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Cefpodoxime Proxetil

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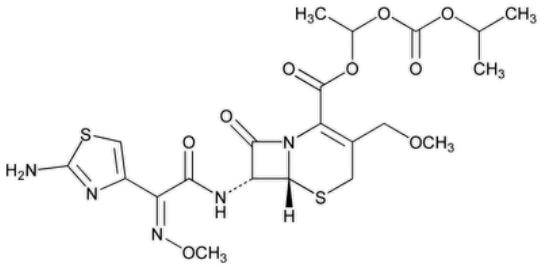

$C_{21}H_{27}N_5O_9S_2$ ▲557.59▲ (CN 1-Aug-2024)

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-,1-[[(1-methylethoxy)carbonyl]oxy]ethyl ester, [6*R*-[6α,7β(*Z*)]]-.

▲(*RS*)-1-[(Isopropoxycarbonyl)oxy]ethyl (6*R*,7*R*)-7-[2-(2-amino-4-thiazolyl)-2-[(*Z*)-methoxyimino]acetamido]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate▲ (CN 1-Aug-2024) CAS RN®: 87239-81-4; UNII: 2TB00A1Z7N.

» Cefpodoxime Proxetil contains the equivalent of not less than 690 µg and not more than 804 µg of cefpodoxime ($C_{15}H_{17}N_5O_6S_2$) per mg, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers, at a temperature not exceeding 25°.

USP Reference standards ⟨11⟩—

USP Cefpodoxime Proxetil RS

Identification—

A: *Spectroscopic Identification Tests ⟨197⟩, Infrared Spectroscopy: 197M*

B: *Spectroscopic Identification Tests ⟨197⟩, Ultraviolet-Visible Spectroscopy: 197U*—

Solution: 15 µg per mL.

Medium: acetonitrile.

C: Dissolve 1 mg of it in 4 mL of water, add 1 mL of 1 N sulfuric acid while cooling in an ice bath, add 1 mL of a freshly prepared solution of sodium nitrite (1 in 100), allow to stand for 2 minutes, then add 1 mL of ammonium sulfamate solution (1 in 100). Allow to stand for 1 minute, and add 1 mL of *N*-(1-naphthyl)ethylenediamine dihydrochloride TS: a red-purple color develops.

Specific rotation ⟨781S⟩**:** between +35.0° and +48.0°.

Test solution: 10 mg per mL, in methanol.

Water Determination, *Method I* ⟨921⟩**:** not more than 3.0%.

Residue on ignition ⟨281⟩**:** not more than 0.2%.

Isomer ratio—Using the chromatogram of the *Assay preparation* obtained in the *Assay,* calculate the ratio of the cefpodoxime proxetil *R*-epimer peak response to the sum of the peak responses of the cefpodoxime proxetil *S*-epimer peak and the cefpodoxime proxetil *R*-epimer peak: the ratio is between 0.5 and 0.6.

Chromatographic purity—

Solution A—Prepare filtered and degassed 0.02 M ammonium acetate.

Solution B—Use filtered and degassed acetonitrile.

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⟩).

Diluent—Prepare a degassed mixture of water and acetonitrile (2:1).

System suitability solution—Dissolve a quantity of USP Cefpodoxime Proxetil RS in *Diluent* to obtain a solution containing about 10 µg per mL. [Note—A volume of methanol not exceeding 10% of the total volume in the final solution may be used to facilitate dissolution.]

Test solution—Transfer about 50 mg of Cefpodoxime Proxetil, accurately weighed, to a 50-mL volumetric flask, dissolve in 5 mL of methanol, using sonication if necessary, dilute with *Diluent* to volume, and mix. This solution should be injected promptly, but may be analyzed within 24 hours when stored at 8°.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 260-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The column temperature is maintained at a constant temperature of about 30°. The flow rate is about

2 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0	90	10	equilibration (10 minutes)
0–10	90→68	10→32	linear gradient
10–40	68	32	isocratic
40–80	68→50	32→50	linear gradient
80–85	50	50	isocratic
85–90	50→25	50→75	linear gradient
90–95	25	75	isocratic
95–100	25→90	75→10	linear gradient

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the retention time for cefpodoxime proxetil *R*-epimer is between 37 and 42 minutes; the relative retention times are about 0.9 for cefpodoxime proxetil *S*-epimer and 1.0 for cefpodoxime proxetil *R*-epimer; the resolution, *R,* between cefpodoxime proxetil *S*-epimer and cefpodoxime proxetil *R*-epimer is not less than 4.0; the column efficiency is not less than 19,000 theoretical plates determined from the cefpodoxime proxetil *R*-epimer peak; and the relative standard deviation for replicate injections determined from the sum of the areas of the cefpodoxime proxetil *S*-epimer and cefpodoxime proxetil *R*-epimer peaks is not more than 2.0%.

Procedure—Inject a volume (about 20 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure all of the peak areas. Calculate the percentage of each impurity in the portion of Cefpodoxime Proxetil taken by the formula:

$$100(r_i/r_s)$$

in which r_i is the peak area for each impurity; and r_s is the sum of the areas of all the peaks: not more than 3.0% of any peak at a relative retention time of about 0.86 is found; not more than 1.0% for any peak at relative retention times of about 1.27, 1.39, and other individual peaks having relative retention times higher than 2.0 is found; not more than 0.5% of any other individual impurity is found; and not more than 6.0% of total impurities is found, impurity peaks of less than 0.05% being disregarded.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of 0.02 M ammonium acetate and acetonitrile (6:4). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a degassed mixture of water and acetonitrile (6:4).

Standard preparation—Transfer about 25 mg of USP Cefpodoxime Proxetil RS, accurately weighed, to a 50-mL volumetric flask, dissolve in 5 mL of methanol, dilute with *Diluent* to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Diluent* to volume, mix, and pass through a filter having a 0.45-µm or finer porosity.

Assay preparation—Transfer about 50 mg of Cefpodoxime Proxetil, accurately weighed, to a 100-mL volumetric flask, dissolve in 10 mL of methanol, dilute with *Diluent* to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Diluent* to volume, mix, and pass through a filter having a 0.45-µm or finer porosity.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 235-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 2 mL per minute. The column temperature is maintained at a constant temperature of about 30°. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.9 for cefpodoxime proxetil *S*-epimer and 1.0 for cefpodoxime proxetil *R*-epimer; the resolution, *R,* between cefpodoxime proxetil *S*-epimer and cefpodoxime proxetil *R*-epimer is not less than 2.5; the tailing factor for cefpodoxime proxetil *R*-epimer is not more than 1.5; and the relative standard deviation determined from the sum of the areas of the cefpodoxime proxetil *S*-epimer and cefpodoxime proxetil *R*-epimer peaks for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 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 cefpodoxime ($C_{15}H_{17}N_5O_6S_2$) in each mg of Cefpodoxime Proxetil taken by the formula:

$$2000(CP/W)(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Cefpodoxime Proxetil RS in the *Standard preparation; P* is the designated potency, in µg per mg, of cefpodoxime ($C_{15}H_{17}N_5O_6S_2$) in USP Cefpodoxime Proxetil RS; *W* is the weight, in mg, of Cefpodoxime Proxetil taken to prepare the

Assay preparation; and r_U and r_S are the sums of the peak responses for cefpodoxime proxetil *S*-epimer and cefpodoxime proxetil *R*-epimer obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
CEFPODOXIME PROXETIL	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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