East 42nd Street  
New York, NY 10017-5755

Dear Dr. Barnes:

Reference is made to your Proposed Pediatric Study Request submitted on June 18, 2003 for Relpax (eletriptan) to NDA 21-016.

To obtain needed pediatric information on eletriptan, 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:

***Type 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 eletriptan 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 eletriptan 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 eletriptan tablets for the acute treatment of migraine in adolescents 12 to 17 years of age with a history of migraine headaches.

***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 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 eletriptan when used to treat multiple migraine attacks over one year. Each patient must treat, on average, approximately 1 or more headaches 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. There must be similar number of patients in the 12 to 14 and 15 to 17 age groups.

***Entry criteria***

**Study 1:** Adolescent patients between 12 and 17 years of age, with an average of 1 to 6 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:***

**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. Include other information as appropriate. 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:***

Study reports are to be submitted to the Agency on or before August 1, 2007. 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 **supplement to an 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.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits in the pediatric population.

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

Sincerely,

Robert Temple, M.D.  
Director  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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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.**  
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/s/

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Robert Temple

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