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] 1*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]-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%.

▲*USP35*

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.
- **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).
  $C_{14}H_{15}N_5O_6S_2$ 413.43

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. Ultraviolet Absorption** ⟨**197U**⟩
  Buffer: Prepare as directed in the *Assay*.
  Blank: Use the *Buffer*.
  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
  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 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 size: 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 for cefdinir from the *Sample solution*
r_S = peak response for 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%–100.0%

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

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
D = dilution factor of the *Sample solution* (mL/mL)
V = volume of *Medium*, 900 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

Change to read:

- **ORGANIC IMPURITIES**
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% 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)
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.
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 of 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) into a 200-mL volumetric flask. Dissolve in 30 mL of *Buffer*, and dilute with *Solution C* to volume to obtain a solution having 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
Column temperature: 40°
Autosampler temperature: 4°
Flow rate: 1 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 1.5 between cefdinir and the third peak of the 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 response, *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 = concentration of the *Sample solution* (mg/mL)
F = relative response factor (see *Table 2*)
▲**Acceptance criteria:** See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Reporting Threshold (% Cefdinir)	Acceptance Criteria, NMT (%)
Thiazolylacetyl glycine oxime[a]	0.10	1.1	0.1	0.5
Thiazolylacetyl glycine oxime acetal[b]	0.13	1.1	0.1	0.5
Cefdinir sulfoxide[c]	0.36	1.0	0.05	0.2
Cefdinir thiazine analog[d]	0.46	1.5	0.05	0.7
3-Methyl cefdinir[e]	0.75	1.0	0.05	0.7
Cefdinir impurity 1[f]	0.77	1.0	0.05	0.3
Cefdinir related compound A (cefdinir open ring lactone a)[g,h]	0.85	1.5	0.1	2.5
Cefdinir related compound A (cefdinir open ring lactone b)[g,h]	0.94	1.5	0.1	
Cefdinir related compound A (cefdinir open ring lactone c)[g,h]	1.11	1.5	0.1	
Cefdinir related compound A (cefdinir open ring lactone d)[g,h]	1.14	1.5	0.1	
7*S*-Cefdinir[i]	1.18	1.1	0.05	0.2
Cefdinir lactone[j]	1.23	1.2	0.05	1.0
Cefdinir related compound B[k]	1.28	1.1	0.05	0.2
Cefdinir isoxazole analog[l]	1.37	1.4	0.05	0.5
Cefdinir impurity 2[e]	1.44	1.0	0.05	0.5
Cefdinir glyoxalic analog[m]	1.49	1.0	0.05	0.2
E-cefdinir[n]	1.51	1.1	0.05	0.7
Cefdinir decarboxy open ring lactone a[o,p]	1.62	1.3	0.05	1.0
Cefdinir decarboxy open ring lactone b[o,p]	1.64	1.3	0.05	
Cefdinir impurity 3[e]	1.82	1.0	0.05	0.2
Individual unidentified impurities	—	1.0	0.05	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 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 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 2 isomers labeled cefdinir decarboxy open ring lactone a and b. The sum of the values is reported. The limit for sum of the 2 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.

▲*USP35*

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight light-resistant containers, and store at controlled room temperature.
- **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).
  $C_{14}H_{15}N_5O_6S_2$ 413.43
  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.
  $C_{14}H_{13}N_4O_4S_2$ 365.41

Cefdinir for Oral Suspension

DEFINITION

Cefdinir for Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of cefdinir ($C_{14}H_{13}N_5O_5S_2$). It may contain one or more suitable buffers, flavors, preservatives, stabilizing agents, sweeteners, and suspending agents.

IDENTIFICATION

Delete the following:

▲• **A. Thin-Layer Chromatographic Identification Test** ⟨201⟩
Buffer: Prepare as directed in the *Assay*.
Standard solution: 600 µg/mL of USP Cefdinir RS in methanol and *Buffer* (3:1)