CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
19-962/S-013

Approvable Letter

McDonald

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 19-962/S-013

JUL 10 2000

AstraZeneca LP
Attention: Steven J. Miller, Ph.D.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Dear Dr. Miller:

Please refer to your supplemental new drug application dated September 10, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Toprol XL (metoprolol succinate) 25, 50, 100 and 200 mg Tablets.

We acknowledge receipt of your submissions dated November 8 and 15, and December 22, 1999; January 6, 17, 18 and 26, February 1, 2, 8 (two), and 23, March 3, 6, and 16, April 13 and 21, May 5, 17 (two), 25 and 30, and June 14 and 23, 2000.

This supplemental new drug application provides for the use of Toprol XL (metoprolol succinate) Tablets for the treatment of congestive heart failure and for a 25 mg dosage strength scored tablet.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed labeling (text for the package insert).

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

Please submit 20 paper copies of the final printed labeling ten of which are individually mounted on heavy weight paper or similar material. Alternately, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999).

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

As agreed to in a telephone conversation with Mr. Len Alansky on June 27, 2000, please incorporate a for Toprol XL Tablets. In addition, please update the storage statement on container labels to conform to the revised statement in the package insert and use your current corporate name in all labeling.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Cardio-Renal Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, please call:

Ms. Zelda McDonald
Regulatory Health Project Manager
(301) 594-5333

Sincerely,

/S/ 7/10/00

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:
Archival NDA 19-962
HFD-110/Div. Files
HFD-110/Z.McDonald
HFD-101/RTemple
HFD-002/ORM
HFD-101/ADRA
HFD-42/DDMAC (with labeling)
DISTRICT OFFICE
Drafted by: ZM/June 21, 2000
Initialed by: R Mittal/6/28/00
K Srinivasachar/6/28/00
N Nguyen/6/28/00
P Marroum/6/28/00
A DeFelice/6/28/00
L Cui/6/28/00
J Hung/6/28/00
C Duarte/6/28/00
N Stockbridge/6/27/00
N Morgenstern/6/30/00
Final: asb/6/30/00

APPROVABLE (AE)

26 pages redacted from this section of the approval package consisted of draft labeling

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
19-962/S-013

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-962/S-013

AstraZeneca LP
Attention: Ms. Cindy M. Lancaster
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Ms. Lancaster:

Please refer to your supplemental new drug application dated September 10, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Toprol-XL (metoprolol succinate) 25, 50, 100, 200 mg Tablets.

We acknowledge receipt of your submissions dated July 19 (two), August 7, September 14, November 27, and December 20, 2000 and January 11, 2001. Your submission of January 11, 2001 constituted a complete response to our July 10, 2000 action letter.

This supplemental new drug application provides for the new use of Toprol-XL (metoprolol succinate) Tablets for the treatment of congestive heart failure and for a 25 mg dosage strength scored tablet.

We have completed the review of this supplemental application, as amended, 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 final printed package insert and immediate container and carton labels included in your January 11, 2001 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

At the time of your next printing, please revise the sentence under Clinical Trials, line 266 as follows:

"However, in the US subgroup (N=1071) and women (N=898), overall mortality and cardiovascular mortality appeared less affected."

A supplement is not needed for this change; please include it in your annual report.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" 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, call:

Ms. Zelda McDonald
Regulatory Health Project Manager
(301) 594-5333.

Sincerely,

/S/

{See appended electronic signature page}

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research