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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

19-386/S-021

Medical Review(s)

To: NDA #19-386, S-019, S-020, S-021

From: Shari Targum, MD

Correspondence Date: 9/30/02, 10/24/02

Date of Review: 1/9/03

Re: Labeling changes

The sponsor has submitted three labeling supplements for Brevibloc (esmolol HCl) Injection. These labeling supplements involve the addition of a Breviblock Double Strength Premixed Injection containing 20 mg/ml concentration of esmolol HCl (S-20) as well as completion of prior Phase 4 commitment (to reduce overage of esmolol HCl added to the formulation).

Under Dosage and Administration, this reviewer noted the following additional language (underlined):
"The Brevibloc Premixed Injection contains Esmolol Hydrochloride at a concentration of 10 milligrams/mL. When using a 10 milligrams/mL concentration, a loading dose of 0.5 milligrams/kg infused over 1 minute period of time, for a 70 kg patient, is 3.5 mL....
The Breviblock Premixed Injection DOUBLE STRENGTH contains Esmolol Hydrochloride at a concentration of 20 milligrams/mL. When using a 20 milligrams/mL concentration, a loading dose of 0.5 milligrams/kg infused over 1 minute period of time, for a 70 kg patient, is 1.75 ml...."

Reviewer: Given the two-fold higher concentration in the Double-Strength formulation, the reviewer concurs with administration of half the loading dose volume.
The reviewer has no objection to the color change proposed in the supplements, so long as these changes serve to clarify and not cause confusion.

APPEARS THIS WAY
ON ORIGINAL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Shari Targum
1/13/03 04:35:09 PM
MEDICAL OFFICER