Ketorolac Tromethamine Injection

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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 Injection**

Ketorolac Trometamol Injection

Ketorolac Tromethamine Injection is a sterile solution of Ketorolac Tromethamine in a suitable vehicle.

Ketorolac Tromethamine Injection contains 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 strengths. 15 mg per ml; 30 mg per 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

pH (2.4.24). 6.9 to 7.9.

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. Dilute a suitable volume of the injection with the solvent mixture to obtain a solution containing 0.024 per cent w/v of Ketorolac Tromethamine.

Reference solution. A solution containing 0.012 per cent w/v, each of, k*etorolac tromethamine IPRS, ketorolac impurity A IPRS, ketorolac 1-hydroxy analog IPRS, ketorolac 1-keto analog IPRS,* and *ketorolac impurity D IPRS* prepared by disssolving in *methanol* (4 per cent of the final volume) and dilute to volume with the solvent mixture. Dilute 2.0 ml of the solution to 100.0 ml with the solvent mixture and further dilute 1.0 ml of the solution to 10.0 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),
- 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]		0.4	
Ketorolac 1-hydroxy analog[2]		0.6	Ketorolac
1-keto analog[3]	0.8		
Ketorolac		1.0	
Ketorolac impurity D[4]		2.1	

[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 the reference solution. The test is not valid until the resolution between the peaks due to ketorolac 1-keto analog and ketorolac is not less than 2 and the relative standard deviation for replicate injections is not more than 2.8 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 ketorolac impurity A and ketorolac impurity D, each of, is not more than twice the area of the corresponding peak in the chromatogram obtained with the reference solution (0.2 per cent), the area of any peak corresponding to ketorolac 1-hydroxy analog and ketorolac 1-keto analog, each of, is not more than 5 times the area of the corresponding peak in the chromatogram obtained with the reference solution (0.5 per cent), the area of any other secondary peak is not more than twice the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 15 times the area of the principal peak in the chromatogram obtained with the reference solution (1.5 per cent). Ignore any peak with an area less than 0.5 times of the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

Bacterial endotoxins (2.2.3). Not more than 5.8 Endotoxin units per mg of ketorolac tromethamine.

Other tests. Comply with the tests stated under Parenteral Preparations (Injections).

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

Test solution. Dilute a volume of injection with the solvent mixture to obtain a solution containing 0.0045 per cent w/v of Ketorolac Tromethamine.

Reference solution. A 0.0045 per cent w/v solution of *ketorolac tromethamine IPRS* in the solvent mixture.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject the reference solution and test solution.

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

Storage. Store in single dose containers preferably of type I glass, protected from light, at a temperature not exceeding 30°.