19-962/S-022

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-962/S-022

AstraZeneca
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 July 6, 2001, 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 December 14, 2001.

This "Changes Being Effected" supplemental new drug application provides for final printed labeling revised as follows:

1. The third paragraph of the CLINICAL PHARMACOLOGY/Clinical Trials subsection has been changed from:

[redacted]

To:

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

2. The following subsection has been added to the ADVERSE REACTIONS section of the labeling:

Post-Marketing Experience
The following adverse reactions have been reported in post-marketing use:
GASTROINTESTINAL: hepatitis.
MUSCULOSKELETAL: arthralgia.

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 labeling included in your July 6, 2001 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

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, please call Ms. Zelda McDonald, Regulatory Health Project Manager, at (301) 594-5333.

Sincerely,

{See appended electronic signature page}

Douglas Throckmorton, M.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Doug Throckmorton
3/5/02 04:35:54 PM

RHPM Review of Final Printed Labeling
NDA 19-962/S-022

Date of Submission: July 6, 2001
Date of Review: February 22, 2002
Applicant Name: AstraZeneca
Product Name: Toprol XL (metoprolol succinate) 25, 50, 100 and 200 mg Tablets

Evaluation:
This submission is a Changes-Being-Effected supplement that provides for final printed labeling with the following revisions:

1. In accordance with our February 5, 2001 approval letter for supplement 13, the following sentence in the third paragraph of the CLINICAL PHARMACOLOGY/Clinical Trials subsection has been changed from:

[redacted]

To:

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

2. The following subsection has been added to the ADVERSE REACTIONS section of the labeling:

Post-Marketing Experience
The following adverse reactions have been reported in post-marketing use:
GASTROINTESTINAL: hepatitis.
MUSCULOSKELETAL: arthralgia.

Other than very minor editorial changes throughout the labeling, there are no other changes from the last approved package insert.

Recommendation:
An approval letter should issue for this supplement as set forth under 21 CFR 314.70 (b) (3) [Any change in labeling].

/S/

Zelda McDonald, RHPM

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/s/

Zelda McDonald
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CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-962/S-022

AstraZeneca
Attention: Cindy M. Lancaster, M.S., M.B.A.
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Ms. Lancaster:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Toprol-XL (metoprolol succinate) Extended-Release Tablets

NDA Number: 19-962

Supplement number: S-022

Date of supplement: July 6, 2001

Date of receipt: July 9, 2001

This supplemental application was submitted as a "Supplement - Changes Being Effected."

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 7, 2001 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
1451 Rockville Pike
Rockville, Maryland 20852
If you have any questions, please call:

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

Sincerely yours,

/S/

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Natalia Morgenstern
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