Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Nepafenac Ophthalmic Suspension

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This draft proposal contains monograph text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

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

Description	Details
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Further follow-up action as required.	

Nepafenac Ophthalmic Suspension

Nepafenac Ophthalmic Suspension is a sterile aqueous suspension of Nepafenac in a suitable aqueous vehicle.

Nepafenac Ophthalmic Suspension contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{15}H_{14}N_2O_2$.

Usual strength. 0.1 per cent w/v.

Identification

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

Tests

pH (2.4.24). 6.4 to 8.4.

Weight per ml (2.4.29). 0.9 g to 1.1 g.

Osmolarity (2.4.23). 250 mOsmol per kg to 350 mOsmol per kg.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 80 volumes of *methanol* and 20 volumes of *water*.

Test solution. Mix the content of 10 vials. Weigh and transfer a quantity of the suspension containing 5 mg of Nepafenac, to a 50-ml volumetric flask, add 30 ml of the solvent mixture and sonicate for 10 minutes with intermittent shaking and dilute to volume with the solvent mixture. Centrifuge a portion of the solution at 4000 rpm for 5 minutes. Use the clear supernatant.

NOTE- Maintain the temperature of the water bath in the sonicator between 15°-20°during sonication.

Reference solution. A 0.0001 per cent w/v solution of *nepafenac IPRS* in the solvent mixture.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS 3),
- mobile phase. a mixture of 65 volumes of buffer solution prepared by dissolving 1.26 g of *ammonium formate* in 1000 ml of *water*, adjusted to pH 5.6 with *orthophosphoric acid* and 35 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 239 nm,
- injection volume: 20 µl.

Name	Relative retention time	Correction factor
Nepafenac impurity A[1]	0.52	1.25
Nepafenac (Retention time: about 14 minutes)	1.00	---
Nepafenac impurity B[2]	1.38	1.08
Nepafenac impurity C[3]	1.66	1.15

[1]3-(phenylcarbonyl)phenyl]acetic acid,
[2]2-[2-amino-3-(phenylcarbonyl)phenyl]-N-methylacetamide,
[3]7-(phenylcarbonyl)-1,3-dihydro-2H-indol-2-one.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, 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 nepafenac impurity A, nepafenac impurity B and nepafenac impurity C, each of, is not more than the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent) and the sum of the areas of all the secondary peaks is not more than 3 times the area of the principal peak in the chromatogram obtained with the reference solution (3.0 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).

Stabilized Oxychloro Complex. Not less than 80.0 per cent of the stated amount of $C_{15}H_{14}N_2O_2$.

Mix the content of 10 vials. Weigh and transfer a quantity of the suspension containing 0.5 mg of Stabilized Oxychloro Complex to a 250-ml conical flask, add 5.0 ml of 0.01 per cent w/v of *disodium edentate solution*, 10 ml of 10 per cent w/v *potassium iodide solution* and 10 ml of 10 per cent v/v of *sulphuric acid solution*. Keep the conical flask in dark place for about 2 minutes and titrate with *0.005 M sodium thiosulphate* until color changes from dark blue to colorless, using 1 ml of *starch solution* as indicator. Carry out a blank titration.

1.0 ml of *0.005 M sodium thiosulphate* is equivalent to 0.000113 g of stabilized oxychloro complex.

Sterility (2.2.11). Complies with the test for sterility.

Other tests. Comply with the tests stated under Eye Drops.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances with the following modifications.

Test solution. Mix the contents of 10 vials. Weigh and transfer a quantity of the suspension containing about 10 mg of Nepafenac to 200-ml volumetric flask, add 100 ml of the solvent mixture, shake to dissolve and sonicate for 10 minutes with intermittent shaking and dilute to volume with the solvent mixture.

Reference solution. A 0.005 per cent w/v solution of *nepafenac IPRS* in the solvent mixture.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, 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.

Determine the weight per ml (2.4.29) of the suspension and calculate the content of $C_{15}H_{14}N_2O_2$ in the suspension.

Storage. Store at a temperature not exceeding 30°.