Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2023
Document Type: USP Monographs
DocId: GUID-ED8E5319-F91E-494D-A823-8DB438663ED7_3_en-US
DOI: https://doi.org/10.31003/USPNF_M2183_03_01
DOI Ref: 86bn4

Cefdinir Capsules

DEFINITION
Cefdinir Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of cefdinir ($C_{14}H_{13}N_5O_5S_2$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

Buffer: Prepare as directed in the *Assay*.

Standard solution: 10 µg/mL of USP Cefdinir RS in *Buffer*

Sample solution: Equivalent to 10 µg/mL of cefdinir from Capsules in *Buffer*. Filter before use.

Cell size: 1 cm

Blank: Use the *Buffer*.

Acceptance criteria: *Sample solution* maxima and minima occur at the same wavelengths as those in the *Standard solution*.

• **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**

Buffer: 10.7 g/L of dibasic sodium phosphate and 3.4 g/L of monobasic potassium phosphate. Adjust with phosphoric acid or sodium hydroxide to a pH of 7.0 ± 0.05 before final dilution.

Solution A: 7 g/L of citric acid monohydrate. Adjust with phosphoric acid to a pH of 2.0 ± 0.05.

Mobile phase: Methanol, tetrahydrofuran, and *Solution A* (111:28:1000)

System suitability solution: 50 µg/mL of USP Cefdinir RS and 175 µg/mL of *m*-hydroxybenzoic acid in *Buffer*

Standard solution: 50 µg/mL of USP Cefdinir RS in *Buffer*

Sample solution: Equivalent to 50 µg/mL of cefdinir, from Capsule contents (NLT 20), in *Buffer*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 1.4 mL/min

Injection volume: 15 µL

System suitability

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

Suitability requirements

Resolution: Greater than 3.0 between cefdinir and *m*-hydroxybenzoic acid, *System suitability solution*

Tailing factor: NMT 2.0 for cefdinir, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cefdinir ($C_{14}H_{13}N_5O_5S_2$) in the portion of Capsules taken:

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

r_U = peak response of cefdinir from the *Sample solution*

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

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

C_U = nominal concentration of cefdinir in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 50 mM phosphate buffer, pH 6.8; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Detector: UV 290 nm

Cell length: 0.1-cm flow cell

Standard solution: 0.33 mg/mL of USP Cefdinir RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with *Medium* to a concentration of about 0.33 mg/mL of cefdinir.

Blank: Dissolve 1 empty Capsule in 100 mL of *Medium*, and dilute to 900 mL. Filter if necessary.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cefdinir ($C_{14}H_{13}N_5O_5S_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution* (mL/mL)

L = label claim (mg/Capsule)

Tolerances: NLT 80% (*Q*) of the labeled amount of cefdinir ($C_{14}H_{13}N_5O_5S_2$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

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

Solution B: 13.6 g/L of monobasic potassium phosphate

Buffer: Combine appropriate amounts of *Solution A* and *Solution B* (about 2:1) to obtain a solution with a pH of 7.0 ± 0.1.

Solution C: Dilute tetramethylammonium hydroxide (10% aqueous) with water to obtain a 0.1% solution. Adjust with dilute phosphoric acid (1 in 10) to a pH of 5.5 ± 0.1.

Solution D: 37.2 mg/mL of edetate disodium

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

Solution F: Acetonitrile, methanol, *Solution C*, and *Solution D* (150:100:250:0.2)

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 stock solution 1: 40 µg/mL of USP Cefdinir Related Compound A RS in *Solution C*

System suitability stock solution 2: 40 µg/mL of USP Cefdinir Related Compound B RS in *Solution C*

System suitability solution: Transfer 37.5 mg of USP Cefdinir RS to a 25-mL volumetric flask. Add about 10 mL of *Buffer*. Add 5.0 mL each of *System suitability stock solution 1* and *System suitability stock solution 2*, and dilute with *Solution C* to volume.

Standard stock solution: 750 µg/mL of USP Cefdinir RS in *Buffer*

Standard solution: 15 µg/mL of USP Cefdinir RS, from the *Standard stock solution*, in *Solution C*

Sample solution: Transfer an equivalent to 300 mg of cefdinir from Capsule contents (NLT 20) to a 200-mL volumetric flask. Dissolve in 30 mL of *Buffer*, and dilute with *Solution C* to volume to obtain a solution with a nominal concentration of about 1.5 mg/mL of cefdinir.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Temperatures

Autosampler: 4°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

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

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

Relative standard deviation: NMT 2.0% for the cefdinir peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response from the *Standard solution*

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Thiazolylacetyl glycine oxime[a]	0.10	1.0	0.5
Thiazolylacetyl glycine oxime acetal[b]	0.13	1.0	0.5
Cefdinir sulfoxide[c]	0.36	1.0	0.2
Cefdinir thiazine analog[d]	0.46	0.68	0.7
3-Methyl cefdinir[e]	0.75	1.0	0.7
Cefdinir impurity 1[f]	0.77	1.0	0.3
Cefdinir related compound A (cefdinir open ring lactone a)[g,h]	0.85	0.65	2.5

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cefdinir related compound A (cefdinir open ring lactone b)[g,h]	0.94	0.65	
Cefdinir related compound A (cefdinir open ring lactone c)[g,h]	1.11	0.65	
Cefdinir related compound A (cefdinir open ring lactone d)[g,h]	1.14	0.65	
7*S*-Cefdinir[i]	1.18	1.0	0.2
Cefdinir lactone[j]	1.23	1.0	1.0
Cefdinir related compound B[k]	1.28	1.0	0.2
Cefdinir isoxazole analog[l]	1.37	0.72	0.5
Cefdinir impurity 2[f]	1.44	1.0	0.5
Cefdinir glyoxalic analog[m]	1.49	1.0	0.2
E-Cefdinir[n]	1.51	1.0	1.2
Cefdinir decarboxy open ring lactone a[o,p]	1.62	1.0	1.0
Cefdinir decarboxy open ring lactone b[o,p]	1.64	1.0	
Cefdinir impurity 3[f]	1.82	1.0	0.2
Individual unidentified impurities	—	1.0	0.2
Total impurities	—	—	5.0

[a] *N*-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetyl]glycine.

[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]-5,8-dioxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[d] (*R*,*Z*)-2-{(*R*)-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido](carboxy)methyl}-5-ethylidene-5,6-dihydro-2*H*-1,3-thiazine-4-carboxylic acid.

[e] (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.

[f] Cefdinir impurity 1, cefdinir impurity 2, and cefdinir impurity 3 are unidentified impurities.

[g] Cefdinir related compound A is a mixture of four 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 four isomers is 2.5%.

[h] 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.

[i] (6*R*,7*S*)-7-[(*Z*)-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.

[j] (*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.

[k] (6*R*,7*R*)-7-[2-(2-Amino-4-thiazolyl)acetamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[l] (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.

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

[n] (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.

[o] Cefdinir decarboxy open ring lactone is a mixture of two isomers labeled cefdinir decarboxy open ring lactone a and b. The sum of the values is reported. The limit for the sum of the two isomers is 1.0%.

[p] (*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.

ADDITIONAL REQUIREMENTS

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

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)

USP Cefdinir Related Compound B RS

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

▲$C_{14}H_{14}N_4O_4S_2$ 366.41▲ (ERR 1-Dec-2023)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 40(2)

Current DocID: GUID-ED8E5319-F91E-494D-A823-8DB438663ED7_3_en-US

DOI: https://doi.org/10.31003/USPNF_M2183_03_01

DOI ref: 86bn4