Tramadol 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.	

Tramadol Injection

Tramadol Hydrochloride Injection

Tramadol Injection is a sterile solution of Tramadol hydrochloride in Water for Injections.

Tramadol Injection contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of tramadol hydrochloride, $C_{16}H_{25}NO_2$,HCl.

Usual strengths. 50 mg per ml; 100 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 reference solution (a).

Tests

pH (2.4.24). 6.0 to 7.0, determined in 5.0 per cent w/v solution of tramadol hydrochloride.

Related substances. Determine by liquid chromatography (2.4.14).
Test solution. Dilute a suitable volume of the injection with the mobile phase to obtain a solution containing 0.05 per cent w/v of Tramadol Hydrochloride.

Reference solution (a). A 0.05 per cent w/v of *tramadol hydrochloride IPRS* in the mobile phase.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 50.0 ml with the mobile phase. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Reference solution (c). A solution containing 0.005 per cent w/v, each of, *tramadol hydrochloride IPRS* and *tramadol impurity A IPRS* in the mobile phase.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Nucleosil 100-5 C18),
- mobile phase: A mixture of 70.5 volumes of 0.2 per cent w/v solution of *trifluoroacetic acid* in *water* and 29.5 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 270 nm,
- injection volume: 20 µl.

Name	Relative retention time
Tramadol impurity D[1]	0.7
Tramadol impurity A[2]	0.9
Tramadol (retention time: about 5 minutes)	1.0
Tramadol impurity 1[3]	1.2
Tramadol impurity 2[4]	1.9
Tramadol impurity C[5]	2.4
Tramadol impurity B[6]	2.7
Tramadol impurity 3[7]	4.2

[1](1RS,2RS)-2-[(dimethylamino)methyl]-1-(3-hydroxyphenyl)cyclohexan-1-ol,
[2](1RS,2SR)-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexan-1-ol,
[3](1RS,2RS)-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol N-oxide,
[4]8a-(3-methoxyphenyl)-3-methyloctahydro-2H-1,3-benzoxazine,
[5][(1RS)-2-(3-methoxyphenyl)cyclohex-2-en-1-yl]-N,N-dimethylmethanamine,
[6][2-(3-methoxyphenyl)cyclohex-1-en-1-yl]-N,N-dimethylmethanamine,

[7]methoxybenzene (anisole).

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to tramadol and tramadol impurity A is not less than 3.0.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

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

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances.

Inject reference solution (a) and (c). The test is not valid unless the resolution between the peaks due to tramadol and tramadol impurity A is not less than 3.0 in the chromatogram obtained with reference solution (c) and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $C_{16}H_{25}NO_2$,HCl.

Storage. Store at a temperature not exceeding 30°.