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Meropenem for Injection

DEFINITION

Meropenem for Injection is a sterile dry mixture of Meropenem and Sodium Carbonate. It contains NLT 90.0% and NMT 120.0% of the labeled amount of meropenem ($C_{17}H_{25}N_3O_5S$).

IDENTIFICATION

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

ASSAY

Change to read:

- **Procedure**

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

Mobile phase: Acetonitrile, methanol, and ▲*Buffer*▲ (ERR 1-Feb-2020) (150:100:750)

Standard solution: 0.11 mg/mL of USP Meropenem RS in *Mobile phase*. Immediately after preparation, store this solution in a refrigerator, and use within 24 h.

Sample stock solution 1 (where it is represented as being a single-dose container)**:** Nominally 1 mg/mL of meropenem, prepared as follows. Constitute a container of Meropenem for Injection with a volume of water, corresponding to the quantity of solvent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and transfer to a suitable volumetric flask. Dilute with water to volume, and mix.

Sample solution 1: Nominally 0.1 mg/mL of meropenem in *Mobile phase* from *Sample stock solution 1*. Hold this *Sample solution 1* for 2 h at 25 ± 1° before testing.

Sample stock solution 2 (where the label states the quantity of meropenem in a given volume of constituted solution)**:** Nominally 1 mg/mL of meropenem, prepared as follows. Constitute a container of Meropenem for Injection with a volume of water corresponding to the quantity of solvent specified in the labeling, and dilute with water.

Sample solution 2: Nominally 0.1 mg/mL of meropenem in *Mobile phase* from *Sample stock solution 2*. Hold this *Sample solution 2* for 2 h at 25 ± 1° before testing.

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 2.0%

Analysis

Samples: *Standard solution* and *Sample solution 1* or *Sample solution 2*

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

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

r_U = peak response of meropenem from *Sample solution 1* or *Sample solution 2*

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 = nominal concentration of meropenem in *Sample solution 1* or *Sample solution 2* (mg/mL)

P = potency of meropenem in USP Meropenem RS (mg/mg)

Acceptance criteria: 90.0%–120.0%

OTHER COMPONENTS

• **Content of Sodium**

Solution A: 38.1 g/L of potassium chloride in water

Standard stock solution: 25.42 µg/mL of sodium chloride (previously dried at 105° for 2 h) in water

Standard solution: 2.5 µg/mL of sodium chloride from the *Standard stock solution* mixed first with *Solution A* to 10% of the final volume and diluted with water to volume

Sample stock solution 1 (where it is represented as being a single-dose container)**:** Nominally 0.125 mg/mL of meropenem, prepared as follows. Constitute a container of Meropenem for Injection with a volume of water corresponding to the quantity of solvent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and transfer to a suitable volumetric flask. Dilute with water to volume.

Sample stock solution 2 (where the label states the quantity of meropenem in a given volume of constituted solution)**:** Nominally 0.125 mg/mL of meropenem, prepared as follows. Constitute a container of Meropenem for Injection with a volume of water, corresponding to the quantity of solvent specified in the labeling. Transfer the constituted solution to a suitable volumetric flask, and dilute with water to volume.

Sample solution: Nominally 0.0125 mg/mL of meropenem from *Sample stock solution 1* or *Sample stock solution 2* mixed first with *Solution A* to 10% of the final volume, and dilute with water to volume

Blank: *Solution A* and water (1:10)

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption spectroscopy

Analytical wavelength: 589.6 nm sodium emission line

Burner: Single-slot

Flame: Air–acetylene

Lamp: Sodium hollow-cathode

Analysis

Samples: *Standard solution, Sample solution,* and *Blank*

Calculate the percentage of sodium (Na) in the portion of Meropenem for Injection taken:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of sodium chloride in the *Standard solution* (µg/mL)

C_U = nominal concentration of meropenem in the *Sample solution* (µg/mL)

M_{r1} = atomic weight of sodium, 22.99

M_{r2} = molecular weight of sodium chloride, 58.44

Acceptance criteria: 80%–120% of the labeled amount of sodium

PERFORMANCE TESTS

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

IMPURITIES

• **Organic Impurities**

Buffer: 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 *Buffer* (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.

Standard solution: 0.029 mg/mL of USP Meropenem RS in *Buffer*. Store this solution in a refrigerator immediately after preparation, and use within 24 h.

Sample solution: Nominally prepare 5 mg/mL of meropenem in *Buffer* from Meropenem for Injection. This solution has to be prepared fresh and used 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

Injection volume: 10 µL

Run time: NLT 3 times the retention time of meropenem

System suitability

Sample: *Standard solution*

Suitability requirements

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*.

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

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

r_U = peak response of each 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 = nominal concentration of meropenem in the *Sample solution* (mg/mL)

P = potency of meropenem in USP Meropenem RS (mg/mg)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Meropenem open ring[a]	0.45	0.8
Meropenem	1.0	—
Meropenem dimer[b]	1.9	0.6
Any individual unspecified impurity	—	0.10
Total unspecified impurities	—	1.0
Total impurities	—	2.0

[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.

SPECIFIC TESTS

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

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

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 65° for 6 h.

Acceptance criteria: 9.0%–12.0%

- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **pH ⟨791⟩**

  Sample solution: 50 mg/mL

  Acceptance criteria: 7.3–8.3
- **Sterility Tests ⟨71⟩:** Meets the requirements

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*. Store at controlled room temperature.
- **Labeling:** Meets the requirements for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*. Label it to state the quantity, in mg, of sodium (Na) in a given dosage of meropenem.
- **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 FOR INJECTION	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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