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Piperacillin for Injection

DEFINITION

Piperacillin for Injection contains an amount of Piperacillin Sodium equivalent to NLT 90.0% and NMT 120.0% of the labeled amount of piperacillin ($C_{23}H_{27}N_5O_7S$).

IDENTIFICATION

Change to read:

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

Sample: Dissolve 250 mg in water. Add 0.5 mL of 2 N hydrochloric acid and 5 mL of ethyl acetate. Stir, and allow to stand for 10 min in ice water. Pass through a suitable sintered-glass filter, applying suction. Wash the crystals with 5 mL of water and 5 mL of ethyl acetate, then dry in an oven at 60° for 60 min.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Methanol, 0.2 M monobasic sodium phosphate, 0.4 M tetrabutylammonium hydroxide, and water (450:100:3:447). Adjust with phosphoric acid to a pH of 5.50.

System suitability solution: 0.1 mg/mL of USP Ampicillin RS and 0.2 mg/mL of USP Piperacillin RS in *Mobile phase*

Standard solution: 0.4 mg/mL of USP Piperacillin RS in *Mobile phase*. Dissolve in a few drops of methanol, and dilute with *Mobile phase* to volume. Use this solution within 1 h.

Sample solution 1 (where it is labeled for use as a single-dose container)**:** Equivalent to 0.4 mg/mL of piperacillin from Piperacillin for Injection constituted as directed below.

Constitute Piperacillin for Injection in a volume of water corresponding to the volume of solvent specified in the labeling. Withdraw all of the withdrawable contents using a suitable hypodermic needle and syringe, and dilute with *Mobile phase*.

Sample solution 2 (where the label states the quantity of piperacillin in a given volume of the constituted solution)**:** Equivalent to 0.4 mg/mL of piperacillin from Piperacillin for Injection constituted as directed below.

Constitute Piperacillin for Injection in a volume of water corresponding to the volume of solvent specified in the labeling. Dilute an aliquot of the constituted solution with *Mobile phase*.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

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

Suitability requirements

Resolution: NLT 16 between ampicillin and piperacillin, *System suitability solution*

Tailing factor: NMT 1.2 for the piperacillin peak, *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution*

Analysis

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

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Calculate the percentage of the labeled amount of piperacillin ($C_{23}H_{27}N_5O_7S$) in the container or in the portion of constituted solution taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

P = potency of piperacillin in USP Piperacillin RS (µg/mg)

F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS

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

IMPURITIES

• **Organic Impurities**

Mobile phase, System suitability solution, Sample solution 1, Sample solution 2, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*. Evaluate the *Relative standard deviation* using the *Standard solution* prepared in the *Assay*.

Standard solution: 40 µg/mL of USP Piperacillin RS in *Mobile phase*. Dissolve in a few drops of methanol, and dilute with *Mobile phase* to volume. Use this solution within 1 h.

Analysis

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

Calculate the percentage of piperacillin penicilloic acid and acetylated penicilloic acid of piperacillin in the portion of Piperacillin for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times (1/F_1) \times F_2 \times 100$$

r_U = peak response of piperacillin penicilloic acid or acetylated penicilloic acid of piperacillin from *Sample solution 1* or *Sample solution 2*

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

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

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

P = potency of piperacillin in USP Piperacillin RS (µg/mg)

F_1 = relative response factor (see *Table 1*)

F_2 = conversion factor, 0.001 mg/µg

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Piperacillin related compound E[a,b]	0.24	—	—
Ampicillin[a]	0.31	—	—

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Acetylated penicilloic acid of piperacillin[c]	0.37	1.1	1.0
Piperacillin penicilloic acid[d]	0.62	0.7	3.5
Piperacillin	1.0	—	—

[a] These are process impurities that are listed here for information only; they are controlled in the drug substance and are not to be reported.

[b] 1-Ethyl-2,3-piperazinedione.

[c] (2*R*,4*S*)-3-Acetyl-2-{(1*R*)-carboxy[2-(4-ethyl-2,3-dioxopiperazine-1-carboxamido)-2-phenylacetamido]methyl}-5,5-dimethylthiazolidine-4-carboxylic acid.

[d] (2*R*,4*S*)-2-{(1*R*)-Carboxy[2-(4-ethyl-2,3-dioxopiperazine-1-carboxamido)-2-phenylacetamido]methyl}-5,5-dimethylthiazolidine-4-carboxylic acid.

SPECIFIC TESTS

• **Constituted Solution:** At the time of use, it meets the requirements in *Injections and Implanted Drug Products ⟨1⟩, Specific Tests, Completeness and clarity of solutions*.

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.07 USP Endotoxin Unit/mg of piperacillin.

• **Sterility Tests ⟨71⟩:** It meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

• **pH ⟨791⟩:** 4.8–6.8, in a solution of 200 mg/mL of piperacillin

• **Water Determination, *Method I* ⟨921⟩:** NMT 0.9%

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

• **Other Requirements:** It meets the requirements in *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*.

• **USP Reference Standards ⟨11⟩**

USP Ampicillin RS

USP Piperacillin RS

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

Topic/Question	Contact	Expert Committee
PIPERACILLIN FOR INJECTION	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

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