Cefuroxime Axetil Oral Suspension

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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.

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Cefuroxime Axetil Oral Suspension

Cefuroxime Axetil Oral Suspension is a suspension cefuroxime axetil in a suitable flavoured vehicle. It is filled in a sealed container.

The suspension is constituted by dispersing the contents of the sealed container in the specified volume of water just before use.

Cefuroxime axetil Oral Suspension contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of cefuroxime, $C_{16}H_{16}N_4O_8S$.

When stored at the temperature and for the period stated on the label during which the constituted suspension may be expected to be satisfactory for use, it contains not less than 90.0 per cent of the stated amount of cefuroxime axetil, $C_{16}H_{16}N_4O_8S$.

Usual strength.125 mg per 5 ml.

Identification

A. Shake a quantity of oral suspension with sufficient *methanol* to produce a solution containing 0.00131 per cent w/v of cefuroxime. When examined, in the range 230 nm to 320 nm, (2.4.7) the resulting solution shows an absorption maximum at about 276 nm.

B. In the Assay, the principal peaks in the chromatogram obtained with the test solution corresponds to the peaks due to diastereo isomers A and B of cefuroxime axetil in the chromatogram obtained with the reference solution.

Tests

pH (2.4.24). 3.5 to 7.0.

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium.900 ml of a buffer solution prepared by dissolving 14.3 g of *disodium hydrogen orthophosphate* and 4.2 g of *sodium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 7.0 with 20 per cent v/v solution of *orthophosphoric acid* or *1 M sodium hydroxide*.

Speed and time. 50 rpm and 30 minutes.

Shake the containers containing the oral suspension under examination for 30 seconds and introduce one dose at a depth of 1 cm below the meniscus to the medium in the each dissolution vessel.

Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, dilute suitably, if necessary, with the dissolution medium, at the maximum at about 282 nm (2.4.7). Calculate the content of $C_{16}H_{16}N_4O_8S$ in the medium from the absorbance obtained from a solution prepared by dissolving a suitable quantity of *cefuroxime axetil IPRS* in 5 ml of *methanol* and dilute to 100.0 ml with the dissolution medium. Further dilute with dissolution medium to obtain a solution having similar concentration as the test solution

1 mg of cefuroxime axetil, $C_{20}H_{22}N_4O_{10}S$ is equivalent to 0.8313 mg of cefuroxime, $C_{16}H_{16}N_4O_8S$.

Q. Not less than 60 per cent of the stated amount of $C_{16}H_{16}N_4O_8S$.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Shake a weighed quantity of oral suspension with *methanol* with the aid of ultrasound for 5 minutes with occasional swirling to obtain a solution containing equivalent of 0.25per cent w/v of cefuroxime. Allow to cool to room temperature, shake vigorously and allow to stand for 10 minutes. Dilute 10.0 ml of resulting solution to 50.0 ml with 23 per

cent v/v of *methanol*, filter. [*NOTE — The solution should be used immediately or store, protected from light, at a temperature of 2° to 8° before analysis*].

Reference solution(a). A solution of *cefuroxime axetil IPRS* containing 0.0005 per cent w/v of cefuroxime in the mobile phase.

Reference solution (b). Heat 5 ml of the test solution at 60º for one hour to generated D^3-isomer.

Reference solution(c). Expose 5 ml of the test solution to ultraviolet light at 254 nm for 24 hours to generate E-isomer.

Chromatographic system

- a stainless steel column 25 cm × 4.6 mm, packed with trimethylsilane bonded to silica (5 µm) (Such as Hypersil SAS),
- mobile phase: a mixture of 38 volumes of *methanol* and 62 volumes of *0.2 M ammonium dihydrogen orthophosphate,*
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 278 nm,
- injection volume: 20 µl.

Name	Relative retention time
Cefuroxime	0.35
Cefuroxime axetil diastereoisomer B	0.9
Cefuroxime axetil diastereoisomer A	1.0
CefuroximeD^3-isomers[1]	1.2
CefuroximeE-isomers[2]	1.7, 2.1

[1]l-(acetyloxy)ethyl (6R,7R)-3-[(carbamoyloxy)methyl]-7[[(2Z}-2-(furao-2-yl)-2-(methoxyimino)acetyl]amino]-8oxo-5-thia-l-azabicyclo[4.2.0]oct-3-ene-2-carboxylate,
[2](1RS)-1-(acetyloxy)ethyl (6R,7R)-3-[(carbamoyloxy)methyl]-7- [[(2E)-2-(furao-2-yl)-2(methoxyimino)acetyl]amino]-8-oxo-5-thia-l-azabicyclo[4.2.0]oct-2-ene-2carboxylale.

Inject reference solution (b) and (c) to identify the peaks due to cefuroxime D^3-isomers and cefuroxime E-isomers, respectively.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to cefuroxime axetil diastereo isomer A and cefuroxime axetil D^3-isomer is not less than 1.5.

Inject reference solution (a)and test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to cefuroxime is not more than the sum of the area of principal peaks in the chromatogram obtained with reference solution (a) (1.0 per cent), the sum of the areas of the peaks corresponding to cefuroxime *E*-isomers is not more than 1.5 times the sum of the area of principal peaks in the chromatogram obtained with reference solution (a) (1.5 per cent), the area of any peak corresponding to cefuroxime D^3-isomers is not more than twice the sum of the area of principal peaks in the chromatogram obtained with reference solution (a) (2.0 per cent), the area of any other secondary peak is not more than 0.5 times the sum of the area of principal peaks in the chromatogram obtained with reference solution (a) (0.5 per cent), and the sum of all the secondary peaks is not more than 4.5 times the sum of the area of principal peaks in the chromatogram obtained with reference solution (a) (4.5 per cent). Ignore any peak with an area less than 0.05 times the sum of the area of principal peaks in the chromatogram obtained with reference solution (a) (0.05 per cent).

Other tests. Comply with the tests stated under Oral Liquids.

Assay. Determine by liquid chromatography (2.4.14).

[*NOTE —The solutions should be used immediately or store, protected from light, at a temperature of 2° to 8° before analysis*].

Test solution. Shake a weighed quantity of oral suspension with *methanol* with the aid of ultrasound for 5 minutes with occasional swirling to obtain a solution containing equivalent of 0.25 per cent w/v of cefuroxime. Allow to cool to room

temperature, shake vigorously and allow to stand for 10 minutes. Dilute 10.0 ml of the resulting solution to 50.0 ml with 23 per cent v/v of *methanol*, filter.

Reference solution. A solution of *cefuroxime axetil IPRS* in the *methanol* containing 0.25 per cent w/v of cefuroxime in *methanol*. Dilute 10.0 ml of the solution to 50.0 ml with *23 per cent v/v of methanol*.

Use the chromatographic system as described under Related substances.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to cefuroxime axetil diastereo isomer A and cefuroxime axetil diastereo isomer B is not less than 1.5.

Inject the reference solution and the test solution.

Determine the weight per ml of the oral suspension (2.4.29) and calculate the content of $C_{16}H_{16}N_4O_8S$ in the suspension as the sum of the areas of the two peaks corresponding to diastereo isomers A and B.

1 mg of cefuroxime axetil, $C_{20}H_{22}N_4O_{10}S$ is equivalent to 0.8313 mg of cefuroxime, $C_{16}H_{16}N_4O_8S$.

Storage. Store protected from light, at a temperature not exceeding 30°.

Labelling. The quantity of active ingredient is stated in terms of the equivalent amount of cefuroxime.