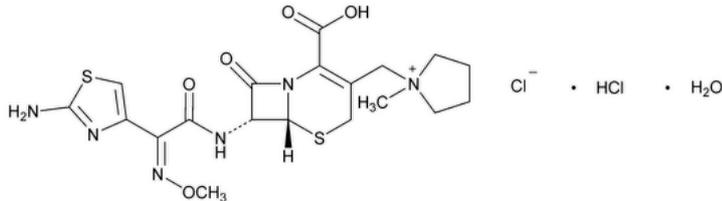


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Cefepime Hydrochloride

Change to read:



$C_{19}H_{25}ClN_6O_5S_2 \cdot HCl \cdot H_2O$

▲571.49

Pyrrolidinium, 1-[(7-[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino)-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl)methyl]-1-methyl-, chloride, monohydrochloride, monohydrate, [6R-[6 α ,7 β (Z)]]-;▲ (USP 1-May-2024)

1-▲(▲ (USP 1-May-2024) (6R,7R)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl)▲ (USP 1-May-2024) methyl)▲ (USP 1-May-2024) -1-methylpyrrolidinium chloride, 7²-(Z)-(O-methyloxime), monohydrochloride, monohydrate CAS RN®: 123171-59-5; ▲UNII: 18X100607P.▲ (USP 1-May-2024)

DEFINITION

Cefepime Hydrochloride contains the equivalent of NLT 825 µg/mg and NMT 911 µg/mg of cefepime ($C_{19}H_{24}N_6O_5S_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** ▲197A, 197K, or ▲ (USP 1-May-2024) 197M

Sample: Proceed as directed in the chapter, but do not dry.

Acceptance criteria: Meets the requirements

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

Add the following:

- ▲ **C. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride:** Meets the requirements▲ (USP 1-May-2024)

ASSAY

Change to read:

PROCEDURE

Solution A: 0.68 mg/mL of [monobasic potassium phosphate](#) in [water](#)

Solution B: [Acetonitrile](#) and *Solution A* (10:90). Adjust with 2% [phosphoric acid](#) or 2% [potassium hydroxide](#) to a pH of 5.0.

Solution C: [Acetonitrile](#) and *Solution A* (50:50). Adjust with 2% [phosphoric acid](#) or 2% [potassium hydroxide](#) to a pH of 5.0.

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
10	100	0
30	50	50
35	50	50
36	100	0

Time (min)	Solution B (%)	Solution C (%)
45	100	0

Standard solution: 1.4 mg/mL of [USP Cefepime Hydrochloride RS](#) in *Solution B*. [NOTE—Sonicate, if necessary. Inject immediately or store in a refrigerator and use within 12 h.]

Sample solution: 1.4 mg/mL of Cefepime Hydrochloride in *Solution B*. [NOTE—Sonicate, if necessary. Inject immediately or store in a refrigerator and use within 12 h.]

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT ▲0.73%▲ (USP 1-May-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity, in µg, of cefepime (C₁₉H₂₄N₆O₅S₂) in each milligram of Cefepime Hydrochloride taken:

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

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

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

C_S = concentration of [USP Cefepime Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

P = content of cefepime in [USP Cefepime Hydrochloride RS](#) (µg/mg)

Acceptance criteria: 825–911 µg/mg on the anhydrous basis

IMPURITIES

• **RESIDUE ON IGNITION (281):** NMT 0.1%

• **LIMIT OF N-METHYLPYRROLIDINE**

Mobile phase: [Acetonitrile](#) and [0.01 N nitric acid](#) (5:95)

Standard solution: 0.05 mg/mL of [N-methylpyrrolidine](#) in 0.002 N [nitric acid](#)

Sample solution: 5 mg/mL of Cefepime Hydrochloride in 0.002 N [nitric acid](#). [NOTE—Inject this solution immediately.]

Chromatographic system

(See [Chromatography \(621\), System Suitability.](#))

Mode: LC

Detector: Conductivity

Column: 4.0-mm × 25-cm; 5-µm packing [L76](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 6 times the retention time of *N-methylpyrrolidine*

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 4.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of *N-methylpyrrolidine* in the portion of Cefepime Hydrochloride taken:

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

r_U = peak response of *N*-methylpyrrolidine from the *Sample solution*

r_S = peak response of *N*-methylpyrrolidine from the *Standard solution*

C_S = concentration of *N*-methylpyrrolidine in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.3%

Change to read:

• **ORGANIC IMPURITIES**

Solution A, Solution B, Solution C, Mobile phase, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

System suitability solution: 1.4 mg/mL of [USP Cefepime Hydrochloride RS](#) and 15 µg/mL each of [USP Cefepime Related Compound D RS](#) and [USP Cefepime Related Compound E RS](#) in *Solution B*

▲Sensitivity solution: 0.0007 mg/mL of [USP Cefepime Hydrochloride RS](#) in *Solution B* ▲ (USP 1-May-2024)

System suitability

Samples: *System suitability solution* ▲ and *Sensitivity solution* ▲ (USP 1-May-2024)

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between cefepime related compound E and cefepime related compound D, *System suitability solution*

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

▲Signal-to-noise ratio: NLT 10, *Sensitivity solution* ▲ (USP 1-May-2024)

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Cefepime Hydrochloride taken:

$$\text{Result} = (r_U / r_T) \times (1/F) \times 100$$

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

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

F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#). [NOTE—The reporting ▲threshold ▲ (USP 1-May-2024) is 0.2% for ▲thiazolyloxime acetaldehyde ▲ (USP 1-May-2024) and 0.05% for all other related compounds.]

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cefepime amine derivative ^a ▲▲ (USP 1-May-2024)	0.4	0.48	0.1
Thiazolyglyoxalic methyloxime▲▲ (USP 1-May-2024) (cefepime related compound D)	0.5	1.0	0.1
Thiazolyloxime acetaldehyde ^b ▲▲ (USP 1-May-2024)	0.6	0.63	0.3
Cefepime dimer ^c ▲▲ (USP 1-May-2024)	0.8	1.0	0.2
Cefepime	1.0	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
E-Cefepime ^d ▲ (USP 1-May-2024)	2.7	0.71	0.3
Cefepime dioxime ^e ▲ (USP 1-May-2024)	4.3	0.71	0.2
Any ▲ (USP 1-May-2024) unspecified impurity	—	1.0	0.1
Total impurities ^f ▲ (USP 1-May-2024)	—	—	1.0

^a (6*R*,7*R*)-7-Amino-3-[(1-methylpyrrolidinium-1-yl)methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate.

^b (Z)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)-N-(2-oxoethyl)acetamide.

^c 1-[[[(6*R*,7*R*)-7-[(Z)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]-2-[(6*R*,7*R*)-2-carboxy-3-[(1-methylpyrrolidinium-1-yl)methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-7-ylcarbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methylpyrrolidinium chloride.

^d 1-[[[(6*R*,7*R*)-7-[(E)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methylpyrrolidinium chloride.

^e 1-[[[(6*R*,7*R*)-7-[(Z)-2-[(Z)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetamido]thiazol-4-yl]-2-(methoxyimino)acetamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methylpyrrolidinium chloride.

^f Excluding N-methylpyrrolidine.

SPECIFIC TESTS

- **BACTERIAL ENDOTOXINS TEST (85):** The level of bacterial endotoxins are such that the requirement under the relevant dosage form monograph(s) in which Cefepime Hydrochloride is used can be met. Where the label states that Cefepime Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Cefepime Hydrochloride is used can be met.
- **STERILITY TESTS (71):** Where the label states that Cefepime Hydrochloride is sterile, it meets the requirements.
- **CRYSTALLINITY (695):** Meets the requirements
- **WATER DETERMINATION (921), Method I:** 3.0%–4.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.
- **USP REFERENCE STANDARDS (11):**
[USP Cefepime Hydrochloride RS](#)
[USP Cefepime Related Compound D RS](#)
 Thiazolyglyoxalic methyloxime;
 (Z)-2-(2-Aminothiazol-4-yl)-2-(methoxyimino)acetic acid.
 $C_6H_7N_3O_3S$ 201.20
[USP Cefepime Related Compound E RS](#)
 Cefepime amine derivative;
 1-[[[(6*R*,7*R*)-7-Amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methylpyrrolidin-1-ium chloride.
 $C_{13}H_{20}ClN_3O_3S$ 333.83

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

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

Chromatographic Database Information: [Chromatographic Database](#)

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