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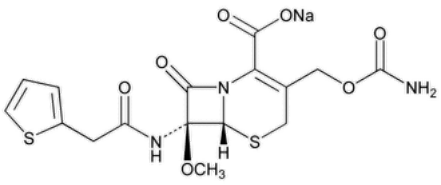
Cefoxitin Sodium



$C_{16}H_{16}N_3NaO_7S_2$ 449.43

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[(aminocarbonyl)oxy]methyl]-7-methoxy-8-oxo-7-[(2-thienylacetyl)amino]-, sodium salt (6*R-cis*)-;

Sodium (6*R*,7*S*)-3-(hydroxymethyl)-7-methoxy-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate carbamate (ester) CAS RN®: 33564-30-6; UNII: Q68050H03T.

DEFINITION

Cefoxitin Sodium contains the equivalent of NLT 927 µg/mg and NMT 970 µg/mg of cefoxitin ($C_{16}H_{17}N_3O_7S_2$), corresponding to NLT 97.5% and NMT 102.0% of cefoxitin sodium ($C_{16}H_{16}N_3NaO_7S_2$), calculated on the anhydrous and acetone- and methanol-free basis.

IDENTIFICATION

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

Change to read:

• **B.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Buffer: 1.0 g/L of monobasic potassium phosphate and 1.8 g/L of anhydrous dibasic sodium phosphate in water

Sample solution: 20 µg/mL in *Buffer*

Acceptance criteria: Meets the requirements

• **C.** **Identification Tests—General, *Sodium*⟨191⟩**

Sample solution: 50 mg/mL

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Buffer: Dissolve 1.0 g of monobasic potassium phosphate and 1.8 g of dibasic sodium phosphate in 900 mL of water. Adjust with phosphoric acid or 10 N sodium hydroxide to a pH of 7.1 ± 0.1, and dilute with water to 1 L. Pass through a membrane filter of 1-µm or finer pore size.

Mobile phase: Acetonitrile, water, and glacial acetic acid (160:840:10). Pass through a membrane filter of 1-µm or finer pore size.

Standard solution: 0.3 mg/mL of USP Cefoxitin RS in *Buffer*. Sonicate, if necessary, to dissolve. Use this solution within 5 h.

Sample solution: 0.3 mg/mL of Cefoxitin Sodium in *Buffer*. Use this solution within 5 h.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 5- to 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2800 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg/mg, of cefoxitin ($C_{16}H_{17}N_3O_7S_2$) in the portion of Cefoxitin Sodium taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

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

P = potency of cefoxitin in USP Cefoxitin RS (mg/mg)

F = conversion factor, 1000 µg/mg

Acceptance criteria: 927–970 µg/mg of cefoxitin, corresponding to NLT 97.5% and NMT 102.0% of cefoxitin sodium, on the anhydrous and acetone- and methanol-free basis

IMPURITIES

• **Limit of Acetone and Methanol**

Standard stock solution 1: 0.5% v/v of acetone in water

Standard stock solution 2: 0.5% v/v of methanol in water

Standard solution: 0.050% v/v of acetone from *Standard stock solution 1* and 0.005% v/v of methanol from *Standard stock solution 2* in water

Sample solution: Transfer 5.0 g of Cefoxitin Sodium to a 50-mL volumetric flask, and dissolve in and dilute with water to volume. Transfer 3.0 mL of the resulting solution to a 15-mL centrifuge tube, cool in an ice-water bath for 2 min, and add 3.0 mL of 0.24 N hydrochloric acid while swirling vigorously. Centrifuge to obtain a clear solution.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Columns

Precolumn: Packed with 60- to 80-mesh silane-treated glass beads

Analytical: 6.3-mm × 1.8-m glass; support S2

Temperatures

Columns: 110°

Injection port: 100°

Detector: 200°

Carrier gas: Nitrogen

Flow rate: 50 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 160 theoretical plates for acetone and NLT 200 theoretical plates for methanol

Tailing factor: NMT 1.3 for acetone and NMT 2.3 for methanol

Relative standard deviation: NMT 5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of acetone and methanol in the portion of Cefoxitin Sodium taken:

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

r_U = peak area of acetone or methanol in the *Sample solution*

r_S = peak area of acetone or methanol in the *Standard solution*

C_S = concentration of acetone or methanol in the *Standard solution* (% v/v)

C_U = concentration of Cefoxitin Sodium in the *Sample solution* (g/mL)

D = density of acetone or methanol at 20° (g/mL)

Acceptance criteria: NMT 0.7% of acetone and NMT 0.1% of methanol

SPECIFIC TESTS

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

Sample solution: 10 mg/mL in methanol

Acceptance criteria: +206° to +214°, calculated on the anhydrous and acetone- and methanol-free basis

• **Crystallinity ⟨695⟩:** Meets the requirements

• **pH ⟨791⟩**

Sample solution: 100 mg/mL

Acceptance criteria: 4.2–7.0

• **Water Determination, *Method I*⟨921⟩**

Analysis: Use a mixture of ethylene glycol and pyridine (3:1) in the titration vessel in place of methanol.

Acceptance criteria: NMT 1.0%

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Cefoxitin Sodium is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 0.13 USP Endotoxin Unit/mg of cefoxitin.

• **Sterility Tests ⟨71⟩:** Where the label states that Cefoxitin Sodium is sterile, it meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store in a cold place.

• **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 Cefoxitin RS

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

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

Chromatographic Database Information: Chromatographic Database

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