June 30, 2003

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Taro Pharmaceuticals U.S.A., Inc.

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 a new strength of Warfarin Sodium Tablets, USP 1.5 mg, based on the reference-listed drug, Bristol-Myers Squibb's Coumadin® Tablets, 2 mg. [See Exhibit 1]

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 Warfarin Sodium Tablets USP, 1.5 mg. The referenced-listed drug is Coumadin® Tablets 2 mg manufactured by Bristol-Myers Squibb. The safety of the proposed strength will be supported by the bioequivalence studies conducted comparing the reference 2 mg strength and Warfarin Sodium Tablet USP, 2 mg (ANDA # 40-301) by Taro. In the studies, 2 mg tablets of both the Taro and reference products were dosed on healthy adult male subjects. Furthermore, safety is supported by the fact that tablets of 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, and 10 mg strengths are the routine oral dosage strengths of this product. Also, this product is pseudo-proportional to Taro's Warfarin Sodium Tablets USP, 2 mg for which an ANDA (40-301) was approved on 7/15/1999.

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B. Statement of Grounds

Warfarin sodium tablets are considered to be a narrow therapeutic range drug; the dosing of warfarin sodium must be individualized according to the patient's sensitivity to the drug as indicated by the PT/INR. Use of dosages in excess of the therapeutic range may increase the incidence of hemorrhagic and other complications, does not offer more rapid protection against thrombus formation, and is not recommended.

Warfarin sodium tablets used in elderly persons have been increased steadily. As patient age increases, less warfarin sodium is required to produce a therapeutic level of anticoagulation. Most patients are satisfactory maintained at a dose of 2 mg to 10 mg daily. Flexibility of dosage is provided by breaking scored tablets in half. The dosage administration can be found in the product insert [Exhibit 1]. The proposed new strength, Warfarin Sodium Tablets USP, 1.5 mg will provide the physicians with greater flexibility in prescribing the drug, as well as enabling the patients to take tablets with greater convenience, which will improve patient compliance.

The proposed Warfarin Sodium Tablets USP, 1.5 mg will be the same as the reference-listed products, Bristol-Myers Squibb's Coumadin® Tablets, 2 mg in respect of:

- Active ingredient, Warfarin Sodium USP
- Indications
- Dosing regimen
- The proposed new strength 1.5 mg is pseudo-proportional to our approved Warfarin Sodium Tablet USP, 2 mg (ANDA # 40-301). In Taro's approved ANDA, Taro's Warfarin Sodium Tablets USP, 2 mg was dosed on healthy adult male subjects.
- We have conducted an in-vitro dissolution profile testing to demonstrate the equivalency between the 1.5 mg and 2 mg strengths. Based upon our bioequivalence study conducted on the 2 mg strength, we request to have a biowavier for the 1.5 mg strength.

Copies of the approved labeling for Coumadin® Tablets [Exhibit 1] and Taro's proposed labeling for warfarin sodium tablets with highlighting of the changes is attached [Exhibit 2].

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 listed product.

D. Economic Impact

This information will be submitted on request of the Commissioner.

E. Advantages

The proposed Warfarin Sodium Tablets USP, 1.5 mg will provide the physicians a greater flexibility in prescribing the drug, as well as the patients able to take tablets without compromising efficacy.

F. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and view 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,

A. Yacobi

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