Cephapirin Benzathine

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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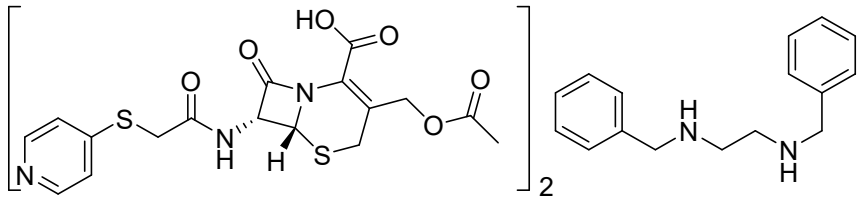
Further follow-up action as required.	

Cephapirin Benzathine



$(C_{17}H_{17}N_3O_6S_2)_2.\ C_{16}H_{20}N_2$ Mol Wt. 1087.3

Cephapirin Benzathine is 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).

Cephapirin Benzathine contains the equivalent of not less than 715 µg and not more than 820 µg of the stated amount of cephapirin, ($C_{17}H_{17}N_4O_2S_2$) per mg.

Category. Mastitis in dairy cattle during the dry period.

Description. A white, crystalline powder.

Identification

Determine by infrared absorption spectrophotometry (2.4.6).Compare the spectrum with that obtained with *cephapirin benzathine IPRS* or with the reference spectrum of cephapirin benzathine.

Tests

Crystallinity (2.4.37). Complies with the test for crystallinity.

pH (2.4.24). 4.0 to 7.0. determined in a 10 per cent w/v solution.

Benzathine content. 20.0 per cent to 24.0 per cent, calculated on the anhydrous basis.

To 1 g of the substance under the examination, add 30 ml of a saturated solution of *sodium chloride* and 10 ml of *5 M sodium hydroxide* and extract with four successive quantities, each of 50 ml of *ether*. Wash the combined *ether* extracts with three successive quantities, each of 10 ml, of *water*. Extract the combined washing with 25 ml of *ether* and add the ether extract to the *water* washed combined *ether* extracts. Evaporate this combined *ether* solution to a volume of about 5 ml, add 2 ml of *ethanol* and evaporate to dryness. Dissolve the residue in 50 ml of *glacial acetic acid* and titrate with *0.1 M perchloric acid* using 1 ml of *p-naphtholbenze* in solution as indicator.

1 ml of *0.1 M perchloric acid* is equivalent to 0.01202 g of $C_{16}H_{20}N_2$,

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals, Method B (20 ppm).

Water (2.3.43). Not more than 5.0 per cent.

Assay. Determine by liquid chromatography (2.4.14).

Solution A. Dissolve 20.5 g of *potassium acetate* in 100 ml of *water*, adjusted to pH 7.5 to 8.2 with *glacial acetic acid*,

Solvent mixture. 40 volumes of *acetic acid* and 60 volumes of *water*.

Test solution. Transfer 60 mg of the substance under examination to a 25-ml volumetric flask, add 2.5 ml of the solvent mixture and 15 ml of solution A, agitate to dissolve. Add 7 ml of *acetonitrile* and dilute to volume with *water*.

Reference solution (a). Transfer 50 mg of *cephapirin sodium IPRS* to a 25-ml volumetric flask, add 2.5 ml of the solvent mixture and 15 ml of solution A, agitate to dissolve. Add 7 ml of *acetonitrile* and dilute to volume with *water*.

Reference solution (b). A 0.2 per cent w/v solution of *cephapirin sodium IPRS* in 10 per cent v/v solution of *acetic acid*. Heat the solution at 50° for 12 hours to 18 hours.

Chromatographic system
- a stainless steel column 15 cm × 3.9 mm, packed with octadecylsilane bonded to porous silica (4 µm) and a guard column 15cm × 3.2 mm, packed with the same column material (7 µm),
- column temperature: 40º,
- mobile phase A: a buffer solution prepared by dissolving 24.78 g of *potassium acetate* in *water*, add 6.55 ml of *glacial acetic acid* and dilute to 1000 ml with *water.*
  B: *acetonitrile,*
- a gradient programme using the conditions given below,
- flow rate: 2 ml per minute,
- spectrophotometer set at 260 nm,
- injection volume: 2 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	91.5	8.5
6	91.5	8.5
10	80	20
12	80	20
21	91.5	8.5
25	91.5	8.5

Inject reference solution (a) and (b). The test is not valid until the percentage of the height of the valley is not more than 25 per cent for impurity peaks adjacent to the cephapirin peak in chromatogram obtained with the reference solution (b) and the relative standard deviation for replicate injections is not more than 3.0 per cent in the chromatogram obtained with the reference solution (a).

Calculate the percentage of height of valley, using following expression;

$$100\frac{r_V}{r_I}$$

Where,

r_V = height of the valley between cephapirin and any impurity.
r_I = height of the impurity 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.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{17}H_{17}N_3O_6S_2$.

Storage. Store protected from moisture, at a temperature not exceeding 30º.

Cephapirin Benzathine:
Solubility: Practically insoluble in *water*, in *ether* and in *toluene*, insoluble in *ethanol*, soluble in *0.1 M hydrochloric acid.*