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Trazodone Tablets

General Notices

Details for the public consultation of this monograph are as follows:

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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Production** statement removed **Dissolution** test solution revised **Related substances** tests A and B replaced by a single method **Impurities** statement revised

Action and use

Monoamine reuptake inhibitor; antidepressant.

DEFINITION

Trazodone Tablets contain Trazodone Hydrochloride.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of trazodone hydrochloride, $C_{19}H_{22}ClN_5O,HCl$

95.0% to 105.0% of the stated amount.

IDENTIFICATION

For film-coated tablets, remove the coating. Shake a quantity of the powdered tablet cores containing 0.3 g of Trazodone Hydrochloride with 50 mL of *acetone*, filter and evaporate to dryness. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of trazodone

hydrochloride *(RS 346)*. In the preparation of the disc, avoid excessive grinding when triturating the substance being examined with *potassium chloride*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1. Carry out the procedure protected from light.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.01M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and filter. Dilute the filtered sample, if necessary, with the dissolution medium to produce a solution expected to contain 0.0055% w/v of Trazodone Hydrochloride and measure the *absorbance* at the maximum at 311 nm, Appendix II B, using 0.01M *hydrochloric acid* in the reference cell.
(2) Measure the *absorbance* of a 0.0055% w/v solution of *trazodone hydrochloride BPCRS* using 0.01M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of trazodone hydrochloride, $C_{19}H_{22}ClN_5O$,HCl, in the medium from the absorbances obtained and using the declared content of $C_{19}H_{22}ClN_5O$,HCl in *trazodone hydrochloride BPCRS*.

LIMITS

The amount of trazodone hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in solution A. Carry out the procedure protected from light.

Solution A Equal volumes of mobile phase A and mobile phase B.

(1) Shake a quantity of powdered tablets containing 0.1 g of Trazodone Hydrochloride in 60 mL for 30 minutes, dilute to 100 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume to 5 volumes.
(3) 0.1% w/v of *trazodone hydrochloride impurity standard BPCRS* and 0.0002% w/v each of impurity A and impurity H.
(4) Dilute 1 volume of solution (2) to 2 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (2.6 µm) (Accucore C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use an autosampler temperature of 8°.
(f) Use a detection wavelength of 254 nm.
(g) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.4 volumes of *diethylamine* and 1000 volumes of *water*.

Mobile phase B *Methanol*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-30	50→30	50→70	isocratic
30-40	30→15	70→85	linear gradient
40-45	15→50	85→50	linear gradient
45-50	50	50	re-equilibration

SYSTEM SUITABILITY

For system suitability, use solution (3):

the *resolution* between the peaks due to impurity C and trazodone is at least 3.0;

the *resolution* between the peaks due to trazodone and impurity D is at least 5.0.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of trazodone in solution (2).

For the reporting threshold, use the concentration of trazodone in solution (4).

For peak identification, use solution (3).

Relative retention: impurity A, about 0.3; impurity C, about 0.9; impurity D, about 1.1; impurity E, about 1.7; impurity H, about 2.5.

LIMITS

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 1.0%;

— reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase. Carry out the procedure protected from light.

(1) Shake a quantity of the powdered tablets containing 0.1 g of Trazodone Hydrochloride in 60 mL for 30 minutes in a volumetric flask and dilute to 100 mL and filter. Dilute 1 volume to 10 volumes.
(2) 0.01% w/v of *trazodone hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Spherisorb C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

40 volumes of a solution containing 0.115% w/v of *diammonium hydrogen orthophosphate*, previously adjusted to pH 6.0 with 10% v/v *orthophosphoric acid* or 1M *sodium hydroxide*, and 60 volumes of *methanol*.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{22}ClN_5O,HCl$ in the tablets using the declared content of $C_{19}H_{22}ClN_5O,HCl$ in *trazodone hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, C, D, E and H listed under Trazodone Hydrochloride.