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Change to read:

▲Cefazolin in Dextrose Injection

(Title for this monograph not to change until November 1, 2024.)

(Prior to November 1, 2024, the current practice of labeling the article of commerce with the name Cefazolin Injection may be continued. Use of the name Cefazolin in Dextrose Injection will be permitted as of May 1, 2022; however, the use of this name will not be mandatory until November 1, 2024. The 30-month extension will provide the time needed by manufacturers and users to make necessary changes.)▲

(Official 1-Nov-2024)

Change to read:

DEFINITION

▲Cefazolin in Dextrose Injection▲ (Official 1-Nov-2024) is a sterile solution ▲containing Cefazolin or Cefazolin Sodium, Dextrose, and suitable pH adjustors▲ (USP 1-May-2022) . It contains NLT 90.0% and NMT 115.0% of the labeled amount of cefazolin ($C_{14}H_{14}N_8O_4S_3$).

IDENTIFICATION

• **A.** 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:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

ASSAY

Change to read:

• **Procedure**

Buffer A: ▲0.9▲ (USP 1-May-2022) g/L of sodium phosphate, dibasic, anhydrous and ▲1.3▲ (USP 1-May-2022) g/L of citric acid monohydrate in water▲▲ (USP 1-May-2022)

Buffer B: ▲5.7▲ (USP 1-May-2022) g/L of sodium phosphate, dibasic, anhydrous and ▲3.6▲ (USP 1-May-2022) g/L of potassium phosphate, monobasic in water▲▲ (USP 1-May-2022)

Mobile phase: Acetonitrile and *Buffer A* (10:90)

▲▲ (USP 1-May-2022)

Standard solution: 0.05 mg/mL of USP Cefazolin RS▲▲ (USP 1-May-2022) in *Buffer B*

Sample stock solution: Allow 1 container of Injection to thaw prior to use, and mix. ▲Nominally▲ (USP 1-May-2022) 1 mg/mL of cefazolin from a suitable volume of Injection in *Buffer B*.

Sample solution: ▲Nominally▲ (USP 1-May-2022) 0.05 mg/mL of cefazolin from *Sample stock solution*▲▲ (USP 1-May-2022) in *Buffer B*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2022)

Column: ▲3.9-mm▲ (USP 1-May-2022) × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*▲▲ (USP 1-May-2022)

Suitability requirements

▲▲ (USP 1-May-2022)

Tailing factor: NMT 1.5

Relative standard deviation: NMT ▲1.0%▲ (USP 1-May-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cefazolin ($C_{14}H_{14}N_8O_4S_3$) in the portion of Injection taken:▲

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

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

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

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

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

P = potency of cefazolin in USP Cefazolin RS (mg/mg)

▲ (USP 1-May-2022)

Acceptance criteria: 90.0%–115.0%

IMPURITIES

Change to read:

• ▲**Organic Impurities**

Solution A: 3.4 g/L of potassium phosphate, monobasic in water

Solution B: Acetonitrile and *Solution A* (1:1)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
10	50	50
14	70	30
15	80	20
20	80	20

Diluent: Transfer 5.0 g of sodium acetate, anhydrous to a 1-L volumetric flask and add 900 mL of water and dissolve. Adjust with phosphoric acid to a pH of 4.5, and dilute with water to volume.

Standard stock solution: 1.0 mg/mL of USP Cefazolin RS in *Diluent*. Sonicate to dissolve, if necessary.

Standard solution: 0.03 mg/mL of USP Cefazolin RS from *Standard stock solution*, in *Diluent*

System suitability solution: Add 3.0 mL of 2.5 N sodium hydroxide TS to 25.0 mL of *Standard stock solution*. Mix and allow to react for 20 min. Dilute 5.0 mL of this solution with *Diluent* to 50 mL.

Sensitivity solution: 0.3 µg/mL of USP Cefazolin RS from *Standard solution*, in *Diluent*

Sample solution: Nominally 0.6 mg/mL of cefazolin from a previously thawed Injection, in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Autosampler temperature: 5°

Flow rate: 2 mL/min

Injection volume: 15 µL

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2.5 between methylthiadiazole thiol and cefazolin; NLT 2.5 between cefazolin and cefazolin epimer, *System suitability solution*

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

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each degradation product in the portion of Injection taken:

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

r_U = peak response of each degradation product from the *Sample solution*

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Methylthiadiazole thiol[a]	0.80	1.0
Cefazolin	1.00	—
Specified unidentified impurity	1.10	0.4
Cefazolin epimer[b,c]	1.20	—
Cefazolin thioxo analog[d]	1.30	0.3
Any individual unspecified degradation product	—	0.3
Total degradation products	—	2.0

[a] 5-Methyl-1,3,4-thiadiazole-2-thiol.

[b] (6*R*,7*S*)-7-[2-(1*H*-Tetrazol-1-yl)acetamido]-3-[(5-methyl-1,3,4-thiadiazol-2-ylthio)methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[c] Process impurity included in the table for identification purposes only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total impurities for the drug product.

[d] (6*R*,7*R*)-7-(2-(1*H*-Tetrazol-1-yl)acetamido)-3-[(5-methyl-2-thioxo-1,3,4-thiadiazol-3(2*H*)-yl)methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

▲ (USP 1-May-2022)

SPECIFIC TESTS

Change to read:

- **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-May-2022)
- **Sterility Tests ⟨71⟩**, *Test for Sterility of the Product to Be Examined, Membrane Filtration*: Meets the requirements
- **pH ⟨791⟩:** 4.5–7.0
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*. Maintain in the frozen state.
- **Labeling:** It meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*. The label states that it is to be thawed just before use, describes conditions for proper storage of the resultant solution, and directs that the solution is not to be refrozen.
- **USP Reference Standards ⟨11⟩**

USP Cefazolin RS

Topic/Question	Contact	Expert Committee
CEFAZOLIN IN DEXTROSE INJECTION	Documentary Standards Support	SM12020 Small Molecules 1

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