DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-615/S-012

Baxter Healthcare Corporation
Attention: Ms. Marcia Marconi
Route 120 and Wilson Road
Round Lake, IL 60073-0490

Dear Ms. Marconi:

Please refer to your supplemental new drug application dated June 22, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Dopamine Hydrochloride and 5% Dextrose Injection, USP in Plastic Container, PL 2207.

We acknowledge receipt of your submission dated March 27, 2001 that constituted a complete response to our April 20, 2000 approvable letter.

This supplemental new drug application provides for final printed labeling revised as follows:

1. The **PRECAUTIONS, Pediatric Use** subsection has been changed to:

   Safety and effectiveness in children have not been established. The clearance of dopamine is affected by age (as much as 2 fold greater in children under 2 years of age), renal and hepatic function (decreasing by 2 fold in the presence of either). In younger children, particularly neonates, clearance is highly variable. Newborn infants may be more sensitive to the vasoconstrictive effects of dopamine.

   The most consistent effects of dopamine in 57 publications (between the years 1966 through 1997) were increases in systolic and mean arterial pressure. Renal function was variably affected, except that in a single publication renal function was preserved in the face of treatment with indomethacin. No consistent effect on heart rate was described. Because of the variability of clearance, especially in the neonate and newborn, low doses of dobutamine and slow deliberate titration should be employed (see **DOSAGE and ADMINISTRATION).**

2. Under **DOSAGE and ADMINSTRATION**, a new **Pediatric Dosing and Administration** subsection has been added. It reads as follows:

   **Pediatric Dosing and Administration**

   In publications, the most common **starting** doses were **1-5** micrograms/kilograms/minute. **Particularly in neonates, such low doses require considerable dilution of this product; careful consideration should be given to the use of this product in such circumstances.** Dosing increments that were reported ranged from 2.5 to 5.0 micrograms/kilogram/minute. Usual maximum doses were 15-20 micrograms/kilogram/minute, with occasional use as great as 50 micrograms/kilogram/minute. The time course of dopamine kinetics are poorly defined. Increasing infusion rates (or dose) should be approached cautiously and only after it is apparent that hemodynamics (mainly systolic blood pressure) have stabilized with respect to the current dose and/or rate of infusion.

There have been occasional reports of vasospastic events when dopamine was infused through umbilical vessels. Due caution should be exercised if infusion of dopamine through umbilical vessels becomes necessary.

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 submitted final printed labeling (package insert included in your submission of March 27, 2001). Accordingly, the supplemental application is approved effective on the date of this letter.

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, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

*{See appended electronic signature page}*

Raymond J. Lipicky, M.D.
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