



Taro Research Institute Ltd.

August 30, 2002

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Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, Maryland 20852

CITIZEN PETITION

The undersigned submits this petition pursuant to section 505 (j) (2) (c) of the Federal Food, Drug, and Cosmetic Act and 21 CFR Parts 314.55 (d) (2) and 10.30 of the Food and Drug Administration's regulations, to request the Commissioner of the Food and Drugs Administration to make a determination of ANDA suitability for Amiodarone Hydrochloride Tablets, 300 mg, based on the reference-listed drugs, Wyeth-Ayerst's Cordarone Tablets, 200 mg [see Exhibit 1] and Eon Laboratories' Amiodarone Hydrochloride Tablets, 400 mg [see Exhibit 2].

A. Action Requested

The petitioner requests the Commissioner of the Food and Drug Administration for a change to a listed drug to allow the undersigned to submit an Abbreviated New Drug Application for Amiodarone Hydrochloride Tablets, 300 mg. The reference-listed drugs are Cordarone Tablets, 200 mg manufactured by Wyeth-Ayerst and Amiodarone Hydrochloride Tablets, 400 mg by Eon Laboratories. The safety of the proposed strength will be supported by a bioequivalence study conducted comparing the reference Amiodarone Hydrochloride Tablets, 400 mg of Eon Laboratories and Amiodarone HCl Tablets, 400 mg manufactured by Taro. In the study, 1 x 400-mg tablet was dosed on healthy adult male subjects (as the Amiodarone Hydrochloride Tablets, 300 mg and 400 mg tablets will be dose proportional, a bioequivalence study on the highest strength, 400 mg tablets will cover the lower strength 300 mg tablets). Furthermore, safety is supported by the fact that tablets of 400 mg and 200 mg are the routine oral dosage strengths of this product. Also, this product is dose proportional to Taro's Amiodarone Hydrochloride Tablets, 200 mg for which an ANDA (75-424) was approved on March 30, 2001.

02P-0394

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B. Statement of Grounds

Amiodarone Hydrochloride Tablets dosage should be adjusted to the needs of the individual patients. Amiodarone Hydrochloride Tablets are approved for use at daily doses up to 1600 mg per day, with a usual maintenance dose of 400 mg per day. Because of the unique pharmacokinetic properties and potential severity of the side effects if patients are improperly monitored, Amiodarone Hydrochloride Tablets should be administered at the lowest effective dosage and should be closely monitored by the physicians. The availability of Amiodarone Hydrochloride Tablets, 300 mg will provide the physician with greater flexibility in prescribing the drug, as well as enabling the patients to take dose appropriate tablets, which will improve patient compliance.

The proposed Amiodarone Hydrochloride Tablets, 300 mg will be the same as the reference-listed products, Wyeth-Ayerst's Cordarone Tablets, 200 mg and Eon Laboratories' Amiodarone Hydrochloride Tablets, 400 mg (which is provided as Pacerone) in respect of:

- Active ingredient, Amiodarone Hydrochloride
- Indications
- Dosing regimen
- Bioequivalence: the proposed strength, 300 mg will be dose proportional to Taro's 400 mg tablets and previously approved 200 mg tablets strength. A bioequivalence study was conducted comparing Taro's Amiodarone Hydrochloride Tablets, 400 mg tablets to the reference-listed product; Eon Laboratories' Amiodarone Hydrochloride Tablets 400 mg. *In-Vitro* dissolution profiles and assay will also be conducted on Taro's Amiodarone Hydrochloride Tablets, 300 mg by comparing them to Taro's 400 mg.

Copies of the approved labeling for Wyeth-Ayerst's Cordarone Tablets, 200 mg [see Exhibit 1] and Eon Laboratories' Amiodarone Hydrochloride Tablets 400 mg [see Exhibit 2] and the proposed labeling for the new Amiodarone Hydrochloride Tablets, 300 mg with highlighting of the changes [see Exhibit 3] are attached.

C. Environmental Impact

The undersigned, hereby requests a categorical exclusion under 21 CFR 25.24 (c) (1). The proposed drug product will not be administered at higher dosage levels, for longer duration, or for different indications than for the reference-listed product.

D. Economic Impact

This information will be submitted on request of the Commissioner.

E. Advantages

The proposed Amiodarone Hydrochloride Tablets, 300 mg will provide the physicians a greater flexibility in prescribing the drug.

F. 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,



Avraham Yacobi, Ph.D.
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