DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 8-762/S-020/021/022/026
NDA 10-151/S-022/029/030/032/033/034

Pfizer Pharmaceuticals
Attention: Rita A. Wittich
Drug Regulatory Affairs
235 East 42nd Street
New York, NY 10017-3184

20 NOV 2001

Dear Ms. Wittich:

Please refer to your new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dilantin-125 (phenytoin oral suspension, USP) Suspension (NDA 8-762) and Dilantin (Phenytoin Sodium Injection, USP) Injection (NDA 10-151).

We additionally refer to the following supplemental applications:

NDA	Supplement	Dated
8-762	S-020	May 25, 1994, and amended on January 28, 1997
8-762	S-021	July 18, 1994
8-762	S-022	January 27, 1995
8-762	S-026	December 3, 1996
10-151	S-022	May 10, 1983 and amended on November 1, 1983
10-151	S-029	September 25, 1987, and amended on May 10, 1988
10-151	S-030	September 25, 1989
10-151	S-032	August 9, 1994
10-151	S-033	January 25, 1995, and amended on January 28, 1997
10-151	S-034	December 3, 1996

These applications provide for the following revisions to product labeling:

Dilantin-125 (phenytoin oral suspension, USP) Suspension

8-762/S-020

1. The addition and deletion of several inactive ingredients items under the **DESCRIPTION** section.
2. The deletion of several phenytoin products which are no longer marketed which include Dilantin 30 mg/5 ml suspension and Dilantin ampules throughout the labeling. We additionally note the deletion of several of the quantity sizes under the **HOW SUPPLIED** section since they are no longer marketed.
3. A complete revision to the **WARNINGS** section in regard to use during pregnancy and risks to the fetus to provide for updated information. The addition to the **PRECAUTIONS-General** section regarding adverse events associated with the combination use of phenytoin, cranial radiation, and reduction of corticosteroids.
4. The addition to the **PRECAUTIONS-Information for Patients** section reminding patients that they should use a calibrated measuring device.
5. The addition of the terms cimetidine, fluoxetine, ticlopidine, and paroxetine to the **PRECAUTIONS-Drug Interactions** section.
6. The addition of a new subsection under the **PRECAUTIONS** section entitled **Drug-Enteral Feeding/Nutritional Preparations Interaction**.
7. The addition of a cautionary statement under the **PRECAUTIONS-Drug/Laboratory Test Interactions** regarding immunoanalytical methods.
8. The addition of the statement "Pregnancy Category D" under the **PRECAUTIONS-Pregnancy** section.
9. The addition of a **Pediatric Use** section under the **PRECAUTIONS** section.

8-762/S-021

This supplement provides for the addition of fluoxetine to the **PRECAUTION-Drug Interactions** section as requested in an Agency letter dated February 3, 1994.

8-762/S-022

This supplement provides for revisions to the container labels as well as to the **PRECAUTIONS-Information for Patients** section stating that a calibrated measuring device should be used to measure the oral suspension.

8-762/S-026

This supplement provides for the following revisions:

1. The addition of a **Pediatric Use** subsection under the **PRECAUTIONS** section.
2. Several minor revisions to the **OVERDOSAGE** and **DOSAGE AND ADMINISTRATION** sections to conform to standard pediatric nomenclature.
3. Remove reference to the 5 ml unit dose pouches under the **HOW SUPPLIED** section since they are no longer marketed.

Dilantin (Phenytoin Sodium Injection, USP) Injection

10-151/S-022

This supplement provides for dosage recommendations for neonates in status epilepticus.

10-151/S-029
This supplement provides for revisions to the **PRECAUTIONS** and **ADVERSE REACTIONS** sections of labeling based upon your review of drug experience reports.

10-151/S-030
This supplement provides for revisions to the **DOSAGE AND ADMINISTRATION** section to strengthen the directions for the administration of parental Dilantin via the bolus method, and added instructions for the administration via the infusion method.

10-151/S-032
This supplement provides for the addition of fluoxetine to the **PRECAUTION-Drug Interactions** section as requested in an Agency letter dated February 3, 1994.

10-151/S-033
This labeling supplement is similar to that submitted for **8-762/SLR-020** (see above). We note that it was submitted by you in order to 1) update the labeling to add pertinent information from the Cerebyx labeling to the Dilantin labeling, and 2) assist the Agency in taking an action for the open labeling supplements.
10-151/S-034
This supplement provides for the following revisions:
1. The addition of a **Pediatric Use** subsection under the **PRECAUTIONS** section.
2. Several minor revisions to the **OVERDOSAGE** and **DOSAGE AND ADMINISTRATION** sections to conform to standard pediatric nomenclature.

We note that supplemental application 8-762/S-020 was submitted as a "prior approval" application and was amended on January 28, 1997. The amendment incorporates all of the revisions made in S-021/022/026 as well as strengthens the labeling to incorporate important safety changes already in the Cerebyx labeling.

Similarly, we note that supplemental application 10-151/S-033 was submitted as a "prior approval" application and was amended on January 28, 1997. The amendment incorporates all of the revisions made in S-022/029/030/032/034 as well as strengthens the labeling to incorporate important safety changes already in the Cerebyx labeling.

We have completed our review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in your draft labeling submitted on January 28, 1997 except for your proposed addition to the **PRECAUTIONS-General** section regarding adverse events associated with the combination use of phenytoin, cranial radiation, and reduction of corticosteroids.

We are currently evaluating these data in conjunction with the Agency's Office of Postmarketing Drug Risk Assessment, and we will comment on these changes in a separate letter.

Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) for 8-762/S-020 and 10-151/S-033 must be identical to the draft labeling submitted on January 28, 1997, except for your proposed addition to the **PRECAUTIONS-General** section regarding adverse events associated with the combination use of phenytoin, cranial radiation, and reduction of corticosteroids.

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 8-762/S-020 and NDA 10-151/S-033." Approval of these submissions by FDA is not required before the labeling is used.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Mr. Paul David, R.Ph., Senior Regulatory Project Manager, at (301) 594-5530.

Sincerely,

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