LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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June 28, 2013

OVERNIGHT COURIER 6/28/13

Division of Dockets Management
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, Dapsone Tablets, 50 mg, are 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 the drug product, Dapsone, 50 mg, is suitable for submission as an ANDA. The reference listed drug product (RLD), upon which this petition is based, is Dapsone Tablets USP, 100 mg, ANDA 86-842 held by Jacobus. Another approved ANDA also provides for Dapsone® Tablets in a 25 mg dosage strength (ANDA 86-841). Therefore, the petitioner seeks a change in strength (from 100 mg to 50 mg) from that of the listed drug product.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a drug product that differs in dosage strength from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The reference listed drug, Dapsone® Tablets, 100 mg, held by Jacobus, is a tablet product containing 100 mg of Dapsone. See copy of the page from the current Electronic Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations* (Attachment 1). The proposed drug product also represents a tablet dosage form, but contains 50 mg of Dapsone. This petition is thus seeking a change in strength (from 100 mg to 50 mg) from that of the RLD. Please note that the proposed change in strength represents a dosage strength that is clearly contemplated in the approved labeling for the RLD.

The current dosing instructions in the approved labeling of the RLD are as follows:

> **Dermatitis herpetiformis:** The dosage should be individually titrated starting in adults with 50 mg daily and correspondingly smaller doses in children. If full control is not achieved within the range of 50-300 mg daily, higher doses may be tried. Dosage should be reduced to a minimum maintenance level as soon as possible. In responsive patients, there is a prompt reduction in pruritus followed by clearance of skin lesions. There is no effect on the gastrointestinal component of the disease. Dapsone levels are influenced by acetylation rates. Patients with

high acetylation rates, or who are receiving treatment affecting acetylation may require an adjustment in dosage.

A strict gluten free diet is an option for the patient to elect, permitting many to reduce or eliminate the need for Dapsone; the average time for dosage reduction is 8 months with a range of 4 months to 2 1/2 years and for dosage elimination 29 months with a range of 6 months to 9 years.

Leprosy: In order to reduce secondary Dapsone resistance, the WHO Expert Committee on Leprosy and the USPHS at Carville, LA recommended that Dapsone should be commenced in combination with one or more anti-leprosy drugs. In the multidrug program, Dapsone should be maintained at the full dosage of 100 mg daily without interruption (with corresponding smaller doses for children) and provided to all patients who have sensitive organisms with new or recrudescent disease or who have not yet completed a two year course of Dapsone monotherapy. For advice and other drugs, the USPHS at Carville, LA (1-800-642-2477) should be contacted.

Before using other drugs consult appropriate product labeling.

In bacteriologically negative tuberculoid and indeterminate disease, the recommendation is the co-administration of Dapsone 100 mg daily with six months of Rifampin 600 mg daily. Under WHO, daily Rifampin may be replaced by 600 mg Rifampin monthly, if supervised. The Dapsone is continued until all signs of clinical activity are controlled - usually after an additional six months. Then, Dapsone should be continued for an additional three years for tuberculoid and indeterminate patients and for five years for borderline tuberculoid patients.

In lepromatous and borderline lepromatous patients, the recommendation is the co-administration of Dapsone 100 mg daily with two years of Rifampin 600 mg daily. Under WHO daily Rifampin may be replaced by 600 mg Rifampin monthly, if supervised. One may elect the concurrent administration of a third anti-leprosy drug, usually either Clofazamine 50-100 mg daily or Ethionamide 250-500 mg daily. Dapsone 100 mg daily is continued 3-10 years until all signs of clinical activity are controlled with skin scrapings and biopsies negative for one year. Dapsone should then be continued for an additional 10 years for borderline patients and for life for lepromatous patients.

Secondary Dapsone resistance should be suspected whenever a lepromatous or borderline lepromatous patient receiving Dapsone treatment relapses clinically and bacteriologically, solid staining bacilli being found in the smears taken from the new active lesions. If such cases show no response to regular and supervised Dapsone therapy within three to six months or good compliance for the past 3-6 months can be assured, Dapsone resistance should be considered confirmed clinically. Determination of drug sensitivity using the mouse footpad method is recommended and, after prior arrangement, is available without charge from the USPHS, Carville, LA. Patients with proven Dapsone resistance should be treated with other drugs.

Thus, 50 mg tablets would provide for greater flexibility and convenience in administration of the dose within the labeled dosing range. Providing the additional strength of 50 mg will increase the healthcare practitioner's ability to conveniently titrate to the recommended doses while limiting the potential of adverse effects.

There are no proposed changes in labeling with the exception of the obvious change in strength sought in this petition. The uses, indications, warnings, and directions for use will remain the same as that of the RLD. Draft labeling for the proposed product is included in Attachment 2, and the RLD's approved labeling is provided in Attachment 3.

Therefore, the petitioner's request for the Commissioner to find that a change in strength from 100 mg to 50 mg for Dapsone Tablets should raise no questions of safety or effectiveness, and the Agency should 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,

Christine Miller

Christine Miller, Pharm.D.
Associate Director

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Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, accessed June 19, 2013
2. Draft Insert Labeling Proposed for Dapsone Tablets, 50 mg
3. Labeling for the RLD Dapsone® Tablets by Jacobus

cc: Martin Shimer (OGD)

Suitability Petition for Dapsone

From: (516) 683-1881 Origin ID: RMEA
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J13111302120326

Ship Date: 28JUN13
ActWgt: 1.0 LB
CAD: 105332656/INET3370

Delivery Address Bar Code

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Ref # Citizen Petition
Invoice #
PO #
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