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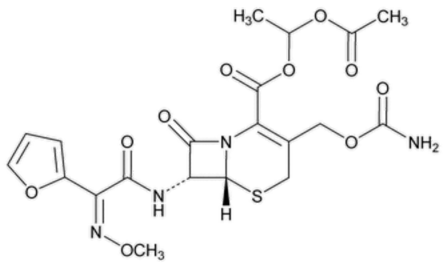
Cefuroxime Axetil



$C_{20}H_{22}N_4O_{10}S$ 510.47

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[(aminocarbonyl)oxy]methyl]-7-[[2-furanyl(methoxyimino)acetyl]amino]-8-oxo-, 1-(acetyloxy)ethyl ester, [6*R*-[6α,7β(*Z*)]]-;

(*RS*)-1-Hydroxyethyl (6*R*,7*R*)-7-[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7^2-(*Z*)-(*O*-methyloxime), 1-acetate 3-carbamate CAS RN®: 64544-07-6; UNII: Z49QDT0J8Z.

DEFINITION

Cefuroxime Axetil is a mixture of the diastereoisomers of cefuroxime axetil ($C_{20}H_{22}N_4O_{10}S$). It contains the equivalent of NLT 745 µg/mg and NMT 875 µg/mg of cefuroxime ($C_{16}H_{16}N_4O_8S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020) **:** Meets the requirements
- **B.** The retention times of cefuroxime axetil diastereoisomers A and B of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 23 g/L of monobasic ammonium phosphate

Mobile phase: Methanol and *Solution A* (38:62)

System suitability stock solution: 0.1 mg/mL of USP Cefuroxime Axetil Delta-3 Isomers RS in methanol

System suitability solution: 10 µg/mL of cefuroxime axetil delta-3 isomers from *System suitability stock solution* and 0.2 mg/mL of USP Cefuroxime Axetil RS in *Mobile phase*

Standard solution: 0.2 mg/mL of USP Cefuroxime Axetil RS in *Mobile phase*. Protect the solution from light, refrigerate, and use on the day prepared.

Sample solution: 0.2 mg/mL of Cefuroxime Axetil in *Mobile phase*. Protect the solution from light, refrigerate, and use on the day prepared.

Chromatographic system

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

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 25-cm; 5-µm packing L13

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between cefuroxime axetil diastereoisomers A and B; NLT 1.5 between cefuroxime axetil diastereoisomer A and cefuroxime axetil delta-3 isomers, *System suitability solution*

Relative standard deviation: NMT 2.0% for the sum of cefuroxime axetil diastereoisomers A and B, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg/mg, of cefuroxime ($C_{16}H_{16}N_4O_8S$) in the portion of Cefuroxime Axetil taken:

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

r_U = sum of the peak responses of cefuroxime axetil diastereoisomers A and B from the *Sample solution*

r_T = sum of the peak responses of cefuroxime axetil diastereoisomers A and B from the *Standard solution*

C_S = concentration of USP Cefuroxime Axetil RS in the *Standard solution* (mg/mL)

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

P = potency of cefuroxime, on the anhydrous basis, in USP Cefuroxime Axetil RS (µg/mg)

Acceptance criteria: 745–875 µg/mg on the anhydrous basis

IMPURITIES

• **Organic Impurities**

Solution A, Mobile phase, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Peak identification solution: 30 µg/mL of USP Cefuroxime Axetil E-Isomers RS in *Mobile phase*

Reference solution: 2 µg/mL of USP Cefuroxime Axetil RS in *Mobile phase*. Protect the solution from light, refrigerate, and use on the day prepared.

System suitability

Samples: *System suitability solution* and *Peak identification solution*

[Note—See *Table 1* for relative retention times. Use the *Peak identification solution* to identify the locations of the cefuroxime axetil *E*-isomers.]

Suitability requirements

Resolution: NLT 1.5 between cefuroxime axetil diastereoisomers A and B; NLT 1.5 between cefuroxime axetil diastereoisomer A and cefuroxime axetil delta-3 isomers, *System suitability solution*

Analysis

Samples: *Sample solution* and *Reference solution*

Calculate the percentage of each impurity in the portion of Cefuroxime Axetil taken:

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

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

r_T = sum of the peak responses of cefuroxime axetil diastereoisomers A and B from the *Sample solution*

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05 times the sum of the responses of the two major peaks from the *Reference solution*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Methoxyiminofuranyl acetic acid[a]	0.24	0.30
Cefuroxime[b]	0.30	0.5
Cefuroxime lactone[c]	0.42	0.30
Cefuroxime axetil diastereoisomer B	0.9	—
Cefuroxime axetil diastereoisomer A	1.0	—
Cefuroxime axetil delta-3 isomers[d,e]	1.2	1.20
Cefuroxime axetil *E*-isomers[d,f]	1.7 2.1	1.0
Cefuroxime axetil dimer[g,h]	2.5	0.5

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
	3.4	
	3.8	
Any other individual impurity	—	0.30
Total impurities	—	3.0

[a] (*Z*)-2-(Furan-2-yl)-2-(methoxyimino)acetic acid.

[b] (6*R*,7*R*)-3-[(Carbamoyloxy)methyl]-7-[(*Z*)-2-(furan-2-yl)-2-(methoxyimino)acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[c] (*Z*)-*N*-((5a*R*,6*R*)-1,7-Dioxo-1,3,4,5a,6,7-hexahydroazeto[2,1-*b*]furo[3,4-*d*][1,3]thiazin-6-yl)-2-(furan-2-yl)-2-(methoxyimino)acetamide.

[d] The system may resolve two isomers. The limit is for the sum of the two isomers.

[e] (1*RS*,6*R*,7*R*)-1-Acetoxyethyl 3-[(carbamoyloxy)methyl]-7-[(*Z*)-2-(furan-2-yl)-2-(methoxyimino)acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylate.

[f] (1*RS*,6*R*,7*R*)-1-Acetoxyethyl 3-[(carbamoyloxy)methyl]-7-[(*E*)-2-(furan-2-yl)-2-(methoxyimino)acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate.

[g] The system may resolve three isomers. The limit is for the sum of the three isomers.

[h] (6*R*,6'*R*,7*R*,7'*R*,*Z*)-Oxybis(ethane-1,1-diyl)bis{3-[(carbamoyloxy)methyl]-7-[(*Z*)-2-(furan-2-yl)-2-(methoxyimino)acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate}.

SPECIFIC TESTS

• **Crystallinity ⟨695⟩:** Particles that do not show birefringence or exhibit extinction positions are amorphous, and particles that show birefringence and exhibit extinction positions are crystalline.

• **Water Determination, *Method I*⟨921⟩:** NMT 1.5%

• **Diastereoisomer Ratio**

Solution A, Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the ratio of cefuroxime axetil diastereoisomer A to the sum of cefuroxime axetil diastereoisomers A and B:

$$\text{Result} = r_A/r_T$$

r_A = peak response of cefuroxime axetil diastereoisomer A

r_T = sum of the peak responses of cefuroxime axetil diastereoisomers A and B

Acceptance criteria: 0.48–0.55

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **Labeling:** Label it to indicate whether it is amorphous or crystalline.

• **USP Reference Standards ⟨11⟩**

USP Cefuroxime Axetil RS

USP Cefuroxime Axetil Delta-3 Isomers RS

(1*RS*,6*R*,7*R*)-1-Acetoxyethyl 3-[(carbamoyloxy)methyl]-7-[(*Z*)-2-(furan-2-yl)-2-(methoxyimino)acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylate.

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USP Cefuroxime Axetil E-Isomers RS

(1*RS*,6*R*,7*R*)-1-Acetoxyethyl 3-[(carbamoyloxy)methyl]-7-[(*E*)-2-(furan-2-yl)-2-(methoxyimino)acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate.

$C_{20}H_{22}N_4O_{10}S$ 510.47

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

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

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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