April 10, 2024

Division of Dockets Management
U.S. Food and Drug Administration
Department of Health and Human Services
Room 1061, 1-IFA-305
5630 Fishers Lane
Rockville, MD 20852

ANDA Suitability Petition for Amphotericin B Liposome for Injection 100 mg/vial
*******Priority Review Requested*******

Dear Sir/Madam:

The undersigned submits this suitability 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, to request that the Food and Drug Administration ("FDA") determine that the drug product, Amphotericin B Liposome for Injection, 100 mg/vial lyophilized powder, is suitable for submission in an Abbreviated New Drug Application ("ANDA").

A. Action Requested

The petitioner requests that the FDA declare that the drug product, Amphotericin B Liposome for Injection, 100 mg/vial lyophilized powder is suitable for submission in an ANDA. The listed drug upon which this petition is based, ASTELLAS PHARMACEUTICALS's AmBisome® (Amphotericin B Liposome) for Injection, 50 mg/vial. The listed drug is approved under NDA 050740 on Aug 11, 1997. This petition seeks a change in strength from 50 mg/vial to 100 mg/vial. Note this is only a change in total drug content and not concentration.

Priority review of this petition is requested pursuant to Section III.B.6.c of the GDUFA Reauthorization Performance Goals and Program Enhancement Fiscal Years 2023-2027 (GDUFA III Commitment Letter) as the proposed product represents a new strength of a parenteral product that could aid in eliminating pharmaceutical waste or mitigating the number of vials needed per dose by addressing differences in patient weight, body size, or age.

B. Statement of Grounds

The FD&C Act § 505(j)(2)(A) permits the submission of an ANDA for a drug product that differs in strength from the listed drug provided the FDA has approved a petition that proposed filing such an application. The listed drug for the proposed drug product, AmBisome (Amphotericin B Liposome) for Injection, 50 mg/vial by ASTELLAS PHARMACEUTICALS is a sterile, non-pyrogenic lyophilized product for intravenous infusion, available in vials containing 50 mg of Amphotericin B. A copy of the relevant excerpt from the current electronic edition of the Approved Drug Products with Therapeutic Equivalence Evaluations is provided as **Attachment 1**. A copy of the current labeling for AmBisome (Amphotericin B Liposome) for Injection, 50 mg/vial is provided as **Attachment 2**. This petition is seeking a change in strength (Only total drug content) from 50 mg/vial to 100 mg/vial.

Like AmBisome (Amphotericin B Liposome) for Injection, 50 mg/vial, the proposed drug product would be a sterile non-pyrogenic lyophilized product for intravenous infusion. The proposed strength (total drug content) is contemplated by the approved labeling for the listed drug. The recommended initial dose of AmBisome for adult and pediatric patients is as follows:

Indication	**Dose (mg/kg/day)**
Empirical Therapy	3
Systemic Fungal Infections: Aspergillus, Candida, Cryptococcus	3-5
Cryptococcal meningitis in HIV infected patients (see DESCRIPTION OF CLINICAL STUDIES)	6

Doses recommended for visceral leishmaniasis are presented below:

Visceral Leishmaniasis	**Dose (mg/kg/day)**
Immunocompetent patients	3 (days 1-5) and 3 on Days 14, 21
Immunocompromised patients	4 (days 1-5) and 4 on days 10, 17, 24, 31, 38

(See **Attachment 2** for AmBisome PI, **Dosage and Administration**).

As shown above, a typical dose will require multiple vials. For example, a 60 kg patient (5 mg/kg*60 kg = 300 mg) would require 6 vials. Thus, a 100 mg/vial reduces the number of vials (i.e., 3 vials) required to prepare a typical dose.

This petition seeks a change in strength from that of the listed drug product, from 50 mg/vial to 100 mg/vial. There is only a change in total drug content and not concentration. As per RLD PI, reconstitution is required for this product. So, there would be changes in the reconstitution instruction in Proposed Product PIL. The following table presents the comparison between the approved and petitioner's proposed drug product's reconstitution instruction.

Comparison of Approved Drug Product to Petitioner's Proposed Drug Product

Reconstitution From the PIL	
Approved Product AmBisome (Amphotericin B Liposome) for Injection, 50 mg/vial	**Proposed Product** Amphotericin B Liposome for Injection, 100 mg/vial
1. Aseptically add 12 mL of Sterile Water for Injection, USP to each amphotericin B liposome for injection vial to yield a preparation containing 4 mg amphotericin B/mL. **CAUTION: DO NOT RECONSTITUTE WITH SALINE OR ADD SALINE TO THE RECONSTITUTED CONCENTRATION, OR MIX WITH OTHER DRUGS.** The use of any solution other than those recommended, or the presence of a bacteriostatic agent in the solution, may cause precipitation of amphotericin B liposome for injection.	1. Aseptically add 24 mL of Sterile Water for Injection, USP to each amphotericin B liposome for injection vial to yield a preparation containing 4 mg amphotericin B/mL. **CAUTION: DO NOT RECONSTITUTE WITH SALINE OR ADD SALINE TO THE RECONSTITUTED CONCENTRATION, OR MIX WITH OTHER DRUGS.** The use of any solution other than those recommended, or the presence of a bacteriostatic agent in the solution, may cause precipitation of amphotericin B liposome for injection.
2. Immediately after the addition of water, SHAKE THE VIAL VIGOROUSLY for 30 seconds to completely disperse the amphotericin B liposome for injection. Amphotericin B liposome for injection forms a yellow, translucent suspension. Visually inspect the vial for particulate matter and continue shaking until completely dispersed.	2. **Immediately after the addition of water, SHAKE THE VIAL VIGOROUSLY** for 30 seconds to completely disperse the amphotericin B liposome for injection. Amphotericin B liposome for injection forms a yellow, translucent suspension. Visually inspect the vial for particulate matter and continue shaking until completely dispersed.

There are no proposed changes in labeling with the exception of the obvious changes in strength and reconstitution instruction sought in this petition. The active ingredient, dosage form, and route of administration are the same as those of the current listed drug, as are the uses, indication, warnings, and directions for use. The proposed labeling is provided as **Attachment 3**; with the changes annotated in track changes from the FDA approved labeling**.**

Considering the formulation release property and the desired bioequivalence to the RLD formulation, the bioavailability of the proposed drug product shall be studied against the RLD AmBisome in vivo and in vitro required by Product-Specific Guidance for Amphotericin B Liposome for Injection, as provided in **Attachment 4**.

Therefore, the petitioner's request for the Commissioner to find that a change in strength for Amphotericin B Liposome for Injection (i.e., a change in total drug content) from 50 mg/vial to 100 mg/vial should raise no questions of safety or effectiveness, and the FDA should approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 C.F.R. § 25.31(a) from the requirement to submit an environmental assessment.

D. Economic Impact Statement

The Petitioner will, upon request by the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b).

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 unfavourable to the petition.

Sincerely,

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