CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-678/S003

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

NDA 20-678/S-003

Food and Drug Administration
Rockville MD 20857

Baxter Healthcare Corporation
Attention: Marcia Marconi
Vice President Regulatory Affairs
Route 120 and Wilson Road
Round Lake, IL 60073

APR 12 2000

Dear Ms. Marconi:

Please refer to your supplemental new drug application dated July 6, 1999, received July 7, 1999, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Clinimix E™ sulfite-free (Amino Acid with Electrolytes in Dextrose with Calcium) Injections in Clarity™ Dual Chamber Container.

We acknowledge receipt of your submissions dated March 28 and 31, 2000.

This supplemental new drug application provides for changes in the WARNINGS, PRECAUTIONS, and DOSAGE and ADMINISTRATION sections of the package insert labeling in response to the Final Rule published in the Federal Register on December 13, 1994, titled *"Specific Requirements on Content and Format of labeling for Human Prescription Drugs: Revision of Pediatric Use Subsection in the Labeling"*, vol. 59, No. 238, Pages 64240-64250.

We have completed the review of this supplemental application, 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 the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted March 28, 2000).

Please submit 20 copies of the FPL as soon as it is available, in no case 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, this submission should be designated "FPL for approved supplement NDA 20-678/S-003." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Steve McCort, Regulatory Project Manager, at (301) 827-6415.

Sincerely,

/S/

John K. Jenkins, M.D.
Acting Director
Division of Metabolic and
Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CLINIMIX E (amino acid with electrolytes in dextrose with calcium) Injection
[April 12, 2000: Baxter Healthcare]

WARNINGS:

New last paragraph added -

"In very low birth weight infants, excessive or rapid administration of dextrose injection may result in increased serum osmolality and possible intracerebral hemorrhage."

PRECAUTIONS:

Pediatric Use: New subsection -

"Dextrose is safe for the stated indications in pediatric patients (see Indications and Usage). As reported in the literature, the dosage selection and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low birth weight infants, because of an increased risk of hyperglycemia/hypoglycemia. Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly neonates and low birth weight infants.

"Safety and effectiveness of Clinimix - sulfite-free (amino acid with electrolytes in Dextrose with Calcium) Injections in pediatric patients have not been established by adequate and well-controlled studies. However, the use of amino acid injections in pediatric patients as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance is referenced in the medical literature. See Dosage and Administration."

DOSAGE AND ADMINISTRATION:

Third paragraph, third sentence revised -

"Daily amino acid doses of approximately 1.0 to 1.5 g/kg of body weight for adults ["and 2 to 3 g/kg body weight for infants" deleted] with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance."

Pediatric Use: New subsection -

"Use of Clinimix - sulfite-free (Amino Acid in Dextrose) Injections in pediatric patients is governed by the same considerations that affect the use of any amino acid solution in pediatrics. The amount administered is dosed on the basis of grams of amino acids/kg of body weight/day. Two to 3 g/kg of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance. Solution administrations by peripheral vein should not exceed twice normal serum osmolality (718 mOsmol/L).

Peripheral Vein Administration: New second sentence -

"In pediatric patients, the final solution should not exceed twice normal serum osmolality (718 mOsmol/L)."

Return to Quick Reference