CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212156Orig1s000

SUMMARY REVIEW

NDA Summary Review

NDA #	NDA 212156
Applicant	Par Sterile Products, LLC
Date of Submission	December 21, 2020 (Response to Complete Response)
PDUFA Goal Date	June 21, 2021
Proprietary Name / Established (USAN) names	Micafungin for Injection*
Dosage forms/Strength	Powder for injection (50 mg/single-dose vial & 100 mg/single-dose vial)
Proposed Indication	Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses
Regulatory Action	Approval

** No proprietary/trade name was proposed for the drug product*

1. Background

Micafungin is a member of the echinocandin class of antifungal agents. This 505(b)(2) NDA provides for a new formulation of micafungin for injection, 50 mg/vial and 100 mg/vial, to be used for the treatment of the same indications as for the listed drug (LD), Mycamine® (micafungin for injection) approved under NDA 21506 from Astellas Pharma. Micafungin for injection proposed by the current Applicant, Par Sterile Products, LLC, contains the same drug substance as Mycamine® (micafungin free base, as micafungin sodium). In addition, the proposed drug has the same dosage form, strengths, route of administration, and dosing regimen as the LD; however, it differs from the LD in that it contains sucrose instead of lactose (b) (4).

This NDA was originally submitted on November 19, 2018 and was refused to file (RTF) due to the insufficient drug product stability data. The NDA was resubmitted (after RTF) on July 18, 2019, and it was issued a Complete Response (CR) letter on May 18, 2020 due to a number of deficiencies identified by the OPQ Review Team (refer to the OPQ Review # 1, dated April 10, 2020, and the CR letter dated May 18, 2020, in DARRTS).

2. Current Submission

The current NDA resubmission provides information to address the deficiencies and comments included in the CR letter dated May 18, 2020.

Non-clinical

Micafungin for Injection does not contain any impurities, degradants, or extractables/leachables that are likely to pose a safety concern from a Pharmacology/Toxicology perspective. The nonclinical deficiencies identified in the May 18, 2020 Complete Response Letter regarding the proposed impurity acceptance criterion and leachables assessment have been adequately addressed. The acceptance criterion for impurities have been tightened to NMT (b) (4)%, with exception of Impurity (b) (4). The Applicant's request to increase the acceptance criterion of Impurity (b) (4) to NMT (b) (4)% was found acceptable, as impurity (b) (4) detected (b) (4) at levels ranging from (b) (4) From a Pharmacology/Toxicology perspective, the NDA is recommended for approval (for additional information, please see the Nonclinical Review for this NDA submission in DARRTS [6/9/21]).

OPQ

The current NDA resubmission provides information to address the Product Quality deficiencies identified in the OPQ Review # 1 dated April 10, 2020. These deficiencies included: inadequate status of one of the manufacturing facilities, drug substance intermediate manufacturer, (b) (4) inadequate data from in-use stability studies and lack of proper justification for acceptance criteria proposed for several impurities, including any unspecified impurity. These issues, including several other Product Quality comments listed in the CR letter, which were not considered approvability issues, have been addressed satisfactorily in the current NDA resubmission. In addition, the results of the of the extractable/leachable assessment submitted in the amendment eCTD 0014 dated April 6, 2020 (which was not reviewed in the previous review cycle), were also found adequate. Furthermore, all manufacturing and testing facilities are deemed acceptable and an overall "Approve" recommendation was entered into Panorama by the Office of Pharmaceutical Manufacturing Assessment (OPMA) on January 15, 2021. Therefore, this NDA is now recommended for approval by the Office of Pharmaceutical Quality (OPQ). For details refer to the OPQ Review # 2 dated June 3, 2021, in DARRTS.

Clinical Pharmacology, Clinical Microbiology, Clinical/Statistical

There were no Clinical Pharmacology, Clinical Microbiology, or Clinical/Statistical information/data submitted in this NDA; thus, no detailed discipline reviews were necessary.

Labeling

Review of the Applicant's proposed label, packaging and product labeling was conducted. The listed drug, Mycamine (NDA 21-506), received approval on December 20, 2019 to extend the indication of treatment of candidemia, acute disseminated candidiasis, *Candida* peritonitis and abscesses to patients younger than 4 months of age (a new patient

population); therefore, the labeling information supporting the use of Mycamine for this indication/population is protected by exclusivity and will be carved out from the labeling of generic micafungin products or any 505(b)(2) micafungin applications for 3 years since the time of approval. Specific sections of the prescribing information (PI) affected by this carve out are: Highlights, Indications and Usage (1), Dosage and Administration (2.2), Adverse Reactions (6.1), Use in Specific Populations (8.4), Overdosage (10) and Clinical Pharmacology (12.3) . The recommended carve out will be accompanied by the following statements: "*Additional pediatric use information is approved for Astellas Pharma US., Inc.'s Mycamine® (micafungin for injection). However, due to Astellas Pharma US., Inc.'s marketing exclusivity rights, this drug product is not labeled with that information*".

Labeling changes were also made to the storage of the reconstituted and diluted solution recommendations in the Dosage and Administration (2.3) subsection of the prescribing information.

The Applicant agreed to the Division's recommended changes to the labeling.

3. Regulatory Action

This New Drug Application (NDA 212156) for Micafungin for Injection, 50 mg/vial and 100 mg/vial will receive an approval action.

Reviewers:

Pharmacology/Toxicology Reviewer: Kelly Brant, PhD
Cross-Discipline Team Leader: Terry Miller, PhD
Division Deputy Director: Dmitri Iarikov, MD, PhD

Signatures: *{See appended electronic signature page}*

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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