DEPARTMENT OF HEALTH & HUMA N SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED VIA FACSIMILE

Priya Jambhekar
Director, Regulatory Affairs
Baxter Pharmaceutical Products Inc.
95 Spring Street
New Providence, New Jersey 07974

RE: NDA #19-368
Brevibloc (esmolol hydrochloride) Injection
MACMIS ID # 9860

Dear Ms. Jambhekar:

This letter concerns Baxter Pharmaceutical Products Inc.'s (BPP) dissemination of promotional materials for Brevibloc. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a calendar (748285) for Brevibloc as part of its routine monitoring and surveillance program. From its review, DDMAC has concluded that this piece is in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations because it lacks fair balance.

Lack of Fair Balance

Promotional materials are lacking in fair balance if they fail to present information relating to side effects and contraindications with a prominence and readability reasonably comparable with the presentation of information relating to effectiveness of the drug, taking into account all implementing factors such as typography, layout, contrast, headlines, paragraphing, white space, and any other technique apt to achieve emphasis.

Your calendar lacks fair balance because it includes efficacy claims that are prominently presented with bullets, white space, and large headings. In contrast, the majority of your risk information is presented in a small font size and block format, with minimal white space and without headings or other means of signaling the reader specifically to important warnings and contraindications. In addition, you fail to disclose the warning that Brevibloc should not be used as the treatment for hypertension in patients in whom the increased blood pressure is primarily due to the vasoconstriction associated with hypothermia.

We refer you to our untitled letter dated October 1, 1999, in which we outlined similar objections to violative materials and your October 15, 1999, response to our untitled

letter stating that you would discontinue violative materials and correct the misleading risk presentation in future promotional pieces.

Furthermore, your calendar includes the efficacy claim "In clinical studies, about 60-70% of patients treated with Brevibloc achieved a desired therapeutic effect." Presenting this efficacy claim as the first bullet introducing your risk information minimizes the importance of the contraindications, warnings, precautions, and adverse reactions associated with Brevibloc therapy that follow.

BPP should immediately cease dissemination of promotional materials or activities that contain these and similar claims or presentations concerning Brevibloc. In addition, BPP should respond in writing no later than April 9, 2001, describing its plan to comply. BPP should also include a list of materials being discontinued, as well as the date of discontinuation.

Your response should be directed to me by facsimile at 301-594-6771 or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

We remind you that only written communications are considered official. In all future correspondence regarding this particular matter please refer to MACMIS ID #9860 in addition to the NDA number.

Sincerely,

(see accompanying page for electronic signature)

Andrew S.T. Haffer, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

/s/

Andrew Haffer
3/26/01 01:02:05 PM

2001

DECEMBER 2000

S	M	T	W	T	F	S
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

FEBRUARY 2001

S	M	T	W	T	F	S
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28			

January

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
	1 New Year's Day	2	3	4	5	6
7	8	9	10	11	12	13
14	15 Martin Luther King, Jr. Day	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

January March

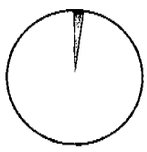
2001-2002 Calendar

from CRITICAL FAST

to CONTROLLED

For control of ventricular rate and/or BP,

Brevibloc® (esmolol HCl) provides:



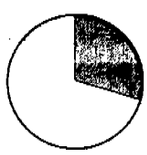
Predictability[1] Onset of action: 2 minutes

Rapid treatment of ventricular rate in critical events, such as:

- Atrial fibrillation
- Atrial flutter

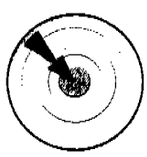
Added control[1] Elimination half-life: 9 minutes

Ability to quickly titrate during critical events



Quick recovery[1] Duration of action: 10–20 minutes

After completion of infusion, reversibility for beta blockade is observed within 10–20 minutes



Flexibility[1] Selective $beta_1$ blockade*

At low doses, may be used with caution in patients with asthma or COPD

*Beta, selectivity is not absolute; at higher doses it begins to inhibit $beta_2$ receptors

WARNING: PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD, IN GENERAL, NOT RECEIVE BETA BLOCKERS.

• In clinical studies, about 60–70% of patients treated with Brevibloc® achieved a desired therapeutic effect • Individual responses may vary based on the patient's condition • Brevibloc® is contraindicated in patients with sinus bradycardia, heart block greater than first degree, cardiogenic shock or overt heart failure • Caution is advised when using any beta blocker due to the potential for serious side effects in particular patient populations • Beta, selectivity is not absolute; at higher doses it begins to inhibit $beta_2$ receptors • The most common side effect is hypotension, asymptomatic in 25%, symptomatic in 12%, mainly dizziness and diaphoresis • Hypotension usually reverses within 30 minutes of the decrease in dose or termination of infusion • Brevibloc® should be used with caution in patients with LV dysfunction, CHF, hypotension, advanced AV block and reactive airway disease • Reduced doses may be necessary in the elderly • The use of Brevibloc® to prevent tachycardia and/or hypertension is not recommended.

Please see accompanying full prescribing information.

Reference: 1. Brevibloc® package insert, revised June 1998. Baxter, New Providence, NJ.

For the reduction of ventricular rate and/or BP

Brevibloc® (esmolol HCl) INJECTION

When Every Minute Counts

Baxter

95 Spring Street, New Providence, NJ 07974. 1-800-ANA-DRUG http://www.baxter.com