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OVERNIGHT COURIER 10/18/02

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

Citizen Petition

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Metoprolol Tartrate Tablets USP, 25 mg is suitable for consideration in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Metoprolol Tartrate Tablets USP, 25 mg are suitable for submission in an ANDA. The designated reference-listed drug product upon which this petition is based is Lopressor® (Metoprolol Tartrate) Tablets, 50 mg and 100 mg manufactured by Novartis Pharmaceuticals (see listing of the Lopressor® application No. NDA 17-963 on Page 3-242 of the 22nd Edition of the Approved Drug Products with Therapeutic Equivalence Evaluations (Attachment 1)). Therefore, the petitioner seeks a change in strength (from a 50 mg and 100 mg to include a 25 mg strength tablet) from that of the listed drug product.

B. Statement of Grounds

The reference-listed drug (RLD) product is currently available in tablets containing 50 mg and 100 mg of Metoprolol Tartrate. The proposed drug product represents a tablet that will contain a lower strength of the drug product (25 mg). This additional proposed strength is consistent with the currently approved RLD product's labeling and is also consistent with the scoring configuration of the 50 mg RLD tablet (the 50 mg tablet contains a bisected score suggesting either a starting dose or titration dose of 25 mg) and will provide a more convenient single-dosage unit to provide the specific single or intermediate dose required by the individual patient and prescribed by the physician. The petition is thus seeking a change in strength (from the existing 50 mg and 100 mg tablets to include a 25 mg tablet product) from that of the reference-listed drug.

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The approved labeling of the RLD provided suggests that the dose of Metoprolol Tartrate should be individualized for each patient. The usual initial dosage for both hypertension and angina pectoris is 100 mg daily, given in single or **divided** doses. Both the 50 mg and 100 mg tablets are scored to allow maximum flexibility in achieving a divided dosage schedule that is tolerated by the individual patient (e.g., 25 mg or 50 mg in multiple doses), or in providing the physician flexibility in selecting an appropriate intermediate dose, as determined by patient response.

In addition, a 25 mg dose is cited as a starting dose for those patients being treated for early myocardial infarction:

"Patients who appear not to tolerate the full intravenous dose should be started on Lopressor Tablets, **25 mg** or 50 mg every six hours...."

Also the labeling recommends the use of the lowest possible dose of Lopressor® in patients with bronchospastic disease and suggests the use of smaller doses three times a day, instead of larger doses two times a day in those patients.

It is thus clear from the labeling of the approved drug product that a 25 mg dosage strength is clearly contemplated for the approved product for individual tablet dosing, or for the purposes of titrating a patient to the required dose.

The petitioner is seeking the requested change in strength from the RLD drug product to provide the physician greater flexibility in administering an appropriate strength product that is consistent with doses contemplated in the labeling of the RLD. The goal being to provide a patient with a 25 mg strength for a single dose, or to allow a patient to utilize the 25 mg product to achieve an intermediate dosage without having to break tablets, a task that may be difficult for the elderly or infirmed. Availability of a 25 mg tablet will likely improve patient convenience, compliance and make it easier to achieve the required dose for those patients that have difficulty in breaking individual tablets.

Copies of labeling of the reference-listed drug product upon which this petition is based and proposed draft labeling for the proposed product are included in Attachments 2 and 3, respectively. The proposed labeling is the "same as" that of the RLD labeling with the exception of changes allowed because the manufacturer of the generic product differs and in the How Supplied section, which lists the additional proposed strength. There are no changes in the indications or dosage and administration sections necessary, as the approved labeling of the RLD already contemplates the use of the proposed dosage strength.

Pursuant to 21 CFR 314.55 (a), the proposed change in strength does not constitute a request to file an application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Therefore, the petitioner believes that the proposed product does not fall under the requirement for an assessment of safety and efficacy in pediatric patients.

Therefore, the petitioner requests that the Commissioner find that a change in strength from 50 mg and 100 mg tablets of Metoprolol Tartrate to include a tablet strength of 25 mg for this

product, raises no questions of safety or effectiveness, and the Agency should, therefore, approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis if requested by the Agency.

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,



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Attachments: 1) *Page 3-242 of the 22nd Edition of the Approved Drug Products with Therapeutic Equivalence Evaluations*
 2) *Label of Reference-Listed Drug*
 3) *Proposed Draft Labeling*

cc: G. Davis, M. Shimer, L. Lachman

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