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APPLICATION NUMBER:

18-227 / S-012

APPROVAL LETTER

NDA 18-227/S-012

Abbott Laboratories
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

Attention: Thomas P. Sampogna
Manager, Regulatory Affairs

Dear Mr. Sampogna:

Please refer to your supplemental New Drug Application (sNDA) dated August 28, 1998, and received on September 01, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Amidate (Etomidate Injection) Fliptop vial 2mg/mL.

This supplemental New Drug Application provide for:
"Geriatric Use" Subsection in the labeling" by updating the currently approved label to incorporate the appropriate geriatric labeling into the package inserts.

We have completed the review of this supplemental application, 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 labeling with the revisions listed below. Accordingly, this supplemental application is approved effective on the date of this letter. The Division's additions are indicated by bold and underline and deletions are indicate by strikethrough. The revisions are as follows :

CLINICAL PHARMACOLOGY

However, ~~clinical data~~ indicates that etomidate administration in geriatric patients, particularly those with hypertension, may result in decreases in heart rate, cardiac index, and mean arterial blood pressure.

CLINICAL PHARMACOLOGY

In clinical ~~studies~~, elderly patients demonstrated decreased initial distribution volumes and total clearance of etomidate. Protein binding of etomidate to serum albumin was also significantly decreased in these individuals.

PRECAUTIONS

Geriatric Use

_____ clinical ~~data~~ ___ ndicates that etomidate may induce cardiac depression in elderly patients, particularly those with hypertension (see CLINICAL PHARMACOLOGY and OTHER ADVERSE OBSERVATIONS, Circulatory System).

Elderly patients may require lower doses of etomidate than younger patients. Age – related differences in pharmacokinetic parameters have been observed in clinical studies (see CLINIACL PHARMACOLOGY and DOSAGE AND ADMINISTRATION).

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function, because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

OTHER ADVERSE OBSERVATIONS

Geriatric patients, particularly those with hypertension, may be at increased risk for the development of cardiac depression following etomidate administration (see CLINICAL PHARMACOLOGY).

DOSAGE AND ADMINISTRATION

There are inadequate data to make dosage recommendations for induction of anesthesia in patients below the age of ten (10) or **over the age of sixty-five (65)** years; therefore, such use is not recommended. ~~Geriatric patients may require reduced doses of etomidate.~~

These revisions are terms of the supplemental NDA approval.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. 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 18-227" Approval of this submission by FDA is not required before the labeling is used.

Should additional information related to the safety and effectiveness of the drug becomes available, further revision of that labeling may be required.

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, contact David Morgan, Project Manager, at (301) 827-7410.

Sincerely,

Cynthia G. McCormick, M.D.
Director
Division of Anesthetic, Critical Care,
and Addiction Drug Products, HFD-170
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 18-227
HFD-170/Div. Files/
HFD-170/D.Morgan
HFD-170/C. G. McCormick
HFD-170/B. Rappaport/M. Roberts/A. W. Longmire
HFD-170/S. Doddapaneni
HFD-170/C. P. Moody
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-103/ADRA (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-95/DDMS (with labeling)
DISTRICT OFFICE

Drafted by: DM/February 22, 1999
Initialed by:
Final:
Filename: 18-22/S-012

APPROVAL (AP)