Ketorolac Tromethamine Tablets

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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.	

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Change **to**: **Ketorolac Tromethamine Tablets**

Ketorolac Trometamol Tablets

Ketorolac Tromethamine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of ketorolac tromethamine $C_{15}H_{13}NO_3,C_4H_{11}NO_3$.

Usual strength. 10 mg.

Identification

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

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 600 ml of *water,*
Speed and time. 50 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with the medium if necessary, at the maximum at about 322 nm (2.4.7). Calculate the content of $C_{15}H_{13}NO_3,C_4H_{11}NO_3$ in the medium from the absorbance obtained from a solution of known concentration of *ketorolac tromethamine IPRS* in the dissolution medium.

Q. Not less than 75 per cent of the stated amount of $C_{15}H_{13}NO_3,C_4H_{11}NO_3$.

Related substances. Determine by liquid chromatography (2.4.14).

NOTE - Protect the solutions from light.

Solvent mixture. Equal volumes of *methanol* and *water.*

Test solution. Transfer 10 intact tablets into a suitable volumetric flask, disperse in *water* (10 per cent of the final volume), with the aid of ultrasound, add *methanol* (40 per cent of the final volume), sonicate for 10 minutes and dilute to volume with *methanol*. Centrifuge and dilute a suitable volume of the solution with the solvent mixture to obtain a solution containing 0.002 per cent w/v of Ketorolac Tromethamine.

Reference solution (a). A 0.02 per cent w/v solution of *ketorolac tromethamine IPRS* in *methanol*. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (b). A solution containing 0.0025 per cent w/v, each of, *ketorolac impurity A IPRS, ketorolac 1-hydroxy analog IPRS, ketorolac 1-keto analog IPRS,* and *ketorolac impurity D IPRS* in *methanol*. Dilute 1.0 ml of the solution to 100.0 ml with reference solution (a).

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 55 volumes of *methanol*, 44 volumes of *water* and 1 volume of *glacial acetic acid*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 100 µl.

Name	Relative retention time

Ketorolac impurity A[1]	0.5
Ketorolac 1-hydroxy analog[2]	0.8
Ketorolac	1.0
Ketorolac 1-keto analog[3]	1.2
Ketorolac impurity D[4]	2.6

[1]5-Benzoyl-*N*-[1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl]-2,3-dihydro-1H-pyrrolizine-1-carboxamide,
[2]5-Benzoyl-2,3-dihydro-1*H*-pyrrolizin-1-ol,
[3]5-Benzoyl-2,3-dihydro-1*H*-pyrrolizin-1-one,
[4]5-Benzoyl-2,3-dihydro-1*H*-pyrrolizine.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to ketorolac and ketorolac 1-hydroxy analog is not less than 1.5 and between ketorolac and ketorolac 1-keto analog is not less than 1.5 and the relative standard deviation for replicate injections is not more than 5.0 per cent for ketorolac impurity A, ketorolac 1-hydroxy analog, ketorolac 1-keto analog and ketorolac impurity D.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to ketorolac impurity A, ketorolac 1-hydroxy analog and ketorolac impurity D, each of, is not more than 0.4 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.5 per cent), the area of any peak corresponding to ketorolac 1-keto analog is not more than 0.64 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.8 per cent), the area of any other secondary peak is not more than 0.5 per cent, calculated by area normalization

The sum of all the impurities is not more than 1.0 per cent.

Uniformity of content. Complies with the test stated under Tablets.

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

Test solution. Transfer 1 intact tablet into a suitable volumetric flask, disperse in *water* (10 per cent of the final volume), with the aid of ultrasound, add *methanol* (40 per cent of the final volume), sonicate for 10 minutes and dilute to volume with *methanol*. Centrifuge and dilute a suitable volume of the solution with the solvent mixture to obtain a solution containing 0.02 per cent w/v of Ketorolac Tromethamine. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{15}H_{13}NO_3$,$C_4H_{11}NO_3$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

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

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to ketorolac and ketorolac 1-hydroxy analog is not less than 1.5 and between ketorolac and ketorolac 1-keto analog is not less than 1.5 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.5 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $C_{15}H_{13}NO_3$,$C_4H_{11}NO_3$ in the tablets.

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