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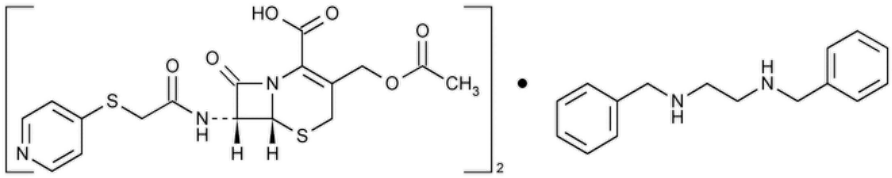
Cephapirin Benzathine



$(C_{17}H_{17}N_3O_6S_2)_2 \cdot C_{16}H_{20}N_2$ 1087.27

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyl-oxy)methyl]-8-oxo-7-[[(4-pyridinylthio)ace tyl]amino]-, (6*R-trans*)-, compd. with *N,N'*-bis(phenylmethyl)-1,2-ethanediamine (2:1).

(6*R,*7*R*)-3-(hydroxymethyl)-8-oxo-7-[2-(4-pyridylthio) acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid compound with *N,N'*-dibenzylethylenediamine (2:1) CAS RN®: 97468-37-6; UNII: 90G868409O.

» Cephapirin Benzathine contains the equivalent of not less than 715 µg and not more than 820 µg of cephapirin ($C_{17}H_{17}N_3O_6S_2$) per mg.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate that it is for veterinary use only.

USP Reference standards ⟨11⟩—

USP Cephapirin Benzathine RS
USP Cephapirin Sodium RS

Change to read:

▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: 197K.▲ (CN 1-May-2020)

Crystallinity ⟨695⟩: meets the requirements.

pH ⟨791⟩: between 4.0 and 7.0, in a suspension (1 in 10).

Water Determination, *Method I* ⟨921⟩ : not more than 5.0%.

Benzathine content—Using about 1 g of Cephapirin Benzathine, accurately weighed, proceed as directed in the test for *Benzathine content* under *Penicillin G Benzathine:* between 20.0% and 24.0% of benzathine ($C_{16}H_{20}N_2$), calculated on the anhydrous basis, is found.

Assay—

Solution A—Transfer about 26.2 mL of acetic acid and about 99.12 g of potassium acetate to a 4-L volumetric flask. Add 2000 mL of water, and mix to dissolve. Dilute with water to volume, and pass through a 0.45-µm nylon filter.

Solution B—Use 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⟩).

Extraction solution: a mixture of 400 mL of acetic acid and 600 mL of water.

Dilution buffer—Dissolve about 205 g of potassium acetate in about 800 mL of water. Adjust with acetic acid to a pH of 7.5 to 8.2. Dilute with water to 1000 mL, and pass through a 0.45-µm nylon filter.

10% Acetic acid solution—Add about 10.0 mL of acetic acid to a 100-mL volumetric flask. Mix, and dilute with water to volume.

System suitability solution—Dissolve an accurately weighed quantity of USP Cephapirin Sodium RS in *10% Acetic acid solution* to prepare a solution containing a known concentration of about 2.0 mg per mL. Heat the solution at 50° for 12 to 18 hours.

Standard preparation—In duplicate, accurately weigh about 50 mg of USP Cephapirin Sodium RS, and transfer into a 25-mL volumetric flask. Add about 2.5 mL of *Extraction solution* and about 15.0 mL of *Dilution buffer,* and agitate to dissolve. Add 7.0 mL of acetonitrile, and mix well. Allow the solution to return to room temperature, and dilute with water to volume.

Assay preparation—In duplicate, weigh about 60 mg of Cephapirin Benzathine, and transfer into a 25-mL volumetric flask. Add about 2.5 mL of *Extraction solution* and 15.0 mL of *Dilution buffer,* and mix to dissolve. Add 7.0 mL of acetonitrile, and mix. Allow the flask to return to room temperature, and dilute with water to volume.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 260-nm detector, a 3.2-mm × 15-mm guard column that contains 7-µm packing L1 and a 3.9-mm × 15-cm analytical column that contains 4-µm packing L1. The flow rate is about

2.0 mL per minute, and the columns are heated to 40°. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–6	91.5	8.5	isocratic
6–10	91.5→80.0	8.5→20.0	linear
10–12	80.0	20.0	isocratic
12	80.0→91.5	20.0→8.5	return to initial
12–21	91.5	8.5	re-equilibration

Chromatograph the *System suitability solution* and the *Standard preparation,* and record the peak heights and valleys as directed for *Procedure.* Using the results from the *System suitability solution,* calculate the percentage of the height of the valley taken by the formula:

$$100(r_V/r_i)$$

in which r_V is the height of the valley between cephapirin and any impurity; and r_i is the impurity peak height. The percentage of the height of the valley is not more than 25% for the impurity peaks adjacent to the cephapirin peak.

[NOTE—The *System suitability solution* is acceptable as long as the cephapirin peak is larger than the two peaks on either side of the cephapirin peak.]

The relative standard deviation for replicate injections of the *Standard preparation* is not more than 3.0%.

Procedure—Separately inject equal volumes (about 2 µL) of the duplicate *Standard preparation* and the duplicate *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in µg, of $C_{17}H_{17}N_3O_6S_2$ in each mg of Cephapirin Benzathine taken by the formula:

$$P(W_S/W_U)(V_U/V_S)(r_U/r_S)$$

in which P is the assigned potency, in µg of cephapirin per mg, of USP Cephapirin Sodium RS; W_S and W_U are the quantities of USP Cephapirin Sodium RS and Cephapirin Benzathine, in mg, used to prepare the *Standard preparation* and the *Assay preparation,* respectively; V_S and V_U are the final volumes, in mL, of the *Standard preparation* and the *Assay preparation,* respectively; and r_U and r_S are the average peak areas of the cephapirin peaks 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
CEPHAPIRIN BENZATHINE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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