AMIVAS

Citizen Petition

Date: 17 April 2024

The undersigned submits this petition under 21 CFR 10.20, 10.30, and 314.93 Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to request a change from a listed drug in accordance with 314.93 Petition to request a change from a listed drug.

A. Action Requested

In accordance with Section 505(j)(2)(C) of the Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)(2)(C)), as well as under 21 CFR 10.20, 10.30, and 314.93, this petition is being submitted to obtain permission to submit an ANDA for a change to a listed drug that is not identical to the listed drug in strength but otherwise is identical in the active ingredient, route of administration, and dosage form. The sponsor of this ANDA will be Amivas, Inc., 1209 Orange Street, Wilmington, DE, USA 19801.

Proposed Drug Product:

Drug Product Name: Methylene Blue Injection, USP
(AMIVAS BLUE – will be submitted as proposed proprietary name)
Strengths: 50 mg/5 mL (10 mg/mL) vial

Dosage Form: solution for intravenous injection

Reference Listed Drug (RLD):

RLD Drug Product Name: ProvayBlue® (methylene blue) injection, USP
NDA Number: 204630
Sponsor: PROVEPHARM SAS

Requested Type of Change:

Change in Strength:

RLD: ProvayBlue® Dosage Form and Strengths

50 mg/10 mL (5 mg/mL) vial
10 mg/2 mL (5 mg/mL) vial
50 mg/10 mL (5 mg/mL) ampule
10 mg/2 mL (5 mg/mL) ampule

Note: The excipient in both products is water

B. Statement of Grounds

In accordance with 21 CFR 314.93:

A person who wants to submit an ANDA for a drug product which is not identical to a listed drug in route of administration, dosage form, and strength, or in which one active ingredient is

substituted for one of the active ingredients in a listed combination drug, must first obtain permission from FDA to submit such an ANDA.

The petitioner shall also include information to show that:

(1) The active ingredients of the proposed drug product are of the same pharmacological or therapeutic class as those of the reference listed drug.

(2) The drug product can be expected to have the same therapeutic effect as the reference listed drug when administered to patients for each condition of use in the reference listed drug's labeling for which the applicant seeks approval.

The reference listed drug (RLD) as summarized in Section A above is ProvayBlue® (methylene blue) injection, USP, approved by the FDA in 2016, and is indicated for the treatment of pediatric and adult patients with acquired methemoglobinemia. A copy of the most recent prescribing information is provided in Attachment A. ProvayBlue® is supplied as a sterile solution in water in either a vial or ampoule at a concentration of 5 mg/mL. It is supplied in 50 mg/vial and 10 mg/vial strengths (or similarly in ampules). Following dilution in a solution of 5% dextrose in water, the route of administration is intravenous (IV), at a concentration of 1 mg/kg over a period of 5-30 minutes.

The drug product that is subject of the ANDA is Methylene Blue Injection, USP (proposed proprietary name AMIVAS BLUE). The proposed prescribing information for this drug product is provided in Attachment B. Methylene Blue Injection, USP, is also indicated for the treatment of pediatric and adult patients with acquired methemoglobinemia. Methylene Blue Injection, USP is supplied as sterile solution in water in a vial at a concentration of 10 mg/mL. It is supplied as a 50 mg/vial strength. Thus, the proposed drug product is at a higher concentration (10 mg/mL vs 5 mg/mL), but the same amount is provided in a single vial, for one of the strengths of Methylene Blue. It is also diluted in a solution of 5% dextrose in water at a concentration of 1 mg/kg and given IV over a period of 5-30 minutes. Thus, the same amount of active ingredient with the same excipients, with the same diluent, at the same concentration and dosage regimen is given for both products.

As both drugs are given IV, there are no concerns for bioequivalence. As both drugs are methylene blue, USP, they are both of the same pharmacological class and would be expected to have the same therapeutic effect and same safety profile.

For Amivas Inc's, ANDA, the drug product will be manufactured by Phebra Pty LTD (17-19 Orion Road Lane Cove West, NSW, 2066 Australia). The drug product utilizes methylene blue drug substance that is manufactured by BioIndustria (L.I.M. Via Giustizia 1, 15064 FRESONARA (AL) ITALY). Phebra currently has marketing authorization for Methylene Blue Injection in Australia (since Oct 2014), United Kingdom (since March 2014) and Canada (since April 2019).

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C. Environmental Impact

Pursuant to 21 CFR 25.15 (d), Amivas hereby claims a categorical exclusion from the requirement of an Environmental Impact Analysis statement.

- Under 21 CFR 25.31 (a), a categorical exclusion exists for action on an ANDA if the drug product will not be administered at higher dosage levels, for longer duration, or for different indications than were previously in effect and if data available to the agency do not establish that, at the expected level of exposure, the substance may be toxic to organisms in the environment.
- To the best of Amivas' knowledge, no extraordinary circumstances exist.

The methods employed in the manufacture of the referenced product are in compliance with all applicable local, state, and federal environmental regulations.

D. Economic Impact

An economic impact will be submitted if requested; however, at this time, no economic impact is anticipated.

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.

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