



October 18, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
Room 1061
5630 Fishers Lane
Rockville, MD 20852

CITIZEN PETITION

The undersigned submits this petition in triplicate pursuant to 21 CFR U.S.C. 355(j)(2)(C) and 21 CFR § 10.30 and 314.93. Caraco requests that the Food and Drug Administration (FDA) determine that 25 mg tablets of metoprolol tartrate are suitable for a 505(b)(2) or Abbreviated New Drug Application (ANDA) based on the listed drug Lopressor® Tablets, 50 mg.

A. ACTION REQUESTED

Caraco Pharmaceutical Laboratories, Ltd. (Caraco) seeks a determination that a 25 mg metoprolol tartrate tablet drug product is suitable for a 505(b)(2) New Drug Application submitted to FDA October 18, 2002. Alternatively, as an ANDA supplement to Caraco's previously submitted ANDA #74-644 for Metoprolol Tartrate Tablets, 50 mg and 100 mg, approved on December 10, 1996.

B. STATEMENT OF GROUNDS

The reference listed drug for the proposed generic drug product will be Lopressor® Tablets (metoprolol tartrate), 100 mg. Lopressor® Tablets are approved for use at daily doses up to approximately 400 mg per day. Lopressor® Tablets are labeled for individualized doses based on diagnosis (hypertension, angina pectoris and myocardial infarction) and patient tolerance.

The approved Lopressor® Tablets labeling for myocardial infarction, states:

“... Patients who appear not to tolerate the full intravenous dose should be started on Lopressor® tablets either 25 mg or 50 mg every 6 hours (depending on the degree of intolerance) 15 minutes after the last intravenous dose or as soon as their clinical condition allows.”

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For many patients, 25 mg is a sufficient dose and, in fact, 31% of patients receiving metoprolol tartrate take the drug at a dose below 50 mg. Another 2% of patients take a 1 ½ tablet dose. See IMS Audit (February 2002), copy provided as **Attachment 1**. In fact, the 50 mg version of Lopressor ® (metoprolol tartrate) tablet is scored, to facilitate breaking the tablet into two 25 mg doses. The availability of 25 mg metoprolol tartrate tablets will make it easier and more convenient for patients prescribed smaller daily doses of metoprolol tartrate tablets to take their medication at an accurate dose.

Therefore, Caraco seeks a determination that a 25 mg metoprolol tartrate tablet is suitable for approval, with Lopressor ® tablets, 100 mg and the previously approved ANDA #74-644 for Metoprolol Tartrate tablets, 50 mg and 100 mg. The active ingredient of the proposed drug product will be the same as that in the above mentioned approved drug products.

The new 25 mg strength, which is the subject of the new drug application, is dose-proportional to the previously approved products. The product contains the same active and inactive ingredients and should be considered bioequivalent to Lopressor ® tablets. The proposed drug product is expected to have the same therapeutic effect as Lopressor ® Tablets when administered to patients under the same conditions of use contained in the RLD labeling. In accordance with FDA regulations and policies, Caraco has requested a bioequivalency waiver in 505(b)(2) New Drug application submitted October 18, 2002. However, to facilitate review, the submitted application provides a copy, of the previously approved bioequivalence studies, submitted in support of ANDA #74-644, which includes comparison of Caraco's 100 mg strength of Metoprolol Tartrate Tablets to the 100 mg strength of Lopressor ® Tablets, the RLD.

Pursuant to 21 CFR § 314.54 and 314.3 (d), a copy of the approved labeling for Lopressor ® Tablets is provided as **Attachment 2**. A copy of the proposed labeling for Caraco's generic labeling for the 25mg, 50 mg and 100 mg is also attached in **Attachment 3**, containing labeling for the addition of the 25 mg strength. No major changes to the labeling are necessary other than those necessitated by the addition of a different strength and manufacturer specific information. The brand name Lopressor ® Tablets will be replaced by the generic name and descriptions of the strength and details of the "How Supplied" section were modified.

C. ENVIRONMENTAL IMPACT

Pursuant to 21 CFR § 25.31(a), this petition qualifies for a categorical exclusion from the requirement for submission of an environmental assessment.

D. ECONOMIC IMPACT

According to 21 CFR § 10.30(b), information on economic impact is to be submitted only upon request by the Commissioner following review of this petition.

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E. CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

 10/17/02
Robert Kurkiewicz
Sr. Vice-President, Technical
Caraco Pharmaceutical Laboratories, Ltd.