CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-450/S-004

ADMINISTRATIVE DOCUMENTS

REGULATORY PROJECT MANAGER
LABELING REVIEW

DRUG: NDA 20-450 Cerebyx® (fosphenytoin sodium) Injection

Supplements: S-004, S-005, & —

(last approved) Original Approval (August 5, 1996)
Label Code: Package Insert: #4007G030 July, 1996 (original approval)

(pending action) SLR-004 (dated: March 1, 1999)
(amended: April 9, 1999)
SLR-005 (dated: June 24, 1999)

NOTE: The original approval of Cerebyx® was based on draft labeling submitted to the application on July 12, 1996. The August 5, 1996 approval letter referenced this submitted draft labeling and requested additional editorial changes. FPL for both carton/container and the package insert was submitted to the NDA after approval on August 26, 1996. Carton/container labeling was further modified soon after the original approval (S-001 approved December 26, 1996). The package insert FPL submitted on August 26, 1996 has not previously been reviewed for compliance with the original approval letter.

REVIEW

SLR-004
Dated: March 1, 1999
Amended: April 9, 1999
CBE: Yes
Carton/Container Labels:

The supplement provides for revision of carton/container labeling to reflect concentration as a function of total container content rather than content per mL. This change was effected in response to several reports of overdose where health care providers mistakenly assumed that the amount of Cerebyx® per mL was the final amount provided by the total vial.

Reviewed by Chemist: Not Approvable. See review dated March 18, 1999.

1. The Chemistry review notes that the submitted labeling does not comply with recommendations made by the CDER Medication Errors Committee in a memo dated May 28, 1998. These recommendations were conveyed to the firm in a labeling change request letter dated January 6, 1999.

2. A review of the administrative files indicates that the firm and the Division negotiated and reached agreement on the content of the container labels in a series of communications in late January/early February, 1999 subsequent to receipt of the January 6th letter. The supplemental application submitted on March 1, 1999 includes labels that comply with the

agreements reached. The chemistry review does not include comments that indicate that the reviewer was aware of the agreements reached between the firm and the Division.

SLR-005
Dated: June 24, 1999
CBE: Yes
Package Insert Label Code: # 4007G211 May, 1999

The supplement provides for revisions to the OVERDOSAGE section of the package insert to include specific adverse events that have been reported during cases of overdosage with Cerebyx®.

Reviewed by Medical Officer: Acceptable

1. A line-by-line comparison of this package insert was conducted using the "draft" package insert from the July 12, 1996 submission as a base. No changes beyond those provided for in S-005 or in the original approval letter were noted.

CONCLUSIONS

1. S-004: The clinical team leader should assess the recommendations from the chemistry review in light of the previous agreements reached with the firm. Based upon this assessment, an action letter can issue which either approves the supplement or asks for further revision of the container labeling in an approvable letter.

2. S-005: This supplemental application may be approved.

Robbin Nighswander, R.Ph.
Supervisory Regulatory Health Project Manager

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/s/

Robbin Nighswander
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CSO