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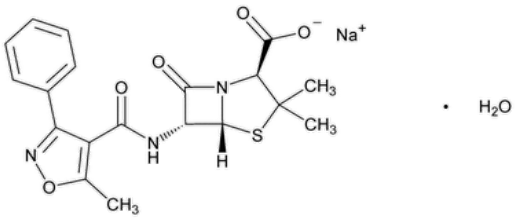
Oxacillin Sodium



$C_{19}H_{18}N_3NaO_5S \cdot H_2O$ 441.43

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-6-[[(5-methyl-3-phenyl-4-isoxazolyl)-carbonyl]amino]-7-oxo-, monosodium salt, monohydrate, [2*S*-(2α,5α,6β)]-;

Monosodium (2*S*,5*R*,6*R*)-3,3-dimethyl-6-(5-methyl-3-phenyl-4-isoxazolecarboxamido)-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate CAS RN®: 7240-38-2; UNII: G0V6C994Q5.

Anhydrous

$C_{19}H_{18}N_3NaO_5S$ 423.43 CAS RN®: 1173-88-2; UNII: 4TWD2995UP.

DEFINITION

Oxacillin Sodium contains the equivalent of NLT 815 µg/mg and NMT 950 µg/mg of oxacillin ($C_{19}H_{19}N_3O_5S$).

IDENTIFICATION

Change to read:

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

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

• **C.** **Identification Tests—General ⟨191⟩, *Sodium*:** Meets the requirements

ASSAY

• **Procedure**

Protect solutions containing oxacillin from light.

Solution A: 1.18 g/L of sodium 1-hexanesulfonate monohydrate and 0.8 mL/L of ammonium hydroxide in water, adjusted with phosphoric acid to a pH of 2.8–3.2

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20	30	70

Return to the original conditions and re-equilibrate the system.

Diluent: Acetonitrile and water (15:85)

System suitability stock solution: 0.1 mg/mL of USP Oxacillin Related Compound C RS in *Diluent*. Sonicate as needed to dissolve.

System suitability solution: 0.01 mg/mL of USP Oxacillin Related Compound C RS from *System suitability stock solution* and 1 mg/mL of USP Oxacillin Sodium RS in *Diluent*. Store this solution at 4°.

Standard solution: 1 mg/mL of USP Oxacillin Sodium RS in *Diluent*. Sonicate as needed to dissolve. Store this solution at 4°.

Sample solution: 1 mg/mL of Oxacillin Sodium in *Diluent*. Sonicate as needed to dissolve. Store this solution at 4°.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

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

Temperatures

Column: 40°

Autosampler: 4°

Flow rate: 1.5 mL/min

Injection volume: 2 µL

System suitability

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

[NOTE—The relative retention times for oxacillin related compound C and oxacillin are about 0.96 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between oxacillin related compound C and oxacillin, *System suitability solution*

Tailing factor: 0.8–1.5, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg/mg, of oxacillin ($C_{19}H_{19}N_3O_5S$) in the portion of Oxacillin Sodium taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

P = potency of oxacillin in USP Oxacillin Sodium RS (µg/mg)

Acceptance criteria: 815–950 µg/mg

IMPURITIES

• **ORGANIC IMPURITIES**

Protect solutions containing oxacillin from light.

Solution A: 6 g/L of anhydrous monobasic sodium phosphate, 0.56 g/L of sodium 1-hexanesulfonate monohydrate, and 0.05 g/L of edetate disodium. Adjust with phosphoric acid to a pH of 3.0–3.2.

Solution B: Acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	90	10
3	90	10
30	50	50
40	15	85
45	15	85

Return to the original conditions and re-equilibrate the system.

Diluent: Acetonitrile and water (15:85)

System suitability stock solution: 0.1 mg/mL of USP Oxacillin Related Compound C RS in *Diluent*. Do not sonicate.

System suitability solution: 0.01 mg/mL of USP Oxacillin Related Compound C RS from *System suitability stock solution* and 1 mg/mL of USP Oxacillin Sodium RS in *Diluent*. Store this solution at 4°.

Standard solution: 0.01 mg/mL of USP Oxacillin Sodium RS in *Diluent*. Do not sonicate. Store this solution at 4°.

Sample solution: 1 mg/mL of Oxacillin Sodium in *Diluent*. Do not sonicate. Store this solution at 4°.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

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

Temperatures

Column: 22°

Autosampler: 4°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between oxacillin related compound C and oxacillin, *System suitability solution*

Tailing factor: 0.8–1.5, *Standard solution*

Relative standard deviation: NMT 2.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Oxacillin Sodium taken:

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

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

P = potency of oxacillin in USP Oxacillin Sodium RS (µg/mg)

F_1 = conversion factor, 0.001 mg/µg

F_2 = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Amoxicillin related compound A[a]	0.08	0.22	0.5
Oxacillin penicilloic acid[b,c]	0.66	0.40	1.5
	0.69		

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Imidazothiazole analog[d]	0.68	1.0	0.5
Oxacillin penilloic acid[c,e]	0.83 0.84	0.79	0.5
Thiooxacillin[f]	0.93	1.0	0.5
Oxacillin related compound C[g]	0.97	2.0	0.5
Oxacillin	1.0	—	—
Cloxacillin	1.09	1.0	1.0
Cloxacillin isomers[h]	1.17	1.0	0.5
N-(Penicillan-6-yl) oxacillinamide[i]	1.19	1.0	0.5
N-(Penicillan-6-yl) open ring oxacillinamide[j]	1.31	1.0	0.5
Any individual unspecified impurity	—	1.0	0.2
Total impurities	—	—	3.0

[a] 6-Aminopenicillanic acid; (2*S*,5*R*,6*R*)-6-Amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

[b] (4*S*)-2-[Carboxy(5-methyl-3-phenylisoxazole-4-carboxamido)methyl]-5,5-dimethylthiazolidine-4-carboxylic acid.

[c] The system resolves two isomers. The limit is for the sum of the isomers.

[d] (3*S*,7*R*)-2,2-Dimethyl-5-(5-methyl-3-phenylisoxazol-4-yl)-2,3,7,7a-tetrahydroimidazo[5,1-*b*]thiazole-3,7-dicarboxylic acid.

[e] (4*S*)-5,5-Dimethyl-2-[(5-methyl-3-phenylisoxazole-4-carboxamido)methyl]thiazolidine-4-carboxylic acid.

[f] (2*R*,5*R*,6*R*)-3,3-Dimethyl-6-(5-methyl-3-phenylisoxazole-4-carboxamido)-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carbothioic acid.

[g] Isoxazole carboxylic analog; 5-Methyl-3-phenylisoxazole-4-carboxylic acid.

[h] (2*S*,5*R*,6*R*)-6-[3-(Chlorophenyl)-5-methylisoxazole-4-carboxamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

[i] (2*S*,5*R*,6*R*)-6-{(2*S*,5*R*,6*R*)-3,3-Dimethyl-6-(5-methyl-3-phenylisoxazole-4-carboxamido)-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxamido}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

[j] (2*S*,5*R*,6*R*)-6-{(*R*)-2-[(2*R*,4*S*)-4-Carboxy-5,5-dimethylthiazolidin-2-yl]-2-(5-methyl-3-phenylisoxazole-4-carboxamido)acetamido}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid.

SPECIFIC TESTS

- **Crystallinity ⟨695⟩:** Meets the requirements
- **pH ⟨791⟩**

  Sample solution: 30 mg/mL

  Acceptance criteria: 4.5–7.5
- **Water Determination, *Method I*⟨921⟩:** 3.5%–5.0%
- **Sterility Tests ⟨71⟩:** Where the label states that Oxacillin Sodium is sterile, it meets the requirements.

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Oxacillin Sodium is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 0.2 USP Endotoxin Units/mg of oxacillin.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, at controlled room temperature.

• **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.

• **USP Reference Standards ⟨11⟩**

USP Oxacillin Related Compound C RS

Isoxazole carboxylic analog;
5-Methyl-3-phenylisoxazole-4-carboxylic acid.
$C_{11}H_9NO_3$ 203.20

USP Oxacillin Sodium RS

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

Topic/Question	Contact	Expert Committee
OXACILLIN SODIUM	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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