HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BREVIBLOC safely and effectively. See full prescribing information for BREVIBLOC.

BREVIBLOC (esmolol hydrochloride) injection, for intravenous use
Initial U.S. Approval: 1986

----------INDICATIONS AND USAGE----------

BREVIBLOC is a beta adrenergic blocker indicated for the short-term treatment of:

- Control of ventricular rate in supraventricular tachycardia including atrial fibrillation and atrial flutter and control of heart rate in noncompensatory sinus tachycardia (1.1)
- Control of perioperative tachycardia and hypertension (1.2)

----------DOSAGE AND ADMINISTRATION----------

- Administer intravenously (2.1, 2.2)
- Titrate using ventricular rate or blood pressure at ≥ 4-minute intervals (2.1, 2.2)
- Supraventricular tachycardia (SVT) or noncompensatory sinus tachycardia (2.1)
  - Optional loading dose: 500 mcg per kg infused over one minute
  - Then 50 mcg per kg per minute for the next 4 minutes
  - Adjust dose as needed to a maximum of 200 mcg per kg per minute
  - Additional loading doses may be administered
- Perioperative tachycardia and hypertension (2.2)
  - Loading dose: 500 mcg per kg over 1 minute for gradual control (1 mg per kg over 30 seconds for immediate control)
  - Then 50 mcg per kg per minute for gradual control (150 mcg per kg per minute for immediate control) adjusted to a maximum of 200 (tachycardia) or 300 (hypertension) mcg per kg per minute (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

- Injection: 100 mg/10 mL (10 mg/mL) in 10 mL vial (3)
- Injection: 2500 mg/250 mL (10 mg/mL) in 250 mL Premixed Injection bag (3)
- Injection: 2000 mg/100 mL (20 mg/mL) in 100 mL Double Strength Premixed Injection bag (3)

----------CONTRAINDICATIONS----------

- Severe sinus bradycardia (4)
- Heart block greater than first degree (4)
- Sick sinus syndrome (4)
- Decompensated heart failure (4)
- Cardiogenic shock (4)
- Coadministration of IV cardiodepressant calcium-channel antagonists (e.g. verapamil) in close proximity to BREVIBLOC (4, 7)
- Pulmonary hypertension (4)
- Known hypersensitivity to esmolol (4)

----------WARNINGS AND PRECAUTIONS----------

- Risk of hypotension, bradycardia, and cardiac failure: Reduce or discontinue use (5.1, 5.2, 5.3, 5.10)
- Risk of exacerbating reactive airway disease (5.5)
- Diabetes mellitus: Increases the effect of hypoglycemic agents and masks hypoglycemic tachycardia (5.6)
- Risk of unopposed alpha-agonism and severe hypertension in untreated pheochromocytoma (5.9)
- Risk of myocardial ischemia when abruptly discontinued in patients with coronary artery disease (5.12, 5.15)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence> 10%) are symptomatic hypotension (hyperhidrosis, dizziness) and asymptomatic hypotension (6)

To report SUSPECTED ADVERSE REACTIONS, contact Baxter Healthcare Corporation at 1-866-888-2472 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------

- Digitalis glycosides: Risk of bradycardia (7)
- Anticholinesterases: Prolongs neuromuscular blockade (7)
- Antihypertensive agents: Risk of rebound hypertension (7)
- Sympathomimetic drugs: Dose adjustment needed (7)
- Vasoconstrictive and positive inotropic effect substances: Avoid concomitant use (7)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the Full Prescribing Information are not listed

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Supraventricular Tachycardia or Noncompensatory Sinus Tachycardia

BREVIBLOC (Esmolol Hydrochloride) is indicated for the rapid control of ventricular rate in patients with atrial fibrillation or atrial flutter in perioperative, postoperative, or other emergent circumstances where short term control of ventricular rate with a short-acting agent is desirable. BREVIBLOC is also indicated in noncompensatory sinus tachycardia where, in the physician's judgment, the rapid heart rate requires specific intervention. BREVIBLOC is intended for short-term use.

1.2 Intraoperative and Postoperative Tachycardia and Hypertension

BREVIBLOC (Esmolol Hydrochloride) is indicated for the short-term treatment of tachycardia and hypertension that occur during induction and tracheal intubation, during surgery, on emergence from anesthesia and in the postoperative period, when in the physician's judgment such specific intervention is considered indicated.

Use of BREVIBLOC to prevent such events is not recommended.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing for the Treatment of Supraventricular Tachycardia or Noncompensatory Sinus Tachycardia

Brevibloc is administered by continuous intravenous infusion with or without a loading dose. Additional loading doses and/or titration of the maintenance infusion (step-wise dosing) may be necessary based on desired ventricular response.

Table 1 Step-Wise Dosing

Step	Action
1	Optional loading dose (500 mcg per kg over 1 minute), then 50 mcg per kg per min for 4 min
2	Optional loading dose if necessary, then 100 mcg per kg per min for 4 min
3	Optional loading dose if necessary, then 150 mcg per kg per min for 4 min
4	If necessary increase dose to 200 mcg per kg per min

In the absence of loading doses, continuous infusion of a single concentration of esmolol reaches pharmacokinetic and pharmacodynamic steady-state in about 30 minutes.

The effective maintenance dose for continuous and step-wise dosing is 50 to 200 mcg per kg per minute, although doses as low as 25 mcg per kg per minute have been adequate. Dosages greater than 200 mcg per kg per minute provide little added heart-rate lowering effect, and the rate of adverse reactions increases.

Maintenance infusions may be continued for up to 48 hours.

2.2 Intraoperative and Postoperative Tachycardia and Hypertension

In this setting it is not always advisable to slowly titrate to a therapeutic effect. Therefore two dosing options are presented: immediate control and gradual control.

Immediate Control

- Administer 1 mg per kg as a bolus dose over 30 seconds followed by an infusion of 150 mcg per kg per min if necessary.
- Adjust the infusion rate as required to maintain desired heart rate and blood pressure. Refer to Maximum Recommended Doses below.

Gradual Control

- Administer 500 mcg per kg as a bolus dose over 1 minute followed by a maintenance infusion of 50 mcg per kg per min for 4 minutes.
- Depending on the response obtained, continue dosing as outlined for supraventricular tachycardia (refer to Figure 1). Refer to Maximum Recommended Doses below.

Maximum Recommended Doses

- For the treatment of tachycardia, maintenance infusion dosages greater than 200 mcg per kg per min are not recommended; dosages greater than 200 mcg per kg per min provide little additional heart rate-lowering effect, and the rate of adverse reactions increases.
- For the treatment of hypertension, higher maintenance infusion dosages (250-300 mcg per kg per min) may be required. The safety of doses above 300 mcg per kg per minute has not been studied.

2.3 Transition from BREVIBLOC Therapy to Alternative Drugs

After patients achieve adequate control of the heart rate and a stable clinical status, transition to alternative antiarrhythmic drugs may be accomplished.

When transitioning from BREVIBLOC to alternative drugs, the physician should carefully consider the labeling instructions of the alternative drug selected and reduce the dosage of BREVIBLOC as follows:

1. Thirty minutes following the first dose of the alternative drug, reduce the BREVIBLOC infusion rate by one-half (50%).

2. After administration of the second dose of the alternative drug, monitor the patient's response, and, if satisfactory control is maintained for the first hour, discontinue the BREVIBLOC infusion.

2.4 Directions for Use

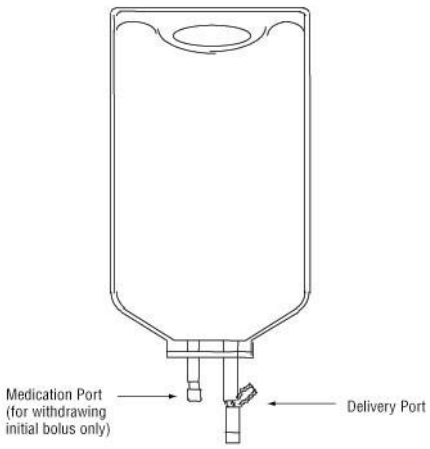
BREVIBLOC is available in a pre-mixed bag and ready-to-use vial. BREVIBLOC is not compatible with Sodium Bicarbonate (5%) solution (limited stability) or furosemide (precipitation).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Premixed Bag

- The medication port is to be used solely for withdrawing an initial bolus from the bag.
- Use aseptic technique when withdrawing the bolus dose.
- Do not add any additional medications to the bag.

Figure 2: Two-Port IntraVia Bag



Ready-to-Use Vial

The Ready-to-use Vial may be used to administer a loading dosage by hand-held syringe while the maintenance infusion is being prepared *[see How Supplied/Storage and Handling (16.2)]*.

Compatibility with Commonly Used Intravenous Fluids

BREVIBLOC was tested for compatibility with ten commonly used intravenous fluids at a final concentration of 10 mg Esmolol Hydrochloride per mL. BREVIBLOC was found to be compatible with the following solutions and was stable for at least 24 hours at controlled room temperature or under refrigeration:

- Dextrose (5%) Injection, USP
- Dextrose (5%) in Lactated Ringer's Injection
- Dextrose (5%) in Ringer's Injection
- Dextrose (5%) and Sodium Chloride (0.45%) Injection, USP
- Dextrose (5%) and Sodium Chloride (0.9%) Injection, USP
- Lactated Ringer's Injection, USP
- Potassium Chloride (40 mEq/liter) in Dextrose (5%) Injection, USP
- Sodium Chloride (0.45%) Injection, USP
- Sodium Chloride (0.9%) Injection, USP

3 DOSAGE FORMS AND STRENGTHS

All BREVIBLOC dosage forms are iso-osmotic solutions of Esmolol Hydrochloride in Sodium Chloride.

Table 1 BREVIBLOC Presentations

Product Name	BREVIBLOC PREMIXED INJECTION (Esmolol Hydrochloride)	BREVIBLOC DOUBLE STRENGTH PREMIXED INJECTION (Esmolol Hydrochloride)	BREVIBLOC INJECTION (Esmolol Hydrochloride)
Total Dose	2500 mg / 250 mL	2000 mg / 100 mL	100 mg / 10 mL
Esmolol Hydrochloride Concentration	10 mg/mL	20 mg/mL	10 mg/mL
Packaging	250 mL Bag	100 mL Bag	10 mL Vial

4 CONTRAINDICATIONS

BREVIBLOC (Esmolol Hydrochloride) is contraindicated in patients with:

DOCKET ALARM

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