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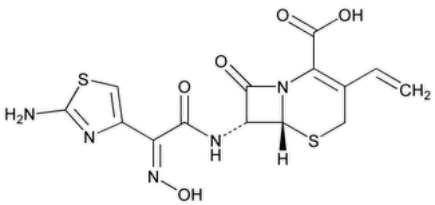
Cefdinir



$C_{14}H_{13}N_5O_5S_2$ 395.41

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-3-ethenyl-8-oxo-, [6*R*-[6α,7β(*Z*)]]-; (−)-(6*R*,7*R*)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7^2-(*Z*)-oxime CAS RN®: 91832-40-5; UNII: CI0FAO63WC.

DEFINITION

Cefdinir contains NLT 940 µg/mg and NMT 1030 µg/mg of cefdinir ($C_{14}H_{13}N_5O_5S_2$), calculated on the anhydrous basis.

IDENTIFICATION

- **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 14.2 g/L of anhydrous dibasic sodium phosphate

Solution B: 13.6 g/L of monobasic potassium phosphate

Solution C: Dilute tetramethylammonium hydroxide (10%) with water to obtain a 0.1% solution. Adjust with 10% phosphoric acid to a pH of 5.5.

Solution D: 37.2 mg/mL of edetate disodium

Buffer: Combine appropriate amounts of *Solution A* and *Solution B* (about 2:1) to obtain a solution with a pH of 7.0.

Mobile phase: Acetonitrile, methanol, *Solution C*, and *Solution D* (300:200:4500:2)

System suitability solution: 0.2 mg/mL of USP Cefdinir RS and 0.5 mg/mL of USP Cefdinir Related Compound A RS in *Buffer*

Standard solution: 0.2 mg/mL of USP Cefdinir RS in *Buffer*

Sample solution: 0.2 mg/mL of Cefdinir in *Buffer*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection size: 5 µL

System suitability

Samples: *System suitability solution* and *Standard solution*. USP Cefdinir Related Compound A RS should produce four peaks.

Tailing factor: NMT 1.5 for cefdinir, *System suitability solution*

Resolution: NLT 1.2 between the second peak of cefdinir related compound A and cefdinir, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg/mg, of cefdinir ($C_{14}H_{13}N_5O_5S_2$) in the portion of Cefdinir 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 the *Standard solution* (mg/mL)

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

P = purity of USP Cefdinir RS (µg/mg)

Acceptance criteria: 940–1030 µg/mg on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.20%

Change to read:

• **Organic Impurities**

Solution A, Solution B, Solution C, Solution D, and **Buffer:** Prepare as directed in the *Assay*.

Solution E: To 1000 mL of *Solution C* add 0.4 mL of *Solution D*.

Solution F: Acetonitrile, methanol, *Solution C*, and *Solution D* (300:200:500:0.4)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution E (%)	Solution F (%)
0	95	5
2	95	5
22	75	25
32	50	50
37	50	50
38	95	5
58	95	5

System suitability solution 1: 15 µg/mL of cefdinir from the *Sample solution*, diluted with *Solution C*

System suitability solution 2: 1.5 µg/mL of cefdinir from *System suitability solution 1*, diluted with *Solution C*

System suitability solution 3: 1.5 mg/mL of USP Cefdinir RS and 0.1 mg/mL of USP Cefdinir Related Compound A RS, dissolved initially in *Buffer* corresponding to 15% of the final volume, and diluted with *Solution C* to volume

Sample stock solution: 10 mg/mL of Cefdinir in *Buffer*

Sample solution: 1.5 mg/mL of cefdinir from the *Sample stock solution*, in *Solution C*. [Note—Prepare fresh immediately before use.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Samples: *System suitability solution 1*, *System suitability solution 2*, and *System suitability solution 3*. USP Cefdinir Related Compound A RS should produce four peaks.

Suitability requirements

Response ratio: The response of cefdinir from *System suitability solution 2* is between 7% and 13% of that from *System suitability solution 1*.

Resolution: NLT 1.5 between cefdinir and the third peak of USP Cefdinir Related Compound A RS, *System suitability solution 3*

Relative standard deviation: NMT 2.0% for cefdinir, *System suitability solution 3*

Analysis

Sample: *Sample solution*. Record the chromatogram for at least 1.8 times the retention time of the cefdinir peak.

Calculate the percentage of each impurity in the portion of Cefdinir taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Thiazolylacetyl glycine oxime[a]	0.10	0.5
Thiazolylacetyl glycine oxime acetal[b]	0.12	0.5
3-Methyl cefdinir[c]	0.74	0.7
Cefdinir related compound A (cefdinir open ring lactone a)[d,e]	0.85	0.7
Cefdinir related compound A (cefdinir open ring lactone b)[d,e]	0.93	
Cefdinir related compound A (cefdinir open ring lactone c)[d,e]	1.11	
Cefdinir related compound A (cefdinir open ring lactone d)[d,e]	1.14	
Cefdinir lactone[f]	1.22	0.5
Cefdinir isoxazole analog[g]	1.36	0.5
E-Cefdinir[h]	1.51	0.7
Cefdinir decarboxy open ring lactone a[i,j]	1.61	0.5
Cefdinir decarboxy open ring lactone b[i,j]	1.64	
Any other individual, unidentified impurity	—	0.2
Total impurities	—	3.0

[a] ▲*N*-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetyl]glycine.▲ (ERR 1-Dec-2023)

[b] (*Z*)-2-(2-Aminothiazol-4-yl)-*N*-(2,2-dihydroxyethyl)-2-(hydroxyimino)acetamide.

[c] (6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[d] 2(*R*)-2-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido)]-2-[(2*RS*,5*RS*)-5-methyl-7-oxo-2,4,5,7-tetrahydro-1*H*-furo[3,4-*d*][1,3]thiazin-2-yl]acetic acid.

[e] Cefdinir related compound A is a mixture of 4 isomers labeled cefdinir open ring lactones a, b, c, and d. The sum of the values is reported. The limit for the sum of the 4 isomers is 0.7%.

[f] (*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)-*N*-{(3*RS*,5a*R*,6*R*)-3-methyl-1,7-dioxo-1,3,4,5a,6,7-hexahydroazeto[2,1-*b*]furo[3,4-*d*][1,3]thiazin-6-yl}acetamide.

[g] (6*R*,7*R*)-7-(4-Hydroxyisoxazole-3-carboxamido)-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[h] (6*R*,7*R*)-7-[(*E*)-2-(2-Aminothiazol-4-yl-)-2-(hydroxyimino)acetamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[i] (*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)-*N*-{[(2*RS*,5*RS*)-5-methyl-7-oxo-2,4,5,7-tetrahydro-1*H*-furo[3,4-*d*][1,3]thiazin-2-yl]methyl}acetamide.

[j] Cefdinir decarboxy open ring lactone is a mixture of 2 isomers labeled cefdinir decarboxy open ring lactones a and b. The sum of the values is reported. The limit for sum of the 2 isomers is 0.5%.

SPECIFIC TESTS

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

Sample solution: 10 mg/mL in *Buffer*, as obtained in the *Assay*

Acceptance criteria: −61° to −67° at 20°

• **Water Determination,** *Method I* ⟨921⟩**:** NMT 2.0% for anhydrous; 4.0%–8.5% for hydrated forms. For this monograph, the term “hydrated forms” refers to several known forms of Cefdinir. Use a mixture of formamide and methanol (2:1) as the solvent.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Cefdinir RS

USP Cefdinir Related Compound A RS

(2*R*)-2-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido]-2-[(2*RS*,5*RS*)-5-methyl-7-oxo-2,4,5,7-tetrahydro-1*H*-furo[3,4-*d*][1,3]thiazin-2-yl]acetic acid (three other stereoisomers are also present in this RS).

$C_{14}H_{15}N_5O_6S_2$ ▲413.42▲ (ERR 1-Dec-2023)

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

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

Chromatographic Database Information: Chromatographic Database

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