Trazodone Tablets

Trazodone Hydrochloride Tablets

Trazodone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of trazodone hydrochloride, $C_{19}H_{22}ClN_5O$, HCl.

Usual strengths. 25 mg; 50 mg; 100 mg.

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

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 900 ml of *0.01 M hydrochloric acid*,
Speed and time. 50 rpm and 60 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. Dissolve a quantity of *trazodone hydrochloride IPRS* in the dissolution medium and dilute with the same medium to obtain a solution of known concentration similar to the expected concentration of the test solution.

Chromatographic system
- a stainless steel column 10 cm x 5 mm, packed with octadecylsilane bonded to porous silica (4 µm),
- mobile phase: a mixture of 25 volumes of a buffer solution prepared by dissolving 1.15 g of *ammonium dihydrogen phosphate* in 1000 ml of *water*, adjusted to pH 6.0 with *sodium hydroxide* and 75 volumes of *methanol*,
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 246 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 900 theoretical plates and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution. Run the chromatogram 4.5 times the retention time of the principal peak.

Calculate the content of $C_{19}H_{22}ClN_5O$, HCl in the medium.

Q. Not less than 80 per cent of the stated amount of $C_{19}H_{22}ClN_5O$, HCl.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 65 volumes of *methanol*, 35 volumes of *water* and 0.3 volume of *hydrochloric acid*.

Test solution. Disperse a quantity of the powdered tablets containing 50 mg of trazodone in the solvent mixture, with the aid of ultrasound for 10 minutes and dilute to 100.0 ml with the solvent mixture.

Reference solution (a). An accurately weighed quantity of *trazodone hydrochloride IPRS* containing 0.0005 per cent w/v of trazodone in the solvent mixture. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Reference solution (b). A solution containing 0.00007 per cent w/v of *trazodone hydrochloride IPRS* and 0.00015 per cent w/v of *trazodone related compound C IPRS* in the solvent mixture.

Chromatographic system
- a stainless steel column 15 cm x 4.0 mm, packed with octadecylsilane bonded to porous silica (3 µm),
- mobile phase: A. dissolve 6.75 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, add 1.0 ml of *triethylamine* and mix,

B. *acetonitrile*,

- a gradient programme using the conditions given below,
- flow rate: 0.7 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 10 µl.

Time (In min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	90	10
5	90	10
30	60	40
35	60	40
60	42	58
63	30	70
78	30	70
78.1	90	10
90	90	10

Name	Relative retention time
Triazolopyridinone[1*]	0.1
Chlorophenylpiperazine[2*]	0.6
Hyroxypropyl chlorophenyl piperazine[3*]	0.7
Isotrazodone[4*]	0.8
Trazodone related compound C*	0.97
Trazodone hydrochloride	1.0
Trazodone dimer[5*]	1.5
Trazodone related compound F[6*]	1.6
Bispiperazine analog[7*]	1.8
Bis(3-chlorophenyl)piperazine[8*]	2.2

*Process impurity included for indentification only and not included in the calculation of total degradation products,
[1][1,2,4]Triazolo[4,3-a]pyridin-3(2H)-one,
[2]1-(3-Chlorophenyl)piperazine,
[3]3-[4-(3-chlorophenyl)piperazin-1-yl]propan-1-ol,
[4]1-{3-[4-(3-chlorophenyl)piperazin-1-yl]propyl}-[1,2,4]triazolo[4,3-a]pyridin-1-ium-3-olate,
[5]1,1-Bis{2-chloro-[4-(3-{1,2,4,-triazolo[4,3-a]pyridin-3-(2H)-on-2-yl}propyl)piperazine-1-yl]phenyl}ethane trihydrochloride,
[6]1-(3-chlorophenyl)-4-(3-chloropropyl)piperazine,
[7]1,3-Bis(4-(3-chlorophenyl)piperazin-1-yl)propane,
[8]1,4-bis(3-chlorophenyl)piperazine.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to trazodone related compound C and trazodone is not less than 2.5 in the chromatogram obtained with reference solution (b), the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent) and the sum of the areas of all the secondary peaks is not more than 20 times the area of the principal peak in the chromatogram obtained with reference solution (a) (2.0 per cent).

Other tests. Comply with the tests stated under Tablets.

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

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 50 mg of Trazodone Hydrochloride in *0.01M hydrochloric acid*, with the aid of ultrasound for 30 minutes and dilute to 50.0 ml with *0.01 M hydrochloric acid*. Dilute 5.0 ml of the solution to 50.0 ml with *0.01M hydrochloric acid*.

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

Inject the reference solution and the test solution.

Calculate the content of $C_{19}H_{22}ClN_5O$, HCl in the tablets.

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