DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-956

AstraZeneca LP
Attention: Ms. Paula R. Clark
1800 Concord Pike
P.O. Box 8355
Wilmington, DE 19803-8355

Dear Ms. Clark:

Please refer to your new drug application (NDA) dated October 28, 2005, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Dutoprol™ (metoprolol succinate extended-release/hydrochlorothiazide) 25/12.5, 50/12.5 and 100/12.5 mg Tablets.

We acknowledge receipt of your submissions dated January 5, February 7 and 27, March 30, April 13, 17, and 19, May 1, 15, and 19, June 8, 12, and 26, July 7, August 3 and 8, 2006.

This new drug application provides for the use of Dutoprol™ (metoprolol succinate extended-release/hydrochlorothiazide) 25.12.5, 50/12.5 and 100/12.5 mg Tablets for the management of hypertension.

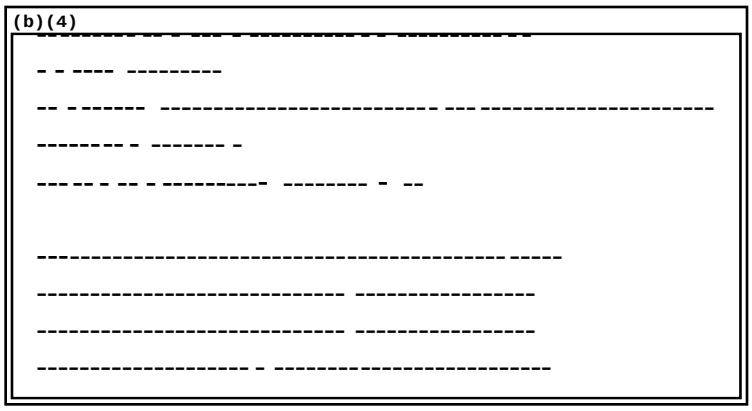
We have completed our review of this application and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling. Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-956**." Approval of this submission by FDA is not required before the labeling is used.

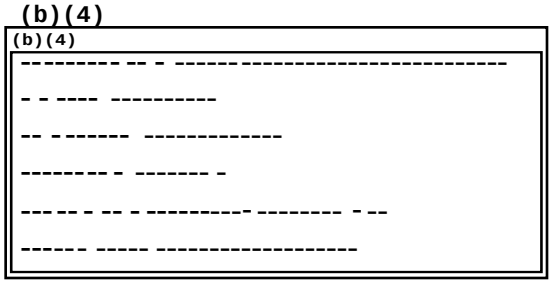
The dissolution method is acceptable. However, the following new specifications for the metoprolol succinate ER component of Dutoprol are recommended:

(b)(4)



The recommended dissolution method and specifications for the HCT component of Dutoprol is as follows:

(b)(4)



A shelf-life of twenty-four months for the drug product will be granted based on stability data provided.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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. We reference our letter dated August 16, 2005 waiving the pediatric study requirement for this combination product.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, please call:

Alisea Sermon, Pharm.D.
Regulatory Project Manager
(301) 796-1144

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Division Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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