CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

NDA 19-386/S-022

Trade Name: Brevibloc

Generic Name(s): (Esmolol hydrochloride in sodium chloride)

Sponsor: Baxter Healthcare Corporation

Agent:

Approval Date: May 28, 2003

Indication: Short-Term control of heart rate in patients with abnormally fast heart rhythms such as artrial fibrillation, atrial flutter or sinus tachycardia.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-386 / S-022

CONTENTS

Reviews / Information Included in this NDA Review.	
Approval Letter	X
Approvable Letter	
Final Printed Labeling	
Medical Review(s)	
Chemistry Review(s)	X
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	X
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative Document(s)	X
Correspondence	
Bioresearch Monitoring	

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 19-386/S-022

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-386/S-022

Baxter Healthcare Corporation, Anesthesia & Critical Care
Attention: Ms. Lidia Mostovy
95 Spring Street
New Providence, NJ 07974

Dear Ms. Mostovy:

Please refer to your supplemental new drug application dated January 28, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Brevibloc Double Strength Injection (esmolol hydrochloride) 20 mg/mL in 5 mL ready-to-use vials.

This supplemental new drug application provides for the marketing of a new double strength formulation in 5 mL vials. This formulation was approved for marketing in 100 mL bags on January 27, 2003 with the approval of S-020.

This supplement proposes the following changes to the package insert:

1. The following changes were made in the title under the **BREVIBLOC PREMIXED** INJECTION:

    a. (Esmolol Hydrochloride) changed to (Esmolol Hydrochloride in Sodium Chloride)

    b. The addition of the following on the next line: 2,500 mg/250 mL (10mg/mL)

    c. Iso-Osmotic Solution of Esmolol Hydrochloride in Sodium Chloride changed to Iso-Osmotic Solution of Esmolol Hydrochloride

2. The following changes were made in the title under **BREVIBLOC PREMIXED** INJECTION **DOUBLE STRENGTH**:

    a. The title was changed from **BREVIBLOC PREMIXED** INJECTION to **BREVIBLOC DOUBLE STRENGTH PREMIXED** INJECTION

    b. (Esmolol Hydrochloride) **DOUBLE STRENGTH** changed to (Esmolol Hydrochloride in Sodium Chloride)

    c. The addition of the following on the next line: 2,000mg/100mL (20mg/mL)

    d. Iso-Osmotic Solution of Esmolol Hydrochloride in Sodium Chloride changed to Iso-Osmotic Solution of Esmolol Hydrochloride

3. The following changes were made in the title under **BREVIBLOC** INJECTION:

    a. (Esmolol Hydrochloride) changed to (Esmolol Hydrochloride in Sodium Chloride)

    b. The addition of the following on the next line: 100 mg/10 mL (10mg/mL)

    c. Iso-Osmotic Solution of Esmolol Hydrochloride in Sodium Chloride changed to Iso-Osmotic Solution of Esmolol Hydrochloride

4. The addition of the following to the title:

   BREVIBLOC DOUBLE STRENGTH INJECTION
   (Esmolol Hydrochloride in Sodium Chloride)
   100 mg/5 mL (20 mg/mL)
   Ready-to-use Vials
   5 mL Vials
   Iso-Osmotic Solution of Esmolol Hydrochloride
   For Intravenous Use
   Can be used for direct intravenous use.
   Esmolol Hydrochloride concentration = 20 milligrams/mL (20,000 micrograms/mL)
   Single Patient Use Only
   No Preservatives Added

5. The following changes were made to the title under **BREVIBLOC** CONCENTRATE:

   a. The addition of the following line: 2,500 mg/10 mL (250 mg/mL)

6. The following paragraph was added at the end of the **Brevibloc Injection** subsection of the **DESCRIPTION** section:

   100 mg, 5 mL DOUBLE STRENGTH Single Dose Vial– Each mL contains 20 mg Esmolol Hydrochloride, 4.1 mg Sodium Chloride, USP and Water for Injection, USP; buffered with 2.8 mg Sodium Acetate Trihydrate, USP and 0.546 mg Glacial Acetic Acid, USP. Sodium Hydroxide and/or Hydrochloric Acid added, as necessary to adjust pH to 5.0 (4.5-5.5).

7. The second sentence in the **PRECAUTIONS/General** subsection was changed from:

   Extravasation of 20mg/mL may lead to a serious local reaction and possible skin necrosis.

   To:

   With BREVIBLOC CONCENTRATE, extravasation of 20mg/mL or higher may lead to a serious local reaction and possible skin necrosis.

8. The third paragraph in the **PRECAUTIONS/General** subsection was changed from:

   Care should be taken in the intravenous administration of BREVIBLOC as sloughing of the skin and necrosis have been reported in association with infiltration and extravasation of intravenous infusions.

   To:

   Care should be taken in the intravenous administration of BREVIBLOC CONCENTRATE as sloughing of the skin and necrosis have been reported in association with infiltration and extravasation of intravenous infusions.

9. The following sentence was added as the third sentence of the first paragraph of the **OVERDOSAGE/Acute Toxicity** subsection:

   Use of BREVIBLOC PREMIXED INJECTION and BREVIBLOC **DOUBLE STRENGTH** PREMIXED INJECTION may reduce the potential for dilution errors.

10. In the **DOSAGE AND ADMINISTRATION** section, the subsection title has been changed from:

    Directions for Use of Brevibloc Premixed Injection and Brevibloc Premixed Injection DOUBLE STRENGTH

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.