Tramadol 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.

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Tramadol Tablets

Tramadol Hydrochloride Tablets

Tramadol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of tramadol hydrochloride, $C_{16}H_{25}NO_2$.HCl.

Usual strengths.50 mg; 100 mg; 200 mg.

Identification

A. Transfer a quantity of the powdered tablets containing 200 mg of Tramadol Hydrochloride to a 50-ml volumetric flask, add 20 ml *dichloromethane,* sonicate and filter. Transfer the clear supernatant to a separating funnel. Extract the *dichloromethane* layer with two 10 ml portions of *2 M sodium hydroxide* and discard the aqueous layer. Dry the *dichloromethane* layer over *anhydrous sodium sulphate* and filter. Evaporate the filtrate to dryness under a stream of nitrogen. The residue complies with the following test.

Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *tramadol hydrochloride IPRS* treated in the same manner or with the reference spectrum of tramadol.

B. 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

Dissolution (2.5.2).

Apparatus No. 1(Basket),

Medium. 900ml of *0.1 M hydrochloric acid*,

Speed and time. 100 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium.

Reference solution. A 0.0055 per cent w/v solution of *tramadol hydrochloride IPRS* in the dissolution medium.

Chromatographic system

- a stainless steel column 15 cm x 3.9 mm, packed with octylsilane bonded to porous silica (5 µm) (Such as Symmetry C8),
- mobile phase: a mixture of 77 volumes of a buffer solution prepared by dissolving 5.0ml of *perchloric acid* in 950 ml of *water*, add 4 ml of 25 per cent v/v of *ammonia* and dilute to 1000 ml with *water,* adjusted to pH 2.2 with 25 per cent v/v of *ammonia* and 23 volumes of *acetonitrile,*
- flow rate: 2 ml per minute,
- spectrophotometer set at 273 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless 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 $C_{16}H_{25}NO_2$. HCl in the medium.

Q. Not less than 80 per cent of the stated amount of $C_{16}H_{25}NO_2$.HCl.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the powdered tablets containing 200 mg of Tramadol Hydrochloride in the mobile phase, with the aid of ultrasound for 5 minutes and shake for 10 minutes, dilute to 50.0 ml with the mobile phase, filter.

Reference solution (a). A 0.0006 per cent w/v solution of *tramadol hydrochloride IPRS* in the mobile phase.

Reference solution (b). A solution containing 0.02 per cent w/v, each of, *tramadol hydrochloride IPRS* and *tramadol impurity A IPRS* in the mobile phase.

Reference solution (c). Dilute 5.0 ml of the reference solution (a) to 100.0 ml with the mobile phase.

Use the chromatographic system as described under Dissolution with the following modification.

– flow rate: 1 ml per minute.

Name	Relative retention time	Correction factor
TramadolimpurityA[1]	0.85	---
Tramadol hydrochloride	1.0	---
1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohex-1-ene hydrochloride	4.27	0.79
1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohex-6-ene hydrochloride	5.27	---

[1]RS, SR-1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohexanol hydrochloride.

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to tramadol impurity A and tramadol is not less than 2.0 in the chromatogram obtained with reference solution (b), the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a) and the relative standard deviation for replicate injections is not more than 10.0 per cent in the chromatogram obtained with reference solution (c).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to tramadol impurity A, 1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohex-1-ene hydrochloride and 1-(3-Methoxyphenyl)-2-(dimethylaminomethyl)cyclohex-6-ene hydrochloride, each of, is not more than1.33 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent), the area of any other secondary peak is not more than 1.33 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 4.66 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.7 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 50 mg of Tramadol Hydrochloride in *0.1 M hydrochloric acid* with the aid of ultrasound for 5 minutes and shake for 10 minutes, dilute to 100.0 ml with *0.1 M hydrochloric acid*, filter. Dilute 10.0 ml of the filtrate to 50.0 ml with *0.1 M hydrochloric acid*.

Reference solution. A 0.01 per cent w/v solution of *tramadol hydrochloride IPRS* in *0.1 M hydrochloric acid*.

Use the Chromatographic system as described under Dissolution.

Inject the reference solution. The test is not valid unless 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 tramadol hydrochloride, $C_{16}H_{25}NO_2$.HCl in the tablets.

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