



NDA 020450/S-008/S-009/S-016/S-019

SUPPLEMENT APPROVAL

Pfizer Inc
Attention: Carol Haley
Director, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Haley:

Please refer to your Supplemental New Drug Applications (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Cerebyx (fosphenytoin sodium) injection.

Application	Submitted on:	Received on:
NDA 020450/S-009	August 4, 2003	August 5, 2003
This “Changes Being Effected” supplement provides for:		
<ul style="list-style-type: none">• Revisions to the Drug Interactions and Adverse Reactions sections.		

Application	Submitted on:	Received on:
NDA 020450/S-008	July 2, 2003	July 3, 2003
NDA 020450/S-016	April 2, 2009	April 2, 2009
NDA 020450/S-019	January 14, 2011	January 14, 2011
These “Prior Approval” supplements provide for:		
<ul style="list-style-type: none">• Revisions to Clinical Pharmacology Pediatrics subsection, Precautions Pediatric Use subsection, and Dosage and Administration Pediatric subsection reflecting that safety and efficacy of Cerebyx in pediatric patients have not been established.• Revisions addressing concerns about dosing errors due to continuing confusion between concentration of fosphenytoin (expressed as phenytoin equivalents) and total drug content in a vial.• Revisions pertaining to:<ol style="list-style-type: none">1) Addition of fluorouracil to the Drug Interactions section2) Revision to the Warnings : Rash Section3) Addition of language about Anticonvulsant Hypersensitivity Syndrome (AHS) to the Precautions section4) Addition of language to the Adverse Reactions section5) Addition of language to the Dosage and Administration and Indications and usage sections to emphasize that the product is for parenteral use only		

We also refer to our November 3, 2010 Joint Meeting of the Peripheral and Central Nervous System Drugs (PCNS) Advisory Committee and Drug Safety and Risk Management (DSRM) Advisory Committee.

We have completed our review of these supplemental applications, and in our review we have amended the labeling for NDA 20450, as amended, as follows: updating information regarding CYP450-mediated metabolism, adding a Contraindication to coadministration with delavirdine, revising the Indications and Usage section and the Dosage and Administration section to recommend that Cerebyx should be used only when oral phenytoin administration is not possible, adding a boxed warning for cardiovascular risk associated with rapid infusion of fosphenytoin and strengthening the Warnings section regarding this risk, adding information about Purple Glove Syndrome to the Precautions section, and additional revisions to the Drug Interactions section, to the Warnings section, and to the Adverse Reactions section. We have also incorporated additional recommendations from the Joint Advisory Committee to your proposed labeling. These supplemental applications are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND IMMEDIATE CONTAINER LABEL

We also refer to our October 28, 2011 request for container label change and your October 31, 2011 telephone correspondence indicating that you are not currently marketing the product.

If you decide to remarket the product, submit the final printed carton and container labels that include the following revision, as soon as they are available, but no more than 30 days after they are printed:

Revise either the 2 mL or 10 mL container labels to incorporate colors that are not used in the other volume, thereby allowing for improved visual differentiation between the 2 mL and 10 mL Cerebyx vials.

Please submit these labels 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 “**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 020450 S-016.**” Approval of this submission by FDA is not required before the labeling is used.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

OTHER

We request that you perform a comprehensive literature search and a comprehensive safety database search (of cases after June 30, 2001) to determine whether the Drug Interactions and Adverse Reactions sections of labeling should be further updated. Please submit an analysis of your findings and proposed related labeling changes as a Prior Approval Supplement within 3 months of the date of this letter.

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 Su-Lin Sun, PharmD, Regulatory Project Manager, at (301) 796-0036.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE:
Content of Labeling

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

/s/

RUSSELL G KATZ
11/13/2011