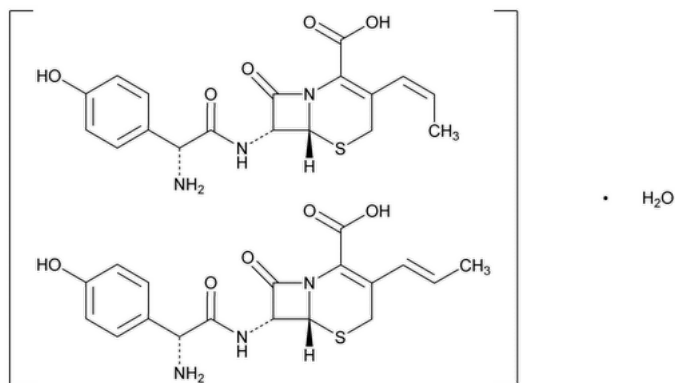


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Cefprozil



$C_{18}H_{19}N_3O_5 \cdot H_2O$ 407.44

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[amino(4-hydroxyphenyl)acetyl]amino]-8-oxo-3-(1-propenyl)-, monohydrate, [6R-[6 α ,7 β (R*)]]-;

(6R,7R)-7-[(R)-2-Amino-2-(p-hydroxyphenyl)acetamido]-8-oxo-3-propenyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate CAS RN®: 121123-17-9.

Anhydrous 389.43 CAS RN®: 92665-29-7.

DEFINITION

Cefprozil contains NLT 900 µg/mg and NMT 1050 µg/mg of cefprozil ($C_{18}H_{19}N_3O_5$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A.** **▲** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy](#): 197A or 197K **▲** (CN 1-May-2020)
- **B.** The retention times of the cefprozil (Z)-isomer and cefprozil (E)-isomer peaks from the *Sample solution* correspond to those of the Standard solutions, as obtained in the Assay.

ASSAY

• PROCEDURE

Buffer: 11.5 g/L of [monobasic ammonium phosphate](#) in [water](#). Adjust, if necessary, with [phosphoric acid](#) to a pH of 4.4.

Mobile phase: [Acetonitrile](#) and *Buffer* (100:900)

System suitability solution: 0.125 mg/mL each of [USP Cefprozil \(Z\)-Isomer RS](#) and [USP Cefprozil \(E\)-Isomer RS](#) in water. Use this solution within 6 h.

Standard solution 1: 0.25 mg/mL of [USP Cefprozil \(Z\)-Isomer RS](#) in water. Use this solution within 6 h.

Standard solution 2: 0.025 mg/mL of [USP Cefprozil \(E\)-Isomer RS](#) in [water](#). Use this solution within 6 h.

Sample solution: 0.3 mg/mL of Cefprozil in [water](#). Shake to dissolve. Use this solution within 6 h.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 30-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *System suitability solution* and *Standard solution 1*

[NOTE—The relative retention times for cefprozil (Z)-isomer and cefprozil (E)-isomer are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.5 between cefprozil (Z)-isomer and cefprozil (E)-isomer, *System suitability solution*

Tailing factor: 0.9–1.1, *Standard solution 1*

Relative standard deviation: NMT 2.0%, *Standard solution 1*

Analysis**Samples:** *Standard solution 1, Standard solution 2, and Sample solution*Calculate the amount (µg/mg) of cefprozil (Z)-isomer (C₁₈H₁₉N₃O₅S) in the portion of Cefprozil taken:

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

 r_U = peak response of cefprozil (Z)-isomer from the *Sample solution* r_S = peak response of cefprozil (Z)-isomer from *Standard solution 1* C_S = concentration of [USP Cefprozil \(Z\)-Isomer RS](#) in *Standard solution 1* (mg/mL) C_U = concentration of Cefprozil in the *Sample solution* (mg/mL) P = potency of [USP Cefprozil \(Z\)-Isomer RS](#) (µg/mg)Calculate the amount (µg/mg) of cefprozil (E)-isomer (C₁₈H₁₉N₃O₅S) in the portion of Cefprozil taken:

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

 r_U = peak response of cefprozil (E)-isomer from the *Sample solution* r_S = peak response of cefprozil (E)-isomer from *Standard solution 2* C_S = concentration of [USP Cefprozil \(E\)-Isomer RS](#) in *Standard solution 2* (mg/mL) C_U = concentration of Cefprozil in the *Sample solution* (mg/mL) P = potency of [USP Cefprozil \(E\)-Isomer RS](#) (µg/mg)Calculate the amount (µg/mg) of cefprozil (C₁₈H₁₉N₃O₅S) in the portion of Cefprozil taken by adding the values, in µg/mg, of the cefprozil (Z)-isomer and the cefprozil (E)-isomer.**Acceptance criteria:** 900–1050 µg/mg on the anhydrous basis**IMPURITIES****• ORGANIC IMPURITIES, PROCEDURE 1**Use *Organic Impurities, Procedure 1* when the impurity profile includes Z-cefprozil open ring, E-cefprozil open ring, and cefprozil related compound K.**Solution A:** 11.5 g/L of [monobasic ammonium phosphate](#) in [water](#). Adjust, if necessary, with [phosphoric acid](#) or [ammonium hydroxide](#) to a pH of 4.4.**Solution B:** [Acetonitrile](#) and *Solution A* (1:1)**Mobile phase:** See [Table 1](#).**Table 1**

Time (min)	Solution A (%)	Solution B (%)
0	81	19
8	81	19
20	36	64
25	36	64
27	81	19
30	81	19

[NOTE—These gradient elution times are established on an HPLC system with a dwell volume of approximately 1.3 mL. The gradient elution times in [Table 1](#) can be adjusted as necessary to achieve the separation described.]**Standard stock solution:** 0.25 mg/mL each of [USP Cefprozil \(Z\)-Isomer RS](#), [USP Amoxicillin Related Compound I RS](#), and [USP Cefprozil Related Compound D RS](#) in a mixture of [1 M hydrochloric acid](#) and *Solution A*. Prepare the solution as follows. Dissolve [USP Amoxicillin Related Compound I RS](#), [USP Cefprozil \(Z\)-Isomer RS](#), and [USP Cefprozil Related Compound D RS](#) in [1 M hydrochloric acid](#), using 20% of the final volume. Dilute with *Solution A* to volume.

Sensitivity solution: 2.5 µg/mL each of cefprozil (Z)-isomer, amoxicillin related compound I, and cefprozil related compound D in *Solution A* from *Standard stock solution*. Store the solution at 4°, and use within 8 h.

Standard solution: 50 µg/mL each of cefprozil (Z)-isomer, amoxicillin related compound I, and cefprozil related compound D in *Solution A* from the *Standard stock solution*. Store the solution at 4°, and use within 12 h.

Sample solution: 5 mg/mL of Cefprozil in a mixture of [1 M hydrochloric acid](#) and *Solution A*, prepared as follows. Dissolve the Cefprozil first in [1 M hydrochloric acid](#) using 4% of the final volume, and then dilute with *Solution A* to volume. Store the solution at 4°, and use within 3 h.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

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

Temperatures

Autosampler: 4°

Column: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[NOTE—[USP Cefprozil Related Compound D RS](#) contains the (Z)- and (E)-isomers of cefprozil related compound D. See [Table 2](#) for relative retention times.]

Suitability requirements

Resolution: NLT 1.4 between the (E)-isomer of cefprozil related compound D and cefprozil (Z)-isomer, *Standard solution*

Relative standard deviation: NMT 10.0% for cefprozil, amoxicillin related compound I, and each isomer of cefprozil related compound D, *Standard solution*

Signal-to-noise ratio: NLT 10 for cefprozil, amoxicillin related compound I, and each isomer of cefprozil related compound D, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amoxicillin related compound I in the portion of Cefprozil taken:

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

r_U = peak response of amoxicillin related compound I from the *Sample solution*

r_S = peak response of amoxicillin related compound I from the *Standard solution*

C_S = concentration of [USP Amoxicillin Related Compound I RS](#) in the *Standard solution* (mg/mL)

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

P = potency of amoxicillin related compound I in [USP Amoxicillin Related Compound I RS](#) (mg/mg)

Calculate the percentage of cefprozil related compound D in the portion of Cefprozil taken:

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

r_U = sum of the responses for cefprozil related compound D (Z)-isomer and cefprozil related compound D (E)-isomer from the *Sample solution*

r_S = peak response of cefprozil related compound D (Z)-isomer from the *Standard solution*

C_S = concentration of [USP Cefprozil Related Compound D RS](#) in the *Standard solution* (mg/mL)

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

P = potency of cefprozil related compound D (Z)-isomer in [USP Cefprozil Related Compound D RS](#) (mg/mg)

Calculate the percentage of each of the other impurities in the portion of Cefprozil taken:

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

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

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

C_S = concentration of [USP Cefprozil \(Z\)-Isomer RS](#) in the *Standard solution* (mg/mL)