



OCT 15 2004

Nabeal M. Saif
112 Holland Avenue
Lackawanna, NY 14218

Docket No. 2003P-0441/CP1

Dear Mr. Saif:

This is in response to your petition filed on September 24, 2003, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Metoprolol Tartrate Tablets, 12.5 mg. The listed drug product to which you refer in your petition is Lopressor® Tablets, 50 mg and 100 mg, manufactured by Novartis Pharmaceuticals and approved under NDA 17-963. For future reference, please be advised that pursuant to 21 CFR 314.93, the petitioner shall identify a listed drug as the drug of reference for requested changes. Generally this should be the reference listed drug identified in *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book).

Your request involves a change in strength (i.e., from 50 mg and 100 mg to 12.5 mg) from that of the listed drug product. The change that you request is the type of change that is authorized under Section 505(j)(2)(C) of the Act.

This petition was reviewed pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). Under Section 505(j)(2)(C)(i) of the Act, such a petition will be approved unless the Agency finds that investigations must be conducted to show the safety and effectiveness of the proposed drug product, or of any of the active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug product.

The Agency has determined that your proposed change in strength raises questions of safety and effectiveness, and has concluded that clinical trials are required for these specific drug products.

FDA acknowledges that the approved labeling makes reference to a 25 mg dose in the treatment of myocardial infarction, to the need to gradually reduce the dose in patients with ischemic heart disease who are discontinuing treatment, and to the need for treating cautiously patients with hypertension and bronchospastic disease. The fact that the innovator's 50 mg tablets are scored is not justification for or evidence of effectiveness of the proposed 12.5 mg dose. In none of these settings or elsewhere in the label is the use of a 12.5 mg dose mentioned. There is mention of a 25 mg dose in the label which can be achieved by breaking the scored 50 mg tablet in half.

Finally, the Agency has determined that the effectiveness of a 12.5 mg dose of metoprolol tartrate has not been established. The use of such a dose could delay treatment with doses known to be

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Metoprolol Tartrate Tablets, 12.5 mg

effective. Therefore, FDA is denying the petition under Section 505(j)(2)(C)(i) because investigations are necessary to show the safety and effectiveness of the proposed drug product and its strength.

If you disagree with our determination concerning the acceptability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR Section 10.20, in the format outlined in Section 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address listed below. If there is additional information, not included as part of your original submission that you would like the Agency to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

A copy of this letter denying your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,



Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research