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Add the following:

▲Micafungin for Injection

DEFINITION

Micafungin for Injection contains an amount of Micafungin Sodium equivalent to NLT 95% and NMT 115% of the labeled amount of micafungin ($C_{56}H_{71}N_9O_{23}S$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Conduct the entire procedure, without exposure to direct sunlight, using a light-resistant vessel.

Buffer: 18.7 g/L of sodium phosphate, monobasic, dihydrate and 7.7 g/L of sodium perchlorate in water. Adjust with 10% phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (450:700)

Diluent: Acetonitrile and water (3:7)

Standard solution: 0.5 mg/mL of USP Micafungin Sodium RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of micafungin from Micafungin for Injection in *Diluent* prepared as follows. Quantitatively transfer the contents of 1 vial of Micafungin for Injection using *Diluent* into a suitable volumetric flask to assure the final nominal concentration. Sonication may be needed. Dilute with *Diluent* to final volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 210 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of micafungin ($C_{56}H_{71}N_9O_{23}S$) in the portion of Micafungin for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of micafungin from the *Sample solution*

r_S = peak response of micafungin from the *Standard solution*

C_S = concentration of USP Micafungin Sodium RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of micafungin in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of micafungin, 1270.27

M_{r2} = molecular weight of micafungin sodium, 1292.27

Acceptance criteria: 95%–115%

IMPURITIES

• **Organic Impurities**

Conduct the entire procedure, without exposure to direct sunlight, using a light-resistant vessel.

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

Solution A: 35.8 g/L of sodium phosphate, dibasic, dodecahydrate

Solution B: 13.6 g/L of potassium phosphate, monobasic

Diluent: *Solution A* and *Solution B* (2:1); pH 7.0

System suitability solution: 4 mg/mL of USP Micafungin Sodium RS in *Diluent*

Sensitivity solution: 0.002 mg/mL of USP Micafungin Sodium RS in *Diluent*

Standard solution: 0.012 mg/mL of USP Micafungin Sodium RS in *Diluent*

Sample solution: Nominally 4 mg/mL of micafungin from Micafungin for Injection in *Diluent* prepared as follows. Quantitatively transfer the contents of 1 vial of Micafungin for Injection using *Diluent* into a suitable size volumetric flask to assure the final nominal concentration. Sonication may be needed.

Chromatographic system: Proceed as directed in the *Assay*, except for the *Injection volume*.

Injection volume: 2 µL

System suitability

Samples: *System suitability solution*, *Sensitivity solution*, and *Standard solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.2 between micafungin and micafungin epimer, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Micafungin for Injection taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of any individual impurity

r_T = sum of all the peak responses

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Micafungin open ring analog[a]	0.73	1.1
Desmethyl micafungin[b]	0.91	1.2
Micafungin serine analog[c]		
Micafungin	1.0	—
Micafungin epimer[d]	1.09	1.1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Deoxy micafungin[e]	1.12	0.5
Any individual unspecified impurity	—	0.3
Total impurities	—	4.5

[a] Sodium 5-[(1*S*,2*S*,3*S*)-4-({(2*S*,3*R*)-5-amino-1-[(2*S*,3*S*,4*S*)-2-carbamoyl-3-hydroxy-4-methylpyrrolidin-1-yl]-3-hydroxy-1,5-dioxopentan-2-yl}amino)-3-[(2*S*,4*R*)-1-{[(2*S*,4*R*)-4,5-dihydroxy-1-(4-{5-[4-(pentyloxy)phenyl]isoxazol-3-yl}benzoyl)pyrrolidine-2-carbonyl]-L-threonyl}-4-hydroxypyrrolidine-2-carboxamido]-1,2-dihydroxy-4-oxobutyl]-2-hydroxyphenyl sulfate.

[b] Sodium 5-[(1*S*,2*S*)-2-{(2*R*,6*S*,9*S*,11*R*,12*R*,14a*S*,15*S*,20*S*,23*S*,25a*S*)-20-[(*R*)-3-amino-1-hydroxy-3-oxopropyl]-2,11,12,15-tetrahydroxy-6-[(*R*)-1-hydroxyethyl]-5,8,14,19,22,25-hexaoxo-9-(4-{5-[4-(pentyloxy)phenyl]isoxazol-3-yl}benzamido)tetracosahydro-1*H*-dipyrrolo[2,1-*c*:2',1'-*l*][1,4,7,10,13,16]hexaazacyclohenicosin-23-yl}-1,2-dihydroxyethyl]-2-hydroxyphenyl sulfate.

[c] Sodium 5-[(1*S*,2*S*)-2-{(2*R*,6*S*,9*S*,11*R*,12*R*,14a*S*,15*S*,16*S*,20*S*,23*S*,25a*S*)-20-[(*R*)-3-amino-1-hydroxy-3-oxopropyl]-2,11,12,15-tetrahydroxy-6-(hydroxymethyl)-16-methyl-5,8,14,19,22,25-hexaoxo-9-(4-{5-[4-(pentyloxy)phenyl]isoxazol-3-yl}benzamido)tetracosahydro-1*H*-dipyrrolo[2,1-*c*:2',1'-*l*][1,4,7,10,13,16]hexaazacyclohenicosin-23-yl}-1,2-dihydroxyethyl]-2-hydroxyphenyl sulfate.

[d] Sodium 5-[(1*S*,2*S*)-2-{(2*R*,6*S*,9*S*,11*R*,12*S*,14a*S*,15*S*,16*S*,20*S*,23*S*,25a*S*)-20-[(*R*)-3-amino-1-hydroxy-3-oxopropyl]-2,11,12,15-tetrahydroxy-6-[(*R*)-1-hydroxyethyl]-16-methyl-5,8,14,19,22,25-hexaoxo-9-(4-{5-[4-(pentyloxy)phenyl]isoxazol-3-yl}benzamido)tetracosahydro-1*H*-dipyrrolo[2,1-*c*:2',1'-*l*][1,4,7,10,13,16]hexaazacyclohenicosin-23-yl}-1,2-dihydroxyethyl]-2-hydroxyphenyl sulfate.

[e] Sodium 5-[(1*S*,2*S*)-2-{(2*R*,6*S*,9*S*,12*R*,14a*S*,15*S*,16*S*,20*S*,23*S*,25a*S*)-20-[(*R*)-3-amino-1-hydroxy-3-oxopropyl]-2,12,15-trihydroxy-6-[(*R*)-1-hydroxyethyl]-16-methyl-5,8,14,19,22,25-hexaoxo-9-(4-{5-[4-(pentyloxy)phenyl]isoxazol-3-yl}benzamido)tetracosahydro-1*H*-dipyrrolo[2,1-*c*:2',1'-*l*][1,4,7,10,13,16]hexaazacyclohenicosin-23-yl}-1,2-dihydroxyethyl]-2-hydroxyphenyl sulfate.

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

SPECIFIC TESTS

• **pH ⟨791⟩**
Sample: 10–20 mg/mL
Acceptance criteria: 5.0–7.0

• **Particulate Matter in Injections ⟨788⟩, *Method 1 Light Obscuration Particle Count Test***
Sample: 1 container when tested as directed
Acceptance criteria: Meets the requirements

• **Bacterial Endotoxins Test ⟨85⟩:** Meets the requirements

• **Sterility Tests ⟨71⟩, *Test for Sterility of the Product to Be Examined, Membrane Filtration*:** Meets the requirements

• **Constituted Solution:** At the time of use, it meets the requirements of *Injections and Implanted Drug Products ⟨1⟩, Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and Clarity of Solutions*.

• **Other Requirements:** It meets the requirements for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*. Store at controlled room temperature. Protect from light.

• **USP Reference Standards ⟨11⟩**
USP Micafungin Sodium RS▲ (USP 1-Aug-2023)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MICAFUNGIN FOR INJECTION	Documentary Standards Support	SM12020 Small Molecules 1

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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