February 9, 2021

VIA ELECTRONIC SUBMISSION

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

SUITABILITY PETITION

Dear Sir or Madam:

The undersigned petitioner submits this petition, on behalf of a client, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act ("FD&C Act"), and in accordance with 21 C.F.R. § 10.20 and 21 C.F.R. § 10.30 requesting the Commissioner of the Food and Drug Administration ("FDA") to declare that the proposed drug product, Methylene Blue Injection, USP, 5 mg/1 mL is suitable for consideration in an Abbreviated New Drug Application ("ANDA").

I. ACTION REQUESTED

The petitioner requests that the Commissioner of the FDA declare that the proposed drug product, Methylene Blue Injection, USP, 5 mg/1 mL is suitable for submission as an ANDA. The listed reference drug product (RLD), upon which this petition is based, is PROVAYBLUE® (methylene blue) injection USP, for intravenous use, 50 mg/10 mL (5 mg/mL) and 10 mg/2 mL (5 mg/mL), held by PROVEPHARM SAS, NDA 204630.

The petitioner, hereby, seeks an additional strength (total drug content) from that of RLD: 5 mg/1 mL (5 mg/mL). It should be noted that the change in strength is only a change in the total drug content and not in concentration (5 mg/mL).

II. STATEMENT OF GROUNDS

The FD&C Act § 505(j)(2)(A) provides for the submission of an ANDA 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.

Dosing recommendations in the RLD package insert are as follows:

Recommended Dosage for Renal Impairment

- The recommended dosage of PROVAYBLUE in patients with moderate or severe renal impairment (eGFR 15-59 mL/min/1.73 m^2) is a single dose of 1 mg/kg.
- If the methemoglobin level remains greater than 30% or if the clinical symptoms persist 1 hour after dosing, consider initiating alternative interventions for the treatment of methemoglobinemia.

The availability of additional strengths would provide additional flexibility in achieving the proper dose.

There are no proposed changes in labelling with the exception of the obvious changes in strength. The active ingredient, dosage form and route of administration, as well as the uses, indications, warnings, and directions for use will remain the same as that of the RLD.

A copy of the relevant excerpt on RLD from the current electronic Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations* is provided as **Attachment 1**. A copy of the current labelling for PROVAYBLUE® (methylene blue) injection USP, for intravenous use, 50 mg/10 mL (5 mg/mL) and 10 mg/2 mL (5 mg/mL) is provided in **Attachment 2**. The draft *Package Insert* incorporating the proposed additional strengths is provided in **Attachment 3.**

This petition is seeking a change in strength (total drug content) and proposes new strengths of 5 mg/1 mL (5 mg/mL). Note that the change in strength from RLD is only a change in the total drug content and not in concentration, as detailed in the Table below.

Table Comparison of RLD vs. Proposed Product

	RLD: PROVAYBLUE® (methylene blue) injection USP, for intravenous use, held by PROVEPHARM SAS, NDA 204630		**Proposed Drug Product**		
Active Ingredient	Methylene Blue		Methylene Blue		
Strength (Total Drug Content)	50 mg	10 mg	50 mg	10 mg	5 mg
Concentration	5 mg/1 mL	5 mg/1 mL	5 mg/1 mL	5 mg/1 mL	5 mg/1 mL
Fill Volume	10 mL	2 mL	10 mL	2 mL	1 mL
Dosage Form	Solution		Solution		
Route of Administration	Intravenous		Intravenous		
Indications and Usage	PROVAYBLUE® USP is indicated for the treatment of pediatric and adult patients with acquired methemoglobinemia.		PROVAYBLUE® USP is indicated for the treatment of pediatric and adult patients with acquired methemoglobinemia.		

In view of the aforesaid, the petitioner's request for the Commissioner to find that a change in strength as proposed in the form of a new strengths of 5 mg/1 mL (5 mg/mL) for Methylene Blue Injection should raise no questions of safety and effectiveness, and the Agency is thereby requested to approve the petition.

C. Inapplicability of the Pediatric Research Equity Act ("PREA")

PREA, which is codified at FD&C Act§ 505B, does not apply to a new strength and a new packaging configuration, such as the one proposed in this petition. As such, PREA should not serve as an impediment to the Agency's granting of this petition.

D. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

E. 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.

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.

Sincerely,

Michelle R. Ryder

Digitally signed by Michelle R. Ryder
Date: 2022.02.17 14:14:25 -07'00'

Michelle R. Ryder
Principal Consultant
Lachman Consulting Services, Inc.

Attachments:

- ATTACHMENT 1: Copy of the relevant excerpt from the current electronic Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations.*

- ATTACHMENT 2: Current labeling for PROVAYBLUE® (methylene blue) injection USP, for intravenous use, 50 mg/10 mL (5 mg/mL) and 10 mg/2 mL (5 mg/mL), held by PROVEPHARM SAS, NDA 204630 (5/2021 version, source: Drugs@FDA)

- ATTACHMENT 3: Draft Package Insert Proposed for Methylene Blue Injection, USP incorporating the proposed additional strengths.