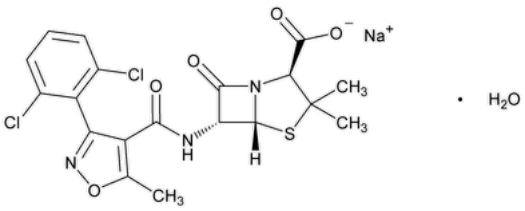
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-8A9D3C85-D755-4D30-9F54-3C87EE828E6F_2_en-US
DOI: https://doi.org/10.31003/USPNF_M24980_02_01
DOI Ref: 7mx0h

Dicloxacillin Sodium



$C_{19}H_{16}Cl_2N_3NaO_5S \cdot H_2O$ 510.32

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

Monosodium (2*S*,5*R*,6*R*)-6-[3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarboxamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate CAS RN®: 13412-64-1; UNII: 4HZT2V9KX0.

Anhydrous

$C_{19}H_{16}Cl_2N_3NaO_5S$ 492.30 CAS RN®: 343-55-5; UNII: 4CKS6MOL6Z.

DEFINITION

Dicloxacillin Sodium contains the equivalent of NLT 850 µg/mg of dicloxacillin ($C_{19}H_{17}Cl_2N_3O_5S$).

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*

Analysis: Ignite about 100 mg. Proceed as directed in the chapter using a solution (1 in 20) of the residue in acetic acid.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Protect solutions containing dicloxacillin 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 2.9–3.1

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	45	55
2	45	55
2.5	35	65
5	35	65

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

Diluent: Acetonitrile and water (50:50)

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

System suitability solution: 0.001 mg/mL of USP Dicloxacillin Related Compound D RS from the *System suitability stock solution* and 0.1 mg/mL of USP Dicloxacillin Sodium RS in *Diluent*. Store this solution at 4°.

Standard solution: 0.1 mg/mL of USP Dicloxacillin Sodium RS in *Diluent*. Sonicate as needed to dissolve. Store this solution at 4°.

Sample solution: 0.1 mg/mL of Dicloxacillin 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

Autosampler: 4°

Column: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

[NOTE—The relative retention times for dicloxacillin and dicloxacillin related compound D are about 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between dicloxacillin and dicloxacillin related compound D, *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 dicloxacillin ($C_{19}H_{17}Cl_2N_3O_5S$) in the portion of Dicloxacillin 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 Dicloxacillin Sodium RS in the *Standard solution* (mg/mL)

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

P = potency of dicloxacillin in USP Dicloxacillin Sodium RS (µg/mg)

Acceptance criteria: NLT 850 µg/mg

IMPURITIES

• **ORGANIC IMPURITIES**

Protect solutions containing dicloxacillin from light.

Solution A, Solution B, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	70	30
10	70	30
30	50	50
35	35	65
45	25	75

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

System suitability stock solution: 0.1 mg/mL of USP Dicloxacillin Related Compound D RS in *Diluent*

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

Standard solution: 0.01 mg/mL of USP Dicloxacillin Sodium RS in *Diluent*. Sonicate as needed to dissolve. Store this solution at 4°.

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

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between dicloxacillin related compound D and dicloxacillin, *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 Dicloxacillin 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 Dicloxacillin Sodium RS in the *Standard solution* (mg/mL)

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

P = potency of dicloxacillin in USP Dicloxacillin Sodium RS (µg/mg)

F_1 = conversion factor, 0.001 mg/µg

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

Acceptance criteria

Individual impurities: NMT 1.0%

Total impurities: NMT 5.0%

See *Table 3* for relative retention times and relative response factors. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor
Amoxicillin related compound A[a]	0.07	0.20
Dicloxacillin penicilloic acid[b,c]	0.23	1.0
	0.25	
Dicloxacillin glycine analog[d]	0.38	1.0
Dicloxacillin *N*-acetyl penicilloic acid[e]	0.43	1.0
Dicloxacillin penilloic acid[b,f]	0.61	0.75
	0.69	
Dicloxacillin related compound D[g]	0.90	1.4
Dicloxacillin	1.0	—
Dicloxacillin penicillamide[h]	1.3	1.0

[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] The system resolves two isomers.

[c] (4*S*)-2-{Carboxy[3-(2,6-dichlorophenyl)-5-methylisoxazole-4-carboxamido]methyl}-5,5-dimethylthiazolidine-4-carboxylic acid.

[d] [3-(2,6-Dichlorophenyl)-5-methylisoxazole-4-carbonyl]glycine.

[e] (2*R*,4*S*)-3-Acetyl-2-{(*R*)-carboxy[3-(2,6-dichlorophenyl)-5-methylisoxazole-4-carboxamido]methyl}-5,5-dimethylthiazolidine-4-carboxylic acid.

[f] (4*S*)-2-{[3-(2,6-Dichlorophenyl)-5-methylisoxazole-4-carboxamido]methyl}-5,5-dimethylthiazolidine-4-carboxylic acid.

[g] 3-(2,6-Dichlorophenyl)-5-methylisoxazole-4-carboxylic acid.

[h] (2*S*,5*R*,6*R*)-6-{(2*S*,5*R*,6*R*)-6-[3-(2,6-Dichlorophenyl)-5-methylisoxazole-4-carboxamido]-3,3-dimethyl-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.

- **Dimethylaniline ⟨223⟩:** Meets the requirements

SPECIFIC TESTS

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

  Sample solution: 10 mg/mL in water

  Acceptance criteria: 4.5–7.5
- **Water Determination ⟨921⟩, *Method I*:** 3.0%–5.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards ⟨11⟩**

  USP Dicloxacillin Sodium RS

  USP Dicloxacillin Related Compound D RS

  3-(2,6-Dichlorophenyl)-5-methylisoxazole-4-carboxylic acid.

  $C_{11}H_7Cl_2NO_3$ 272.08

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

Topic/Question	Contact	Expert Committee
DICLOXACILLIN SODIUM	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(6)

Current DocID: GUID-8A9D3C85-D755-4D30-9F54-3C87EE828E6F_2_en-US

DOI: https://doi.org/10.31003/USPNF_M24980_02_01

DOI ref: 7mx0h