Nepafenac

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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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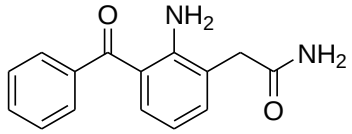
Further follow-up action as required.	

Nepafenac



$C_{15}H_{14}N_2O_2$ Mol. Wt. 254.3

Nepafenac is 2-(2-amino-3-benzoylphenyl) acetamide.

Nepafenac contains not less than 98.0 per cent and not more than 102.0 per cent of the stated amount of $C_{15}H_{14}N_2O_2$, calculated on the dried basis.

Category. Nonsteroidal antiinflammatory.

Description. A yellow colour crystalline powder.

Identification

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

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

Tests

Related substances. Determine by liquid chromatography (2.4.14).

NOTE - Prepare the solutions immediately before use.

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

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Reference solution. A solution containing 0.015 per cent w/v of *nepafenac IPRS*, 0.025 per cent w/v of *nepafenac impurity B IPRS* and 0.0075 per cent w/v, each of, *nepafenac impurity A IPRS* and *nepafenac impurity C IPRS* in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with 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 Inertsil ODS-3,
- mobile phase. a mixture of 65 volumes of *0.02 M ammonium formate* solution, 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
Nepafenac impurity A[1]	0.46
Nepafenac (Retention time; about 14 minutes)	1.00
Nepafenac impurity B[2]	1.37
NepafenacimpurityC[3]	1.64

[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 resolution between the peaks due to nepafenac impurity A and nepafenac is not less than 12.0, the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0, for nepafenac peak and the relative standard deviation for replicate injections is not more than 5.0 per cent, for all the peaks.

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 B is not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.5 per cent), the area of any peak corresponding to nepafenac impurity A and

nepafenac impurity C, each of, is not more than the area of the corresponding peaks in the chromatogram obtained with the reference solution (0.15 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 (0.3 per cent) and the sum of the areas of all the secondary peaks is not more than 3.3 times the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent). Ignore any peak with area less than 0.16 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

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

Sulphated ash (2.3.18). Not more than 0.2 per cent.

Loss on drying (2.4.19). Not more than 0.5 per cent, determined on 1.0 g at 105° for 3 hours.

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

NOTE -Prepare the solutions immediately before use.

Test solution. Dissolve 0.1 g of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Reference solution. A 0.01 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.

Calculate the content of $C_{15}H_{14}N_2O_2$.

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

2.4.26. Solubility.

Insert before **Netilmicin Sulphate.** Page 285

Nepafenac. Soluble in *N,N-Dimethyl formamide*, **s**lightly soluble in *methanol* and *tetrahydrofuran*, practically insoluble in *water*.