CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216142Orig1s000

PRODUCT QUALITY REVIEW(S)

NDA Executive Summary

1. Application/Product Information

NDA Number.	216142
Applicant Name	Baxter Healthcare Corporation
Drug Product Name	Micafungin in sodium chloride injection
Dosage Form.	Solution
Proposed Strength(s)	1 mg/mL (three presentations: 50 mg/50 mL; 100 mg/100 mL; 150 mg/150 mL)
Route of Administration	Intravenous
Maximum Daily Dose	150 mg
Rx/OTC Dispensed	Rx
Proposed Indication	• Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses in adult and pediatric patients 4 months of age and older for whom appropriate dosing with this formulation can be achieved. • Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses without meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age for whom appropriate dosing with this formulation can be achieved. • Treatment of Esophageal Candidiasis in adult and pediatric patients 4 months of age and older for whom appropriate dosing with this formulation can be achieved. • Prophylaxis of Candida Infections in adult and pediatric patients 4 months of age and older undergoing Hematopoietic Stem Cell Transplantation (HSCT) for whom appropriate dosing with this formulation can be achieved.
Drug Product Description	The proposed drug product is a new injectable formulation of micafungin, micafungin in 0.9% sodium chloride injectable solution, 1 mg/mL (50 mg/50 mL, 100 mg/100 mL, and 150 mg/150 mL), packaged in Baxter's [redacted] (b) (4) (GALAXY) container closure system, and to be used for the same indications as the

	listed drug (LD), MYCAMINE® (micafungin for injection), 50 mg/vial and 100 mg/vial (approved under NDA 21506, held by Astellas Pharma US, Inc.). The drug product proposed in the current 505(b)(2) NDA is a “ready to use” premixed, iso-osmotic, sterile, nonpyrogenic solution for intravenous (IV) infusion manufactured using micafungin sodium. The proposed drug product is qualitatively and quantitatively similar to the LD, with differences in excipients. The premixed solution of micafungin is clear and colorless, with a pH range of 4.5 to 5.1.		
Co-packaged product information	N/A		
Device information:	N/A		
Storage Temperature/ Conditions	2-8°C (36°F to 46°F)		
Review Team	**Discipline**	**Primary**	**Secondary**
	Drug Substance	Karina Zuck	Katherine Windsor
	Drug Product	Hudson Roth	Dorota Matecka
	Labeling	Hudson Roth	David Claffey
	Manufacturing	Ephrem Hunde	Yiwei Li
	Biopharmaceutics	Payal Agarwal	Elsbeth Chikhale
	Microbiology	Kelly Ann Miller	Erika Pfeiler
	Other (specify):	N/A	
	RBPM	Anh-Thy Ly	
	ATL	Dorota Matecka	

Consults	N/A

2. Final Overall Recommendation - Approval

3. Action Letter Information

a. Expiration Dating:

12 months [stored in a refrigerator at 2°C to 8°C (36°F to 46°F)].

b. Additional Comments for Action

N/A

4. Basis for Recommendation:

a. Summary of Rationale for Recommendation:

The NDA has provided sufficient CMC information to assure the identity, strength, purity, and quality of the proposed drug substance (micafungin sodium) and the drug product (micafungin in sodium chloride injection). The information for micafungin sodium drug substance is referenced to DMF Type II (b) (4) (held by (b) (4) which was last reviewed on February 15, 2023, in support of the current NDA and found adequate. Also, overall drug substance and drug product information provided in the original NDA and subsequent amendments submitted in response to FDA comments, was found acceptable. Similarly, information provided regarding the drug product manufacturing process and its microbiological quality has been found adequate. From the biopharmaceutics perspective, adequate data were provided to support the bridge between the proposed drug product and the listed drug (LD). In addition, all manufacturing and testing facilities have been found acceptable based on their previous history and status; therefore, an overall "Approve" recommendation for this NDA was entered into Panorama by the Office of Pharmaceutical Manufacturing Assessment (OPMA) on February 21, 2023. Based on the individual subdiscipline assessments, this NDA is recommended for approval by the Office of Pharmaceutical Quality (OPQ).

b. Is the overall recommendation in agreement with the individual discipline recommendations? Yes

Recommendation by Subdiscipline:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Quality Labeling	**-**	**Adequate**
Manufacturing	**-**	**Adequate**
Biopharmaceutics	**-**	**Adequate**
Microbiology	**-**	**Adequate**

Environmental Assessment: Categorical Exclusion - Adequate
QPA for EA(s): No

5. Life-Cycle Considerations

Established Conditions per ICH Q12: No
Comments:

Comparability Protocols (PACMP): No
Comments:

Additional Lifecycle Comments: N/A

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Dorota Matecka

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CHAPTER IV: LABELING

For more details about the items in this template, please see Chapter IV (Labeling) of the NDA IQA Guide

NDA 216142

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: Recommendations for the PI have been conveyed to OND.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Product Title in Highlights		
Established name(s)[1]	Inadequate	Established name should be revised to "Micafungin in sodium chloride injection" based on the FDA Guidance "Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products — Content and Format Guidance"
Route(s) of administration	Adequate	
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system	Inadequate	Revise for conciseness based on best labeling practice in the March 2022 Labeling Review Tool (LRT). "Micafungin in Sodium Chloride Injection: 50 mg in 50 mL, 100 mg in 100 mL, and 150 mg in 150 mL in single-dose Galaxy containers. (3)"
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored".	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk	Adequate	

[1] Established name = [Drug] [Route of Administration] [Dosage Form]

package and imaging bulk package.		
If the drug product contains an active ingredient that is a salt, clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (e.g., Tablets: 10 mg of drug-x hydrochloride).	Adequate	

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	Inadequate	Add additional storage instructions and a reference to Section 16. "Once stored at room temperature, do not place back in the refrigerator. Discard Micafungin in Sodium Chloride Injection after 30 days if stored at room temperature *[see How Supplied/Storage and Handling (16)]*"
Important administration instructions supported by product quality information (e.g., do not crush or chew extended-release tablets, instructions for mixing with food)	Adequate	
For parenteral products: include statement: *"Parenteral drug products must be inspected visually for particulate matter and discoloration prior to administration, whenever*	Inadequate	Include a description of identifying characteristics of the injection after this statement based on best labeling practice in the March 2022 Labeling Review Tool (LRT).

solution and container permit"		
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 11).	N/A	
For radioactive products, include radiation dosimetry for the patient and healthcare practitioner(s) who administer the drug	N/A	
For hazardous products, include the statement *"DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]"* with x numerical citation to "OSHA Hazardous Drugs".	N/A	

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Adequate	
Strength(s) in metric system	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance. Clearly state whether the strength is based on the active moiety (e.g., Tablets: 10 mg of drug-x) or active ingredient (Tablets: 10 mg of drug-x hydrochloride).	Adequate	
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable	Inadequate	Include a description of identifying characteristics of the injection based on best labeling practice in the March 2022 Labeling Review Tool (LRT).
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	Adequate	

Section 11 (DESCRIPTION)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
DESCRIPTION section		
Proprietary and established name(s)	Adequate	
Dosage form(s) and route(s) of administration	Adequate	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per Salt Guidance and MAPP. For example: "TRADENAME contains 100 mg of drug-x (equivalent to 123.7 mg of drug-x hydrochloride)"	Adequate	
List names of all inactive ingredients. Use USP/NF names in alphabetical order. Avoid brand names.	Adequate	
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	Adequate	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Sterility statement (if applicable)	Adequate	
Pharmacological/Therapeutic class	Adequate	
Chemical name, structural formula, molecular weight	Adequate	
If radioactive, statement of important nuclear characteristics.	N/A	
Other important chemical or physical properties (such as pKa or pH)	Inadequate	Include a statement on the sodium content of the drug product based on the Quantitative Sodium Labeling Guidance.

Section 11 (DESCRIPTION) Continued

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
For oral prescription drug products, include gluten statement (if applicable)	Adequate	
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity")	Inadequate	Recommend removing "pre-mixed, iso-osmotic, and non-pyrogenic" from the drug product description. Remove statements about (b) (4)
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled. Note the labeling requirement may be applicable to another section of the PI (e.g., Section 2).	N/A	

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	Adequate	
Strength(s) in metric system	Adequate	
Available units (e.g., bottles of 100 tablets)	Adequate	
Identification of dosage forms (e.g., shape, color, coating, scoring, imprinting, and color and clarity of the solution, when applicable); Include NDC(s)	Inadequate	Include a description of identifying characteristics of the injection based on best labeling practice in the March 2022 Labeling Review Tool (LRT).
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	Adequate	
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g., to protect from light or moisture, to maintain stability, etc.). For hazardous drugs, state "DRUG X is a hazardous drug. Follow applicable special handling and disposal procedures.[x]" with x numerical citation to "OSHA Hazardous Drugs."	Adequate	

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	Adequate	
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: *"Not made with natural rubber latex. Avoid statements such as "latex-free."*	N/A	
Include information about child-resistant packaging	N/A	

1.2.5 Other Sections of Labeling

There may be other sections of labeling that contain product-quality related information. For example, there are specific required/recommended warnings for certain inactive ingredients [e.g., aspartame, aluminum in large and small volume parenterals, sulfites, FD&C Yellow Number 5 (tartrazine), and benzyl alcohol]. Please notify the prescription drug review division if the product contains any of these inactive ingredients.
Please include your comments about other sections of labeling if they contain product quality information.

1.2.6 Manufacturing Information After Section 17 (for drug products)

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments (If an item is Inadequate, provide more details on the issues, as appropriate)
Manufacturing Information After Section 17		
Name and location of business (street address, city, state, and zip code) of the manufacturer, distributor, and/or packer	Adequate	

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guides, Instructions for Use, Patient Information): N/A, there is no patient labeling.

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Established name[2], (font size and prominence)	Adequate	
Strength(s) in metric system	Adequate	
Route(s) of administration	Adequate	
If the active ingredient is a salt, include the equivalency statement per Salt Guidance and MAPP.	Adequate	
Net contents (e.g., tablet count, volume of liquid)	Adequate	
"Rx only" displayed on the principal display	Adequate	
NDC	Adequate	
Lot number and expiration date	Adequate	
Storage conditions. If applicable, include a space on the carton labeling for the user to write the new beyond-use-date (BUD).	Adequate	
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package, and these products require a "Not for direct infusion" statement.	Adequate	
For parenteral injectable dosage forms, include the name and quantities of all active and inactive ingredients in alphabetical order. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.	Adequate	
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Linear Bar code	Adequate	

[2] Established name = [Drug] [Route of Administration] [Dosage Form]

Item	Items in Proposed Labeling (choose "Adequate", "Inadequate", or "N/A")	Assessor's Comments about Carton Labeling (If an item is Inadequate, provide more details on the issues, as appropriate)
Name of manufacturer/distributor /packer	Adequate	
If there is a Medication Guide, must include a statement about dispensing a Medication Guide to each patient.	N/A	
No text on Ferrule and Cap overseal unless a cautionary statement is required.	N/A	
If there is a USP monograph for the drug product and it contains a labeling requirement, ensure the labeling requirement is fulfilled.	N/A	
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.	N/A	
And others, if space is available.	N/A	

Assessment of Carton and Container Labeling: *Adequate*

The following comments were conveyed to the Applicant on May 25, 2023:

1. The active and inactive ingredients are listed in amount per mL as opposed to the net amount in the container. Revise the statement "[redacted (b) (4)] to "Each XX mL bag contains XX mg of micafungin…" in order to express the total amount of each ingredient per container and align with Section 11 of the PI.
2. The amount of micafungin in the list of ingredients is expressed as micafungin sodium. Revise the amount of micafungin in the list of ingredients to comply with the USP Salt Policy (e.g., "XX mg of micafungin (equivalent to XX mg of micafungin sodium)…").
3. The excipients in the list of ingredients each have the USP descriptor (e.g., "Sodium Chloride, USP"). We recommend you remove the USP descriptor from the list of ingredients on both the carton and container labels for clarity and conciseness.
4. The storage temperatures listed on the carton and container labeling put Fahrenheit first. Revise the storage condition temperatures to put Celsius first followed by Fahrenheit in parentheses.

The Applicant **adequately** addressed the comments in a response dated June 16, 2023.

ITEMS FOR ADDITIONAL ASSESSMENT

Recommendations for the Prescribing Information

Highlights of Prescribing Information

1. According to the Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products – Content and Format Guidance, the strength of the vehicle should not be included in the product title. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/product-title-and-initial-us-approval-highlights-prescribing-information-human-prescription-drug-and
2. Capitalize "IN SODIUM CHLORIDE" based on the Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products – Content and Format Guidance.
3. Consider a more concise format for the dosage forms and strength as follows: "Micafungin in Sodium Chloride Injection: 50 mg in 50 mL, 100 mg in 100 mL, 150 mg in 150 mL in single-dose Galaxy containers. (3)"

Section 2

4. Provide a description of identifying characteristics of the injection in accordance with 21 CFR 201.57(c)(17)(iii) after the required statement on visual inspection of parenteral drug products.
5. Include the additional storage statements regarding temporary storage at room temperature and a reference to Section 16 for additional information.
6. Recommend removing the USP descriptor for 0.9% Sodium Chloride Injection from Section 2.6 for clarity and conciseness.

Section 3

7. Provide a description of identifying characteristics of the injection in accordance with 21 CFR 201.57(c)(17)(iii).

Section 11

8. Include a statement on the sodium content in the drug product as per the Quantitative Labeling of Sodium, Potassium, and Phosphorus for Human Over-the-Counter and Prescription Drug Products Guidance. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quantitative-labeling-sodium-potassium-and-phosphorus-human-over-counter-and-prescription-drug
9. Remove the unnecessary drug product descriptors "premixed", "iso-osmotic", and "non-pyrogenic".
10. A description of the [redacted] (b) (4) is not required. We recommend removing this from Section 11.
11. The mechanism of action should not be included in [redacted] (b) (4) it is described in Section 12.4 instead.
12. We recommend removing the USP descriptor for excipients for conciseness and clarity.

Section 16

13. Provide a description of identifying characteristics of the injection in accordance with 21 CFR 201.57(c)(17)(iii).
14. Remove the unnecessary drug product descriptors “refrigerated”, “premixed”, “iso-osmotic”, and “non-pyrogenic”.
15. Consider consolidating the package type information in the “Container” column into the “Number of Containers/Carton” column.
16. Revise storage statements to put °C first and °F in parentheses.
17. Recommend including the statement “…to protect from light.” after “…for up to 30 days in the original carton…” for consistency across the PI.

Overall Assessment and Recommendation:

Recommendations have been conveyed to OND.

Primary Labeling Assessor Name and Date:

Hudson Roth, Ph.D., 08/15/2023

Secondary Assessor Name and Date (and Secondary Summary, as needed):

David Claffey, Ph.D., 08/15/2023

Hudson Roth

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David Claffey

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Yiwei Li

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BIOPHARMACEUTICS REVIEW	
NDA Number	NDA-216142
Submission Type	505(b)(2)
Product Name	Micafungin in 0.9% Sodium Chloride Injection
Applicant	Baxter Healthcare Corporation
Dosage Form	Injectable; Sterile Solution
Strength(s)	50 mg/50 mL; 100 mg/100 mL; 150 mg/150 mL
Route of administration	Intravenous infusion
Proposed Indication	Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses, Treatment of Esophageal Candidiasis
Submission Date(s)	November 30, 2022[1]
Primary Reviewer	Payal Agarwal, Ph. D
Secondary Reviewer	Elsbeth Chikhale, Ph. D
Recommendation	**Adequate**

EXECUTIVE SUMMARY:

In NDA 216142, the Applicant seeks approval for Micafungin in 0.9% Sodium Chloride Injection, 1 mg/mL (packaged as 50 mg/50 mL, 100 mg/100 mL, and 150 mg/150 mL) in Baxter's (b) (4) (GALAXY) container closure system under the 505(b)(2) pathway. This application relies on the previous finding of safety and effectiveness of the listed drug (LD) MYCAMINE® (micafungin for injection), for intravenous use, 50 mg/vial and 100 mg/vial, approved under NDA 021506, which needs to be reconstituted and as per the label could be further diluted before administration. The proposed Micafungin in 0.9% Sodium Chloride Injection drug product is a "ready to use" premixed, iso-osmotic, sterile, nonpyrogenic solution for intravenous (IV) infusion that contains micafungin sodium.

The Biopharmaceutics review is focused on the evaluation of data to support the **bridging between the proposed drug product and the LD for intravenous administration**.

This Application contains the in-vitro comparative physicochemical data, a side by side comparison Table of the proposed drug product and the LD along with the data/justification to demonstrate the lack of impact of the inclusion/exclusion of several excipients on the in vivo physiological disposition or in vivo clinical performance. This submission is based on previous communications with the Applicant through a Type-B Pre-IND meeting package[2].

RECOMMENDATION: Based on the review of the provided information/data, from a Biopharmaceutics perspective, NDA 216142 for Micafungin in 0.9% Sodium Chloride Injection 1 mg/mL (50 mg/50 mL, 100 mg/100 mL and 150 mg/150 mL) is **adequate** and recommended for **Approval**.

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BIOPHARMACEUTICS ASSSESSMENT

1. LIST OF SUBMISSIONS BEING REVIEWED

Submission Reviewed		
SDN #	**Received date**	**Document**
1	November 30th 2022	Original NDA Submission

2. DRUG PRODUCT

In NDA 216142, the Applicant seeks approval of Micafungin in 0.9% Sodium Chloride Injection 1 mg/mL (packaged as 50 mg/50 mL, 100 mg/100 mL and 150 mg/150 mL), in Baxter's (b) (4) (GALAXY) container closure system under the 505(b)(2) pathway.

The proposed Micafungin in 0.9% Sodium Chloride Injection is clear and colorless, with a pH range of 4.5 to 5.1 **(Refer to Appendix 1)** provides the detail composition of the proposed drug product. This proposed product will be supplied as a ready to use, refrigerated, premixed, iso-osmotic, sterile, non-pyrogenic solution for intravenous use:

3. ASSESSMENT OF BRIDGING BETWEEN THE PROPOSED PRODUCT AND THE LISTED DRUG (LD)[3]

This 505(b)(2) application relies on FDA's previous findings of safety and effectiveness of the listed drug (LD) MYCAMINE® (micafungin for injection), for intravenous use, 50 mg/vial and 100 mg/vial, approved under NDA 021506, held by Astellas Pharma US, Inc. MYCAMINE® is supplied as a sterile, lyophilized product for intravenous (IV) infusion that contains micafungin sodium. Each single-dose vial contains 50 mg micafungin (equivalent to 50.86 mg micafungin sodium) or 100 mg micafungin (equivalent to 101.73 mg micafungin sodium), 200 mg lactose, with citric acid and/or sodium hydroxide (used for pH adjustment). MYCAMINE® must be diluted with 0.9% Sodium Chloride Injection, USP, or 5% Dextrose Injection, USP. To justify reliance of the proposed drug product on the LD, bridging between the proposed and the LD/RS needs to be established for intravenous administration.

The proposed product relies on the safety and efficacy information of the LD[4]. As per pre-IND 154875 Meeting Minutes/ Written Response 5/30/21, FDA agreed that it was feasible to establish a scientific bridge between the proposed drug product and the LD and in vivo BE studies would not be required if a bridge is established. In addition, as per the pre-IND 154875 Meeting Minutes/ Written Response 5/30/21, FDA agreed that a review of clinical literature from the date of the listed drug's most recent labeling supplement approval (2019 DEC 20) is sufficient to support thesafety and efficacy of the proposed product and supportive of any required label changes (inclusive of PLLR related updates).

[3] \\CDSESUB1\EVSPROD\nda216142\0001\m1\us\justification-bioequivalence-report-bxu582967.pdf

[4] \\CDSESUB1\EVSPROD\nda216142\0001\m1\us\request-waiver-in-vivo-bioavailability-studies.pdf

Based on the above, Baxter, provided a scientific bridging study BXU582967 that contains:

(a) Side by side table comparing the proposed drug with LD, including formulation (qualitative/quantitative compositions), indications, dosage form, route of administration, drug concentrations, and dosing regimen as shown in **Table 1**.
(b) Comparative physiochemical data including pH, color, osmolality, and measurement of the assay and related substances (total and individual) between the proposed versus the listed drug product.
(c) Data/justification that can adequately address whether any differences between the proposed and LD (e.g., proposed new excipients, change in pH) would not impact the in vivo physiological disposition (e.g., distribution, metabolism, elimination), or in vivo clinical performance (e.g., pharmacodynamic, clinical safety and efficacy) of micafungin.

Side by side table comparing the proposed drug with LD, including formulation (qualitative/quantitative compositions), indications, dosage form route of administration, drug concentrations, and dosing regimen.

- Applicant has provided a comparison table (**Table 2**) between the proposed product and LD product which shows that these two products are administered as the same dosage form, have the same routes of administration, the same drug substance micafungin sodium and use the same diluent for infusion.
- The total drug content in the Baxter proposed 50 mg/50 mL and 100 mg/100 mL presentations are the same as the listed drug MYCAMINE (50 mg/vial and 100 mg/vial)
- Differences are seen with the 150 mg/150 mL which represents a new total drug content of 150 mg, which is not available in one vial of the LD. However, 150 mg as a single dose is approved under the prescribing information for MYCAMINE®, using two or 3 vials. Therefore, even though there is new strength there is no change in the total dose administered.
- Concentration of the proposed product (1.0 mg/mL) falls within the concentration range of the LD product (0.5 mg/mL to 4 mg/mL). Therefore, there is no concern about the safety/efficacy of the proposed drug product (1.0 mg/mL).
- Differences are seen in the dosage form as marketed, where the LD products require reconstitution and subsequent dilution prior to IV administration. For MYCAMINE®, it is recommended for pediatric administration that micafungin concentrations above 1.5 mg/mL should be administered via central catheter. This does not apply to the proposed Baxter products since all concentrations are 1.0 mg/mL.
- The storage conditions also differ between the proposed solution drug products and powder LD products.
- The proposed Baxter formulation contains (b) (4) (citric acid and sodium citrate as (b) (4)), whereas the LD utilizes citric acid and sodium hydroxide as pH adjusters. So, there is no need for pH adjustment in the proposed product.
- Citric acid and sodium citrate are used as excipients and inactive ingredient components in other FDA approved drug products.
- The levels of sodium citrate and citric acid in the proposed drug products are below those found in other products as identified in FDA's Inactive Ingredient Database (IID), and the maximum daily exposure for each of these two components is well below the exposure found with other products that contain citric acid and sodium citrate as inactive ingredients (**Table 3**).

Table 1. Qualitiative and Quantitiatve comparision of Baxter's proposed product and the LD

Ingredient (Function)	Baxter's Proposed Formulations			Listed Drug Product: Astellas Pharma US, Inc. NDA 021506	
	Micafungin in 0.9% Sodium Chloride Injection			MYCAMINE 50 mg/vial	MYCAMINE 100 mg/vial
Micafungin Sodium (API)	50.87 mg/ 50 mL	101.73 mg/ 100 mL	152.60 mg/ 150 mL	50.87 mg/vial Requiring further dilution for injection	101.73 mg/vial Requiring further dilution for injection
Sodium Chloride, USP (b) (4)	9 mg/mL	9 mg/mL	9 mg/mL	N/A	N/A
Citric Acid, Anhydrous, USP (b) (4)	0.72 mg/mL	0.72 mg/mL	0.72 mg/mL	N/A	N/A
Sodium Citrate, Dihydrate, USP (b) (4)	1.84 mg/mL	1.84 mg/mL	1.84 mg/mL	N/A	N/A
Lactose (b) (4)	N/A	N/A	N/A	200 mg/vial	200 mg/vial
Sodium Hydroxide, NF (pH Adjuster)	N/A	N/A	N/A	As Required	As Required
Citric Acid (pH Adjuster)	N/A	N/A	N/A	As Required	As Required
Water for Injection, USP (Diluent)	Quantity Sufficient	Quantity Sufficient	Quantity Sufficient	N/A	N/A
Administered Micafungin Concentration	1 mg/mL	1 mg/mL	1 mg/mL	0.5 – 4 mg/mL	0.5 – 4 mg/mL
pH	4.5 – 5.1	4.5 – 5.1	4.5 – 5.1	5 – 7	5 – 7
Container Closure System	Single-use GALAXY plastic container (50 mL)	Single-use GALAXY plastic container (100 mL)	Single-use GALAXY plastic container (200 mL)	Single-dose Glass Vial	Single-dose Glass Vial
Dosage form as marketed	Solution	Solution	Solution	Powder	Powder
Dosage form as administered	Solution	Solution	Solution	Solution	Solution
Route of Administration	Intravenous	Intravenous	Intravenous	Intravenous	Intravenous

N/A = Not Applicable

Table 2. Comparison between the proposed Baxter's Micafungin sodium in 0.9% NaCl and the LD Mycamine®

Attributes	Baxter's proposed Micafungin sodium in 0.9% NaCl solution	MYCAMINE® (LD)
API	Micafungin Sodium	Micafungin Sodium
Dosage form	Premixed Solution	Lyophilized Powder for Reconstitution
Indication	Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses (Max Daily dose = 100 mg) Treatment of Esophageal Candidiasis (Max Daily dose = 150 mg)	Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses (Max Daily dose = 100 mg) Treatment of Esophageal Candidiasis (Max Daily dose = 150 mg) Prophylaxis of Candida Infections in HSCT Recipients
Route	IV infusion only	IV infusion only
Duration of Infusion	Over one hour	Over one hour
Strengths	50 mg / 50 mL 100 mg / 100 mL 150 mg / 150 mL	50 mg/vial 100 mg/vial
pH	4.5 to 5.1	5-7
Composition	Given in Table 1	Refer to Appendix 1
Inactive ingredients	Sodium Chloride (b) (4) • Citric Acid, Anhydrous: 0.72 mg/mL • Sodium Citrate, Dihydrate: 1.84 mg/mL Water for Injection	Lactose: 200 mg (b) (4) Citric Acid and/or Sodium Hydroxide
Container	Flexible GALAXY Plastic Container	Vial
Diluent	N/A	0.9% Sodium Chloride Injection, USP 5% Dextrose Injection, USP[5]

[5] \\CDSESUB1\EVSPROD\nda216142\0001\m1\us\cover-letter-2022nov30.pdf, https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021506s023lbl.pdf

Label differences	N/A This does not apply to Baxter products since all concentrations are 1.0 mg/mL	LD products require reconstitution and subsequent dilution prior to IV administration For pediatric administration of MYCAMINE, it is recommended that micafungin concentrations above 1.5 mg/mL should be administered via central catheter.
Storage	Baxter's Micafungin solution is stable for up to 30 days in the original carton at room temperature up to 25°C (77°F). Store Micafungin in 0.9% Sodium Chloride Injection in the refrigerator (36°F to 46°F [2°C to 8°C]) in the original carton to protect from light. If needed, Micafungin in 0.9% Sodium Chloride Injection may be stored at room temperature up to 77°F (25°C) for up to 30 days in the original carton. Product does not require light protection during administration. Do not freeze	The reconstituted product should be protected from light and may be stored in the original vial for up to 24 hours at room temperature, 25°C (77°F). The diluted infusion bag should be protected from light and may be stored for up to 24 hours at room temperature, 25°C (77°F). Unopened vials of lyophilized material must be stored at room temperature, 25°C (77°F) Store the reconstituted product at 25°C (77°F) Store the diluted solution at 25°C (77°F) Protect from light

*These excipients have been used in other approved parenteral products.

Table 3. Comparison of the amount of Sodium chloride, citric acid, and sodium citrate dihydrate in the proposed Micafungin in 0.9% Sodium Chloride Injection versus other FDA approved injectable drug products

	Sodium chloride		**Citric Acid**		**Sodium Citrate, Dihydrate**	
	Proposed product	**Brevibloc (Esmolol Hydrochloride) Injection**	**Proposed product**	**ZYVOX IV Injection**	**Proposed product**	**Penicillin G Potassium, USP**
Conc	9 mg/mL	(b) (4)	0.72 mg/mL	0.85 mg/mL	1.84 mg/mL	(b) (4)
MVD*	150 mL		150 mL	600 mL	150 mL	
MDI**	1,350 mg		108 mg	510 mg	276 mg	

*MVD: Maximum Volume per Day
**MDI: Maximum Daily Intake

Comparative physiochemical data including pH, color, osmolality, and measurement of the assay and related substances (total and individual) between the proposed versus the listed drug product.

In bridging study BXU563962, the Micafungin in 0.9% Sodium Chloride Injection test products and LD were tested for visual inspection, pH, osmolality, and color, assay and related substances, after 12 months of refrigerated storage plus short-term storage for 30 days at 25 °C to represent the extremes of the long- term and in-use/short-term storage conditions anticipated for the proposed premix product (**Refer to Appendix 2**). A summary of its findings is given below:

- Clarity: All test articles met the acceptance criteria of clarity, and solutions were found to be essentially free of visible particulate matter. The proposed Micafungin in 0.9% Sodium Chloride Injection product is visually the same as the Listed Drug product after reconstitution and further dilution into 0.9% Sodium Chloride Injection.
- Color: The color of the proposed drug product Micafungin in 0.9% Sodium Chloride Injection is found to be similar (colorless) as the Listed Drug product after reconstitution and further dilution into 0.9% Sodium Chloride Injection.
- pH: The proposed Baxter product measured pH was 4.8 versus the MYCAMINE® reconstituted and further diluted in 0.9% Sodium Chloride Injection measured pH of 5.1 – 5.4. The target pH of the proposed product is (b) (4) which is within the range of approved products for intravenous infusion and is physiologically compatible. The Applicant justifies that pH is not a critical factor in the determination of bioavailability of micafungin administered intravenously, therefore the pH range is clinically acceptable and supportive of a waiver of bioavailability and bioequivalence studies.
- Osmolality: The osmolality of the proposed product is approximately 302- 308 mOsm/kg after 12-months refrigerated plus 30 days room temperature. MYCAMINE® has an osmolality of approximately 290 - 303 mOsm/kg when reconstituted and diluted in 0.9% Sodium Chloride Injection. The osmolality of both the proposed drug product and the Listed Drug product MYCAMINE® after reconstitution and further dilution into 0.9% Sodium Chloride Injection are very close to normal physiological levels therefore, no to minimal impact on serum osmolality is expected.
- Extractable/Leachable: Applicant claims that a direct comparison between the extractable and leachable profiles for the proposed drug products and the listed drug MYCAMINE® is not relevant as the proposed product is provided in a flexible plastic container (GALAXY (b) (4)) and the LD MYCAMINE® is provided as a dry powder in a vial.
- Assay: There is more variability in assay values observed in MYCAMINE® after reconstitution and further dilution into 0.9% Sodium Chloride Injection compared to the proposed Micafungin in 0.9% Sodium Chloride Injection due to reconstitution and dilution practices, which is not needed for the proposed ready-to-use Micafungin in 0.9% Sodium Chloride Injection product.
- Total related substances: The amount of total related substances in Micafungin in 0.9% Sodium Chloride Injection is similar to the amount observed in MYCAMINE®.

Data/justification that can adequately address whether any differences between the proposed and LD (e.g., proposed new excipients, change in pH) would not impact the in vivo physiological disposition (e.g., distribution, metabolism, elimination), or in vivo clinical performance (e.g., pharmacodynamic, clinical safety and efficacy) of micafungin.

- Because the proposed drug product and the LD have different excipients (citric acid anhydrous, lactose, sodium citrate dihydrate, sodium chloride) the Applicant submitted literature sources where no information was found to indicate a potential impact based on the

excipient differences, and therefore, the minor excipient differences can reasonably be expected to have no impact on the in vivo physiological disposition or in vivo clinical performance of micafungin.

- The Applicant provided comparison (**Table 3**) of the amount of these excipients (sodium chloride, citric acid, and sodium citrate) in Micafungin in 0.9% Sodium Chloride Injection with a few other FDA approved Injectable drug products. It was observed that Maximum volume per day and maximum daily intake of these excipients were much lower in the proposed drug product compared to the listed previously approved FDA products for intravenous administration.
- The inactive ingredients in Micafungin in 0.9% Sodium Chloride Injection do not exceed the levels in current CDER-approved drug products with the same route of administration based on Maximum Daily Intake (MDI). The safety of the levels of sodium chloride, citric acid, anhydrous and sodium citrate, dihydrate in the Baxter proposed products can be justified because they do not exceed the Inactive Ingredient Database (IID) levels for the intravenous infusion route of administration based on Maximum Daily Intake as shown in **Table 4**.
- In addition, based on the literature submitted, it was found that the excipients are expected to have low to zero impact on the in vivo physiological disposition (distribution, metabolism, and excretion) of micafungin in human subjects.

Table 4. Comparison of Citric Acid, Anhydrous and Sodium Citrate, Dihydrate in micafungin in 0.9% Sodium Chloride Injection versus the IID

Inactive Ingredient / Excipient	Excipient Amount in Micafungin in 0.9% Sodium Chloride Injection	Excipient Amount per 150 mL Container	Maximum Daily Intake (MDI) of Inactive Ingredient[a]	Maximum Daily Exposure (MDE) based on IID Levels (MDE IID) for Intravenous Route of Administration[b]	Is MDI ≤ IID MDE?
Sodium Chloride, USP	9 mg/mL (0.9%)	1350 mg/150 mL	1350 mg	28773 mg (UNII 451W47IQ8X)	Yes
Citric Acid, Anhydrous, USP	0.72 mg/mL (0.072%)	108 mg/150 mL	108 mg	510 mg (UNII XF417D3PSL)	Yes
Sodium Citrate, Dihydrate, USP	1.84 mg/mL (0.184%)	276 mg/150 mL	276 mg	984 mg (UNII B22547B95K)	Yes
Water for Injection, USP	QS	N/A	N/A	N/A	N/A

IID = Inactive Ingredient Database; USP = United States Pharmacopeia; QS = Quantity Sufficient; N/A = Not Applicable

[a] The Maximum Daily Dose (MDD) of Micafungin is 150 mg. The MDI of an inactive ingredient is taken from the amount in the 150 mg/150 mL strength as this would represent the worst-case exposure.

[b] http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm.

Overall, based on the comparative physicochemical testing between the proposed drug product and the LD Mycamine®, and supporting findings from the given literature review, it can be concluded that for all relevant parameters, Micafungin in 0.9% Sodium Chloride Injection is similar to the LD (MYCAMINE®) after reconstitution and further dilution into 0.9% Sodium Chloride Injection. A scientific bridge between the proposed drug product, Micafungin in 0.9% Sodium

Chloride Injection and the LD (MYCAMINE®) after reconstitution and further dilution into 0.9% Sodium Chloride Injection is established as per 21 CFR 320.24(b)(6).

4. CONCLUSIONS AND RECOMMENDATION

The provided information supports the bridge between the proposed product and the LD for intravenous administration. From a Biopharmaceutics perspective, NDA 216142 for Micafungin in 0.9% Sodium Chloride Injection 1 mg/mL (50 mg/50 mL, 100 mg/100 mL and 150 mg/150 mL) is **adequate** and recommended for **Approval**.

APPENDIX 1

Composition of the proposed Micafungin in 0.9% Sodium Chloride Injection 1 mg/mL (50 mg/50 mL, 100 mg/100 mL and 150 mg/150 mL)

Component	Quality Standard	Function	Component Quantity		
			per 50 mL[a]	per 100 mL[b]	per 150 mL[c]
Micafungin Sodium	In House	Drug substance	50 mg[d]	100 mg[d]	150 mg[d]
Sodium Chloride	USP	(b) (4)	450 mg	900 mg	1350 mg
Citric Acid, Anhydrous	USP		36 mg	72 mg	108 mg
Sodium Citrate, Dihydrate	USP		92 mg	184 mg	276 mg
Water for Injection	USP		QS	QS	QS

USP = United States Pharmacopeia; QS = Quantity Sufficient

[a] Labeled volume: 50 mL. Fill volume: (b) (4)

[b] Labeled volume: 100 mL. Fill volume:

[c] Labeled volume: 150 mL. Fill volume:

[d] Expressed as Micafungin. This value equates to: 50.87 mg Micafungin sodium (per 50 mL), 101.73 mg Micafungin sodium (per 100 mL), and 152.60 mg Micafungin sodium (per 150 mL).

APPENDIX 2[6]

Table 6. Test Methods for Comparative Assessment

Test Method	Analytical Procedure	Acceptance Criteria
Visual Inspection	USP<790> 11-29-22-002/ D1-21-09-406	Pass (Pass means essentially free of visible particulate)
Visual Appearance	USP <1> 11-21-10-895/ D1-21-09-406	Pass (Pass means a clear, colorless solution by visual inspection.)
pH at 25°C	USP <791> (11-21-16-003)	Report Values and Discuss Differences
Osmolality	USP <785> 11-25-15-005/ D1-25-80-0031	Report Values and Discuss Differences
Color	USP <631> (D1-21-80-0003)	Report Values and Discuss Differences
Assay	D1-25-80-0486	Report Values and Discuss Differences
Related Substances	D1-25-80-0486 and D1-25-80-0446	Report Values and Discuss Differences

Table 7. pH Results for Micafungin in 0.9% Sodium Chloride Injection and MYCAMINE

Article	Minimum pH value observed	Maximum pH value observed
Micafungin in 0.9% Sodium Chloride Injection (50 mg/50 mL and 150 mg/150 mL)[a]	4.8	4.8
MYCAMINE (50 mg/vial and 100 mg/vial)[b]	5.1	5.4

[a]12 months refrigerated at 5°C units plus 30 days room temperature, 25°C units.
[b]Reconstituted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C and further diluted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C.

Table 8. Osmolality Results for Micafungin in 0.9% Sodium Chloride Injection and MYCAMINE

Article	Minimum Osmolality value observed (mOsm/kg)	Maximum Osmolality value observed (mOsm/kg)
Micafungin in 0.9% Sodium Chloride Injection (50 mg/50 mL and 150 mg/150 mL)[a]	302	308
MYCAMINE (50 mg/vial and 100 mg/vial)[b]	290	303

[a]12 months refrigerated at 5°C units plus 30 days room temperature, 25°C units.
[b]Reconstituted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C and further diluted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C.

[6] \\CDSESUB1\EVSPROD\nda216142\0001\m1\us\justification-bioequivalence-report-bxu582967.pdf

Table 9. Assay Results for Micafungin in 0.9% Sodium Chloride Injection and MYCAMINE

Article	mg/mL		% Label Claim	
	Minimum Assay value observed	Maximum Assay value observed	Minimum Assay value observed	Maximum Assay value observed
Micafungin in 0.9% Sodium Chloride Injection (50 mg/50 mL and 150 mg/150 mL)[a]	0.95	0.97	94.7	96.9
MYCAMINE (50 mg/vial and 100 mg/vial)[b]	1.02	1.10	101.5	110.1

[a]12 months refrigerated at 5°C units plus 30 days room temperature, 25°C units.
[b]Reconstituted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C and further diluted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C.

Table 10. Total Related Substances Results for Micafungin in 0.9% Sodium Chloride Injection and MYCAMINE

Article	% w/w	
	Minimum Assay value observed	Maximum Assay value observed
Micafungin in 0.9% Sodium Chloride Injection (50 mg/50 mL and 150 mg/150 mL)[a]	2.06	2.61
MYCAMINE (50 mg/vial and 100 mg/vial)[b]	2.12	2.73

[a]12 months refrigerated at 5°C units plus 30 days room temperature, 25°C units.
[b]Reconstituted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C and further diluted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C.

Table 11. Comparison of Highest Related Substance Levels Observed in Micafungin in 0.9% Sodium Chloride Injection and MYCAMINE

Related Substance	Largest Value Observed in Proposed Product Registration Stability Batches (% w/w)[a]	Largest Value Observed in Listed Drug MYCAMINE (% w/w)[b]
		(b) (4)

RRT = Relative Retention Time; NMT = Not More Than
[a]12 months refrigerated at 5°C units plus 30 days room temperature, 25°C units.
[b]Reconstituted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C and further diluted with 0.9% Sodium Chloride Injection and stored 24 hours at 25°C.

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	216142
Assessment Cycle Number	01
Drug Product Name/ Strength	MICAFUNGIN in 0.9% Sodium chloride injection/1 mg/mL (100 mL, 150 mL, 50 mL)
Route of Administration	IV infusion
Applicant Name	Baxter Healthcare Corp
Therapeutic Classification/ OND Division	CDER/OND/OID/DAI
Manufacturing Site	Baxter Healthcare Corporation FEI # 1416980 25212 W. Illinois Route 120 Round Lake, IL 60073, USA
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary: The drug product will be (b) (4) ***. Adequate information was provided to support the sterility assurance of the drug product for the intended shelf-life. This includes*** (b) (4)

List Submissions being assessed (table):

Document(s) Assessed	Date Received
0001 SD 1	**11/30/2022**
0003 SD 3	**01/31/2023**
0004 SD 4	**02/17/2023**

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: The drug product is a refrigerated, premixed, iso-osmotic, sterile, nonpyrogenic solution for intravenous infusion that comes in the following single-dose presentations: 50 mg/50 mL, 100 mg/100 mL, and 150 mg/150 mL in Galaxy (b) (4) containers.

Concise Description of Outstanding Issues: N/A

-

Supporting Documents:

- D (b) (4) M03R02.doc, (b) (4)
- D (b) (4) M07R01.docx, (b) (4)
- D (b) (4) M08R01.pdf, (b) (4)
- D (b) (4) M03R01.doc, (b) (4)
- D (b) (4) M10R01.docx, (b) (4)

S DRUG SUBSTANCE

The drug substance is not provided sterile. Therefore, a product quality microbiology review of the drug substance is not reviewed.

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

Section 3.2.P.1

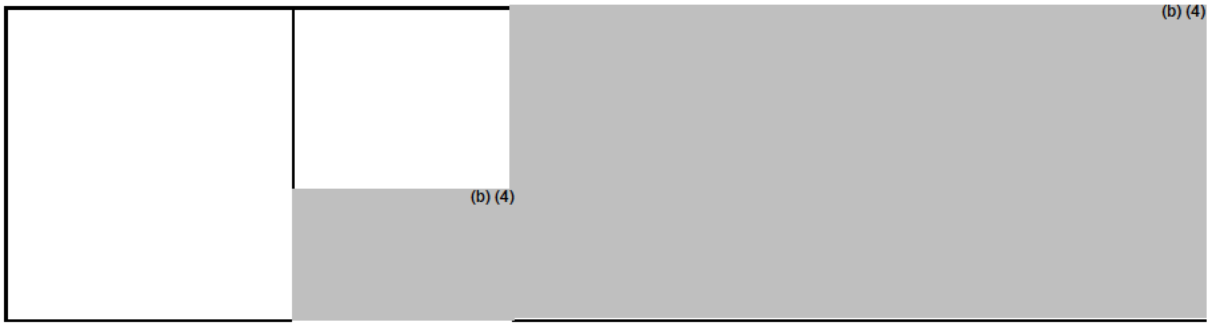
Description of drug product – pre-mixed, iso-osmotic, sterile, nonpyrogenic solution supplied in a flexible GALAXY plastic container (I.V. bag) and is intended for intravenous administration.

Drug product composition –

Ingredient	Quantity (mg per mL)	Function
Micafungin Sodium	1	API
Sodium Chloride, USP	9	(b) (4)
Citric Acid, Anhydrous USP	0.72	
Sodium Citrate, Dihydrate USP	1.84	
Water for Injection, USP	QS	

Description of container closure system – Section 3.2.P.7

Container	Component	Description	Manufacturer
Galaxy (b) (4) container (50 mL, 100 mL, and 200 mL)	(b) (4)	(b) (4)	The GALAXY plastic container is manufactured by Baxter's (b) (4)



The 50 mL, 100 mL, and 200 mL GALAXY containers have identical (b) (4) .

Assessment: Adequate
The applicant provided an adequate description of the drug product composition and container closure system.

Note to reviewer: DMF (b) (4) is referenced for the manufacturing process and controls of the (b) (4) .

P.2 PHARMACEUTICAL DEVELOPMENT

(b) (4)

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