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BY FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, Maryland 20857

SUITABILITY PETITION

Re: **Ribavirin, USP Film-Coated Tablets**

A. THOMAS S. SAFFORD
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PORTER F. FLEMING
Of Counsel

Ladies/Gentlemen:

On behalf of BioPartners GmbH. of Darmstadt, Germany, the undersigned hereby submits in quadruplicate this Suitability Petition pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(j)(2)(C), and FDA regulations 21 CFR §§ 314.93, 10.25 and 10.30.

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A. Action Requested

This Suitability Petition requests a declaration by the Commissioner of Food and Drugs, head of the Food and Drug Administration ("FDA"), that an Abbreviated New Drug Application ("ANDA") may be filed for ribavirin, USP in a water soluble film-coated tablet dosage form.

B. Statement of Grounds

• An ANDA may be filed for the approval of a new drug that is the same as a reference listed drug ("RLD"). 21 U.S.C. § 355(j)(2)(A). An ANDA may also be filed for a new drug which is the same as an RLD except for a difference in dosage form, provided that FDA has granted permission to file such an ANDA upon the submission and approval of a pertinent "suitability" petition. 21 U.S.C. § 355(j)(2)(C); 21 CFR 314.93(b). FDA is authorized to approve a suitability petition seeking a change in dosage form from an RLD. Id.

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- The specific RLD upon which this Petition is based is REBETOL (ribavirin, USP) Capsules, a drug which is indicated in combination with interferon alpha-2b, recombinant for the treatment of chronic hepatitis C virus [see Attachments 1 and 2 hereto]. The NDA for the RLD is held by Schering Corporation. Id.
- The proposed drug product will contain the same active ingredient as the RLD, and will have the same strength (200 mg) and the same route of administration (oral). The proposed drug product will differ from the RLD only in its dosage form - a tablet coated with a water-soluble film, rather than a capsule.
- The labeling of the proposed drug product will also be the same as the currently approved labeling for the RLD, except for changes which are required because of the difference in manufacturer, and the difference in dosage form proposed under this Petition [see proposed labeling in Attachment 3].
- There are demonstrative safety advantages in the availability of ribavirin, USP in a water soluble film-coated tablet. In general, a tablet is smaller and thus more easy to swallow than a capsule. This ease in swallowing will be enhanced by the water-soluble film with which the proposed ribavirin tablet will be coated.

Moreover, capsules are capable of coming apart or becoming crushed (in production, distribution, or in the possession of patients). This phenomenon presents a risk of exposing workers, and particularly patients with hepatitis C virus (and relatives or other persons coming into contact with them), to inhalation of small, dust-like particles of ribavirin, a teratogenic substance. With a tablet, on the other hand, crushing will yield a few larger pieces, which are unlikely to become inhaled.

- In view of the above, and since ribavirin, USP in combination with interferon alpha 2-b has been marketed in the United States for over four years with an established safety and effectiveness profile [see Attachments 2 and 4], there is no reason to question the safety and effectiveness of the proposed ribavirin drug product for its labeled use.

C. Environmental Impact

Petitioner claims a categorical exclusion from the requirement of an environmental assessment or environmental impact statement pursuant to 21 C.F.R. § 25.31.

D. Economic Impact

Pursuant to 21 CFR § 10.30(b), economic impact information is to be submitted only

when requested by the Commissioner following review of this Petition.

E. Requested Waiver of Pediatric Study

Pursuant to FDA regulations 21 CFR § 314.55(c)(2)(ii) and (iii), a full waiver from a pediatric study based on the proposed dosage form change is requested, on the grounds that: (1) a pediatric study is highly impractical because the number of pediatric patients with hepatitis C virus is extremely small; and (2) the adverse events caused by ribavirin therapy render this drug unsafe in pediatric age groups.

Ground (1) above is based on epidemiological data for hepatitis C virus, reporting that: (a) seroprevalence of hepatitis C virus in the United States is approximately 0.2% in children 12 years of age or younger and 0.4% in children between the ages of 12 and 19; and (b) the most common means of transmission of hepatitis C virus to children have been via blood transfusion (now rare after the introduction of hepatitis C screening), and through pregnant mothers (who have a seroprevalence of hepatitis C of 1-2%) [see American Academy of Pediatrics report in Attachment 5].

Ground (2) above is based on the significant adverse events caused by ribavirin therapy (in combination with interferon alfa 2-b), including severe depression and suicidal ideation, hemolytic anemia, suppression of bone marrow function, pulmonary dysfunction, pancreatitis and diabetes [see Warnings section of RLD labeling, Attachment 2]. These adverse events make ribavirin therapy unsafe for pediatric use.

F. Certification

The undersigned certifies that, to their best knowledge and belief, this Suitability Petition includes all information and views upon which the Petition relies, and includes representative data and information known to Petitioner which are unfavorable to the Petition.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP

By 
Charles J. Raubicheck

CJR/bav

Attachments:

1. Approved Drug Products with Therapeutic Equivalence Evaluations (“the Electronic Orange Book”, current through June, 2002): REBETOL (ribavirin, USP) Capsule; Oral; 200 mg.
2. Current approved labeling for REBETOL (ribavirin, USP) Capsules, from FDA’s website.
3. Proposed labeling for Ribavirin, USP Film-Coated Tablets.
4. NDA approval letter for REBETOL (ribavirin, USP) Capsules.
5. Report of American Academy of Pediatrics, Committee on Infectious Diseases, “Hepatitis C Virus Infection (RE9733)” (1997).