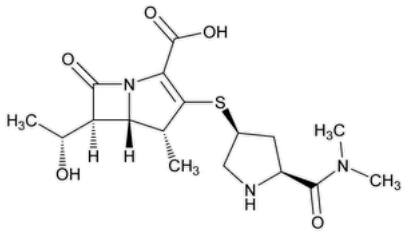
Status: Currently Official on 18-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-0259111D-8037-40AB-8F89-CC5DB2AF07E4_5_en-US
DOI: https://doi.org/10.31003/USPNF_M49434_05_01
DOI Ref: f7q1u

Meropenem

Change to read:



• 3 H_2O

$C_{17}H_{25}N_3O_5S \cdot 3H_2O$ 437.51

$C_{17}H_{25}N_3O_5S$ ▲383.46▲ (USP 1-Dec-2019)

1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[5-[(dimethylamino)carbonyl]-3-pyrrolidinyl]thio]-6-(1-hydroxyethyl)-4-methyl-7-oxo, trihydrate, [4*R*-[3(3*S**,5*S**),4α,5β,6β(*R**)]]-;
(4*R*,5*S*,6*S*)-3-{[(3*S*,5*S*)-5-(Dimethylcarbamoyl)pyrrolidin-3-yl]thio}-6-[(1*R*)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, trihydrate CAS RN®: 119478-56-7; UNII: FV9J3JU8B1.
Anhydrous CAS RN®: 96036-03-2; UNII: YOP6PX0BAO.

DEFINITION

Meropenem contains NLT 98.0% and NMT 101.0% of meropenem ($C_{17}H_{25}N_3O_5S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

Change to read:

• **B.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2019)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** Dilute 15 mL of tetrabutylammonium hydroxide solution (25% in methanol) with water to 750 mL. Adjust with 10% phosphoric acid TS to a pH of 7.5 ± 0.1.

Mobile phase: Acetonitrile, methanol, and *Solution A* (150:100:750)

Standard solution: 0.1 mg/mL of USP Meropenem RS in *Mobile phase*. Immediately after preparation, store this solution in a refrigerator, and use within 24 h.

Sample solution: 0.1 mg/mL of Meropenem in *Mobile phase*. Immediately after preparation, store this solution in a refrigerator, and use within 8 h.

Chromatographic system

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

Mode: LC

Detector: UV 300 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of meropenem ($C_{17}H_{25}N_3O_5S$) in the portion of Meropenem taken:

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

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

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

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

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

P = designated potency of USP Meropenem RS (mg/mg)

▲ (USP 1-Dec-2019)

Acceptance criteria: 98.0%–101.0% on the anhydrous basis

IMPURITIES

Change to read:

• **Residue on Ignition ⟨281⟩**

Analysis: Ignite at 500 ± 50° ▲▲ (USP 1-Dec-2019)

Acceptance criteria: NMT 0.1%

Change to read:

• **Organic Impurities**

Solution A: Mix 1.0 mL of triethylamine and 900 mL of water. Adjust with 10% phosphoric acid TS to a pH of 5.0 ± 0.1, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Solution A* (70:1000)

▲**Peak identification solution:** 5 mg/mL of USP Meropenem RS in *Mobile phase*. Use this solution between 1 and 24 h from preparation.▲ (USP 1-Dec-2019)

Standard solution: 0.025 mg/mL of USP Meropenem RS in *Solution A*

▲Store this solution in a refrigerator and use within 24 h.▲ (USP 1-Dec-2019)

Sample solution: 5 mg/mL of Meropenem in *Solution A*. Use this *Sample solution* immediately.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Column temperature: 40°

Flow rate: 1.6 mL/min

▲▲ (USP 1-Dec-2019)

Injection volume: 10 µL

Run time: NLT 3 times the retention time of meropenem

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-Dec-2019)

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: ▲*Peak identification solution*, *Standard solution*, and *Sample solution*

Chromatograph the *Peak identification solution* and identify the components on the basis of their relative retention times, as shown in *Table 1*.▲ (USP 1-Dec-2019)

Calculate the percentage of each individual impurity in the portion of Meropenem taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \text{▲} \times 100 \text{▲ (USP 1-Dec-2019)}$$

r_U = peak response of any individual impurity from the *Sample solution*

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

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

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

P = ▲potency of meropenem in USP Meropenem RS (mg/mg)▲ (USP 1-Dec-2019)

Acceptance criteria: ▲See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Meropenem open ring[a]	0.45	0.3
Meropenem	1.0	—
Meropenem dimer[b]	1.9	0.3
Any individual unspecified impurity	—	0.05
Total impurities, excluding meropenem open ring and meropenem dimer	—	0.3

[a] (4*R*,5*S*)-5-[(1*S*,2*R*)-1-Carboxy-2-hydroxypropyl]-3-{[(3*S*,5*S*)-5-(dimethylcarbamoyl)pyrrolidin-3-yl]thio}-4-methyl-4,5-dihydro-1*H*-pyrrole-2-carboxylic acid.

[b] (4*R*,5*S*,6*S*)-3-{[(3*S*,5*S*)-1-{(2*S*,3*R*)-2-[(2*S*,3*R*)-5-Carboxy-4-{[(3*S*,5*S*)-5-(dimethylcarbamoyl)pyrrolidin-3-yl]thio}-3-methyl-2,3-dihydro-1*H*-pyrrol-2-yl]-3-hydroxybutanoyl}-5-(dimethylcarbamoyl)pyrrolidin-3-yl]thio}-6-[(*R*)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid.

▲ (USP 1-Dec-2019)

Delete the following:

▲• **Limit of Acetone**

Internal standard solution: 0.05 µL/mL of ethyl acetate in dimethylformamide

Standard stock solution: 0.5 mg/mL of acetone in dimethylformamide

Standard solution: Combine 1.0 mL of *Standard stock solution* and 10.0 mL of *Internal standard solution*.

Sample solution: Dissolve 100 mg of Meropenem in 0.2 mL of dimethylformamide and 2.0 mL of *Internal standard solution*.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 3-mm × 2-m column; support S2

Temperature

Column: 150°

Injection port: 170°

Carrier gas: Nitrogen

Flow rate: Adjusted so that the retention time for acetone is about 3 min

Injection volume: 2 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acetone in the portion of Meropenem taken:

$$\text{Result} = (W_A/5 \times W_U) \times (r_U/r_S)$$

W_A = weight of acetone in the *Standard solution* (mg)

W_U = weight of Meropenem in the *Sample solution* (mg)

r_U = peak area ratio of acetone to the internal standard from the *Sample solution*

r_S = peak area ratio of acetone to the internal standard from the *Standard solution*

Acceptance criteria: NMT 0.05%▲ (USP 1-Dec-2019)

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Meropenem is sterile or that it must be subjected to further processing during the preparation of injectable dosage forms, ▲the level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Meropenem is used can be met.▲ (USP 1-Dec-2019)

• **Optical Rotation ⟨781S⟩**, *Procedures, Specific Rotation*

Sample solution: 5 mg/mL in water

Acceptance criteria: −17° to −21°, at 20°

Change to read:

• **pH ⟨791⟩**

Sample solution: ▲10 mg/mL in water▲ (USP 1-Dec-2019)

Acceptance criteria: 4.0–6.0

Change to read:

• **Sterility Tests ⟨71⟩:** ▲Where the label states that Meropenem is sterile or that it must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements.▲ (USP 1-Dec-2019)

Change to read:

• **Water Determination ⟨921⟩**, *Method I*, ▲*Method Ia*▲ (USP 1-Dec-2019), or *Method Ic*: 11.4%–13.4%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store the dry powder at controlled room temperature.

Change to read:

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms, ▲it is so labeled. Where Meropenem must be subjected to further processing during the preparation of injectable dosage forms to ensure acceptable levels of bacterial endotoxins, it is so labeled.▲ (USP 1-Dec-2019)

• **USP Reference Standards ⟨11⟩**

USP Meropenem RS

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(4)

Current DocID: GUID-0259111D-8037-40AB-8F89-CC5DB2AF07E4_5_en-US

DOI: https://doi.org/10.31003/USPNF_M49434_05_01

DOI ref: f7q1u