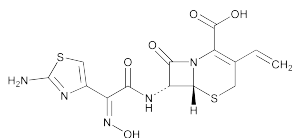


Add the following:

▲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-, [6R-[6 α ,7 β (Z)]]-, (-)-(6R,7R)-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-(Z)-oxime [91832-40-5].

Change to read:

» Cefdinir contains not less than $\bullet 940_{\bullet}$ (RB 1-Oct-2009) μg per mg and not more than $\bullet 1030_{\bullet}$ (RB 1-Oct-2009) μg per mg of $C_{14}H_{13}N_5O_5S_2$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards (11)—*USP Cefdinir RS*. *USP Cefdinir Related Compound A RS*.

Identification—

A: *Infrared Absorption* (197M).

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Specific rotation (781S): between -61° and -67° , at 20° .

Test solution: 10 mg per mL, in *Buffer solution* as prepared in the *Assay*.

Water, Method I (921): not more than 2.0% (anhydrous), or not less than 4.0% and not more than 8.0% (monohydrate), using a mixture of formamide and methanol (2 : 1) as the solvent.

Change to read:

Residue on ignition (281): not more than $\bullet 0.20\%_{\bullet}$ (RB 1-Oct-2009)

Heavy metals, Method II (231): 0.001%.

Related compounds—

Buffer solution, Tetramethylammonium hydroxide solution, and 0.1 M Edetate disodium solution—Proceed as directed in the *Assay*.

Solution A—To 1000 mL of *Tetramethylammonium hydroxide solution* add 0.4 mL of *0.1 M Edetate disodium solution*, filter, and degas.

Solution B—To 500 mL of *Tetramethylammonium hydroxide solution* add 300 mL of acetonitrile, 200 mL of methanol, and 0.4 mL of *0.1 M Edetate disodium solution*. Filter and degas.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

System suitability solution A—Transfer 1 mL of the *Test solution* to a 100-mL volumetric flask. Dilute with *Tetramethylammonium hydroxide solution* to volume, and mix.

System suitability solution B—Transfer 1 mL of *System suitability solution A* to a 10-mL volumetric flask. Dilute with *Tetramethylammonium hydroxide solution* to volume, and mix.

System suitability solution C—Transfer about 30 mg of USP Cefdinir RS and 2 mg of USP Cefdinir Related Compound A RS to a 20-mL volumetric flask, dissolve in 3 mL of *Buffer solution*, dilute with *Tetramethylammonium hydroxide solution* to volume, and mix.

Test solution—Transfer about 100 mg of Cefdinir, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with *Buffer solution* to volume, and mix. Transfer 3 mL of this solution to a 20-mL volumetric flask, dilute with *Tetramethylammonium hydroxide solution* to volume, and mix. [NOTE—Inject this solution immediately.]

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm \times 15-cm column that contains packing L1. The column temperature is maintained at 40° . The flow rate is about 1 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0–2	95	5	isocratic
2–22	95→75	5→25	linear gradient
22–32	75→50	25→50	linear gradient
32–37	50	50	isocratic
37–38	50→95	50→5	linear gradient
38–58	95	5	isocratic

Chromatograph *System suitability solution A* and *System suitability solution B*, and record the peak responses as directed for *Procedure*: the peak response of cefdinir in *System suitability solution B* is about 7% to 13% of that obtained from *System suitability solution A*. Chromatograph *System suitability solution C*, and record the peak responses as directed for *Procedure*: cefdinir related compound A elutes with four peaks. The relative retention times are not less than 1.1 for the third peak of cefdinir related compound A and 1.0 for cefdinir; the column efficiency, determined from the cefdinir peak, is not less than 7000 theoretical plates; the tailing factor for the cefdinir peak is not more than 3.0; and the relative standard deviation for replicate injections, based on the cefdinir peak, is not more than 2.0%.

Procedure—Inject a volume (about 10 μL) of the *Test solution* into the chromatograph, record the chromatogram, and measure all the peak responses. Continue the chromatogram for 40 minutes. Calculate the percentage of each impurity in the portion of Cefdinir taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity, and r_s is the sum of the responses of all the peaks. The limits for the impurities are specified in *Table 1*.

2 Cefdinir

Table 1

Impurity	Relative Retention Time	Limit (w/w, %)
Impurity A ¹	0.10	0.5
Impurity B ²	0.12	0.5
Impurity C ³	0.74	0.7
Cefdinir related compound A (4 peaks) ⁴	0.85, 0.93, 1.11, 1.14	0.7 (total for all 4 peaks)
Impurity E ⁵	1.22	0.5
Impurity F ⁶	1.36	0.5
Impurity G ⁷	1.51	0.7
Impurity H (2 peaks) ⁸	1.61, 1.64	0.5 (total for both peaks)
Individual unknown impurity	—	0.2
Total impurities	—	3.0

¹*N*-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetyl]glycine.²(*Z*)-2-(2-Aminothiazol-4-yl)-*N*-(2,2-dihydroxyethyl)-2-(hydroxyimino)acetamide.³(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.⁴2(*R*)-2-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido]-2-[(2*R*S,5*R*S)-5-methyl-7-oxo-2,4,5,7-tetrahydro-1*H*-furo[3,4-*d*][1,3]thiazin-2-yl]acetic acid.⁵(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)-*N*-[(3*R*S,5*a*R,6*R*)-3-methyl-1,7-dioxo-1,3,4,5*a*,6,7-hexahydroazeto[2,1-*b*]furo[3,4-*d*][1,3]thiazin-6-yl]acetamide.⁶(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.⁷(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.⁸(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)-*N*-{[(2*R*S,5*R*S)-5-methyl-7-oxo-2,4,5,7-tetrahydro-1*H*-furo[3,4-*d*][1,3]thiazin-2-yl]methyl}acetamide.

Assay—

Buffer solution—Dissolve about 7.1 g of anhydrous dibasic sodium phosphate in 500 mL of water (*Solution A*). Dissolve about 6.8 g of monobasic potassium phosphate in 500 mL of water (*Solution B*). Add appropriate amounts of *Solution A* and *Solution B* (approximately 2 : 1 v/v) to obtain a mixture having a pH of 7.0.

Tetramethylammonium hydroxide solution—To 10 mL of tetramethylammonium hydroxide (10%) add 990 mL of water, and adjust with dilute phosphoric acid (1 in 10) to a pH of 5.5.

0.1 M Edetate disodium solution—Dissolve 37.2 g of edetate disodium in 1000 mL of water, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Tetramethylammonium hydroxide solution*, acetonitrile, methanol, and *0.1 M Edetate disodium solution* (900 : 60 : 40 : 0.4). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

System suitability solution—Dissolve accurately weighed quantities of USP Cefdinir RS and USP Cefdinir Related Compound A RS in *Buffer solution* to obtain a solution having a known concentration of about 0.2 mg per mL of USP Cefdinir RS and 0.5 mg per mL of USP Cefdinir Related Compound A RS.

Standard preparation—Dissolve an accurately weighed quantity of USP Cefdinir RS in *Buffer solution*, and dilute quantitatively, and stepwise if necessary, with *Buffer solution* to obtain a solution having a known concentration of about 0.2 mg per mL.

Assay preparation—Transfer about 20 mg of Cefdinir, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Buffer solution* to volume, and mix well.

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains 5-μm packing L1. The flow rate is about 1 mL per minute. The column temperature is maintained at 40°. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure*: cefdinir related compound A elutes with four peaks. The resolution, *R*, between the second peak of cefdinir related compound A and cefdinir is not less than 1.2; and the tailing factor for the cefdinir peak is not more than 1.5. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 5 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in μg, of C₁₄H₁₃N₅O₅S₂ in each mg of Cefdinir taken by the formula:

$$P(C_S / C_U)(r_U / r_S)$$

in which *P* is the purity, in μg per mg, of USP Cefdinir RS; *C_S* is the concentration, in mg per mL, of USP Cefdinir RS in the *Standard preparation*; *C_U* is the concentration, in mg per mL, of Cefdinir in the *Assay preparation*; and *r_U* and *r_S* are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.▲^{USP32}