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Tranylcypromine Sulfate

General Notices

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

EAG/Panel/Working Party	Medicinal Chemicals 2
Contact Details	helen.corns@mhra.gov.uk hannah.bowden@mhra.gov.uk
Deadline for Comment	30 September 2020
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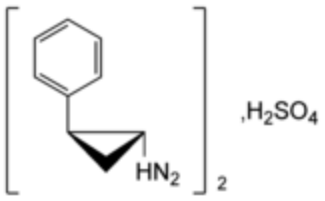
Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Related substances** GC method replaced by LC test & limits revised **Impurities** Section added



and enantiomer

$(C_9H_{11}N)_2,H_2SO_4$ 364.5 *13492-01-8*

Action and use

Monoamine oxidase inhibitor; antidepressant.

Preparation

Tranylcypromine Tablets

DEFINITION

Tranylcypromine Sulfate is (1*RS*,2*SR*)-2-phenylcyclopropylamine sulfate. It contains not less than 98.0% and not more than 101.0% of $(C_9H_{11}N)_2,H_2SO_4$, calculated with reference to the dried substance.

CHARACTERISTICS

A white or almost white, crystalline powder.

Soluble in *water*; very slightly soluble in *ethanol (96%)* and in *ether*.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of tranylcypromine sulfate *(RS 345)*.

B. Yields the reactions characteristic of *sulfates*, Appendix VI.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in solution A.

Solution A: 1 volume of *methanol*, 1 volumes of 0.05M *sulfuric acid* and 3 volumes of *water*.

(1) Dissolve, with the aid of ultrasound, 70 mg of tranylcypromine sulfate in 30 mL *methanol* and 30 mL 0.05M *sulfuric acid*. Add sufficient volume of solution A to produce 100 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes. Dilute 1 volume of this solution to 2 volumes.
(3) 0.00007% w/v of *tranylcypromine sulfate BPCRS* and 0.0003% w/v *cis-2-Phenylcyclopropanamine*.
(4) 0.000035% w/v of *3-phenylallylamine* (impurity B).
(5) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use a column temperature of 35°.
(e) Use detection wavelengths of 249 nm and 220 nm.
(f) Inject 25 µL of each solution.

MOBILE PHASE

Buffer solution Dissolve 3.4 g of *monobasic ammonium phosphate* in 900 mL *water*, adjust to pH 2.2 with *orthophosphoric acid* and dilute to 1000 mL with *water*.

Mobile phase A 3 volumes of *methanol* and 17 volumes of buffer solution.

Mobile phase B 3 volumes of *methanol* and 7 volumes of buffer solution.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-20	100	0	isocratic
20-25	100→0	0→100	linear gradient
25-37	0	100	isocratic

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
37-39	0→100	100→0	linear gradient
39-45	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retention(s) with reference to tranylcypromine sulfate are: impurity A, about 0.8; impurity B, about 1.2, impurity C, about 1.4 and impurity D, about 2.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to tranylcypromine and impurity A is at least 2.0.

LIMITS

For impurity B at 249 nm In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.5%).

For all other impurities at 220 nm In the chromatogram obtained with solution (1):

Identify any peak corresponding to impurity A in the chromatogram obtained with solution (1), using the relative retention times and multiply the area of this peak by a correction factor of 1.4.

the area of any peak corresponding to impurities A, C and D is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any *secondary peak* is not greater than 0.2 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

The total impurity limit is not more than 1%.

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.05%) and any peak corresponding to impurity B.

Loss on drying

When dried to constant weight at 105°, loses not more than 0.5% of its weight. Use 1 g.

Sulfated ash

Not more than 0.1%, Appendix IX A.

ASSAY

Carry out Method I for *non-aqueous titration*, Appendix VIII A, using 0.3 g and determining the end point potentiometrically. Each mL of *0.1M perchloric acid VS* is equivalent to 36.45 mg of $(C_9H_{11}N)_2,H_2SO_4$.

IMPURITIES

 A. (±)-cis-2-Phenylcyclopropanamine (cis-Cypromine)

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 B. 3-Phenylallylamine (Cinnamylamine)

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 C. (±)-cis-2-Phenylcyclopropanecarbohydrazide (cis-tranylcypromine hydrazide)

C. (±)-cis-2-Phenylcyclopropanecarbohydrazide (cis-tranylcypromine hydrazide)

 D. (±)-trans-2-Phenylcyclopropanecarbohydrazide (trans-tranylcypromine hydrazide)

D. (±)-trans-2-Phenylcyclopropanecarbohydrazide (trans-tranylcypromine hydrazide)