Ciprofloxacin for 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.

Document History and Schedule for the Adoption Process

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Ciprofloxacinfor Oral Suspension

Ciprofloxacin for Oral Suspension is a mixture consisting of ciprofloxacin with buffering agent and other excipients. It contains a suitable flavouring agent. 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.

Ciprofloxacin for Oral Suspension contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of ciprofloxacin, $C_{17}H_{18}FN_3O_3$.

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 80.0 per cent of the stated amount of ciprofloxacin, $C_{17}H_{18}FN_3O_3$.

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

Usual strengths. 250 mg per 5 ml; 500 mg per 5 ml.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

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

The constituted suspension complies with the tests stated under Oral liquids and with the following tests.

Dissolution (2.5.2).

Apparatus No. 2 (Paddle),
Medium. 900 ml of buffer solution prepared by dissolving 6.8 g of *sodium acetate* in 1000 ml of *water*, adjusted to pH 4.5 with *glacial acetic acid* and add 0.25 g of *polyoxyethylene23 lauryl ether*,

Speed and time.100 rpm and 30 minutes.

Constitute ciprofloxacin for oral Suspension as directed in the labeling. Using a 5-ml syringe, collect 5 ml of the constituted oral suspension and record the weight, gently empty the contents of each syringe into the bottom of each vessel containing medium. Reweigh each syringe and determine the weight of ciprofloxacin for oral suspension delivered in to each vessel.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium.

Reference solution (a). A 0.0055 per cent w/v solution of *ciprofloxacin IPRS* in the dissolution medium.

Chromatographic system
– a stainless steel column 15 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS-3V),
– column temperature: 30°,
– sample temperature: 10º,
– mobile phase: a mixture of 70 volumes of a buffer solution prepared by dissolving 13.6 g of *sodium acetate* in 1000 ml of *water*, add 1 ml of *triethylamine*, adjusted to pH 4.0 with *orthophosphoric acid* and 30 volumes of *methanol*,

− flow rate: 1.5 ml per minute,
− spectrophotometer set at 278 nm,
− injection volume: 5µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{17}H_{18}FN_3O_3$in the medium.

Q. Not less than 85 per cent of the stated amount of $C_{17}H_{18}FN_3O_2$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture.30 volumes of *0.1 M hydrochloric acid* and 70 volumes of *methanol.*

Test solution. Disperse a quantity of the constituted oral suspension containing 50mg of Ciprofloxacin in 60 ml of solvent mixture with the aid of ultrasound, for 10 minutes with intermittent shaking and dilute to 100.0 ml with the solvent mixture, filter.

Reference solution. A 0.0005 per cent w/v solution of *ciprofloxacin IPRS* in the solvent mixture.

Chromatographic system
- astainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS-3V),
- column temperature: 40°,
- sample temperature: 10º,
- mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 13.6 g of *sodium acetate* in 1000 ml of *water,* add 1 ml of *triethylamine*, adjusted to pH 2.0 with *orthophosphoric acid* and 20 volumes of *methanol*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 278 nm,
- injection volume: 10 µl.

Name retention time	Relative factor	Correction
Ciprofloxacin ethylenediamine analog[1]	0.75	0.77
Ciprofloxacin	1.0	---
7-chloro-6-piperazinyl analog[2]	1.15	2.13
Chlorociprofloxacin[3]	2.20	1.64

[1]7-(2-Aminoethylamino)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid.
[2]7-Chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.
[3]6-Chloro-1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent.

Inject the reference solution and the test solution.In the chromatogram obtained with the test solution, the area of any peak corresponding to ciprofloxacin ethylenediamine analog is not more than 0.3 times the area of the principal peak in the chromatogram obtained with the reference solution (0.3 per cent), the area of any peak corresponding to 7-chloro-6-piperazinyl analog and chloro ciprofloxacin, each of, is not more than 0.2 times the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent), the area of any other secondary peak is not more than 0.2 times the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent) and the sum of areas of all the secondary peaks is not more than of the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the constituted oral suspension containing 0.5 g of Ciprofloxacin in 250 ml of *0.1 M hydrochloric acid* with the aid of ultrasound, for 15 minutes with intermittent shaking, add 25 ml of *methanol*, and dilute to 500.0 ml with*0.1 M hydrochloric acid*. Centrifuge a portion of the solution. Dilute 5.0 ml of the supernatant to 50.0 ml with the mobile phase, filter.

Reference solution. A 0.1 per cent w/v solution of *ciprofloxacin IPRS* in *0.1 M hydrochloric acid*. Dilute 5.0 ml of the solution to 50.0 ml with the mobile phase.

Chromatographic system

- astainless steel column 15 cm × 4.6 mm, packed with base deactivated octadecylsilane bonded to porous silica (5 µm), (Such as Hypersil BDS C18),
- column temperature: 40°,
- sample temperature: 10º,
- mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 13.6 g of *sodium acetate* in 1000 ml of *water*, add 1 ml of *triethylamine*, adjusted to pH 2.0 with *orthophosphoric acid* and 20 volumes of *methanol*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 278 nm,
- injection volume: 5 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution. Run the chromatogram 1.6 times the retention time of the principal peak.

Determine the weight per ml of the oral suspension (2.4.29) and calculate the content of $C_{17}H_{18}FN_3O_3$ in the suspension.

Repeat the procedure using a portion of the constituted suspension that has been stored at the temperature and for the period stated on the label.

Microbial contamination (2.2.9). Total aerobic viable count is not more than 10^3 CFU per g and total fungal count is not more than10^2 CFU per g determined by plate count. 1 g is free from *Escherichia coli*.

Labelling. The label states the temperature of storage and the period during which the constituted suspension may be expected to be satisfactory for use.