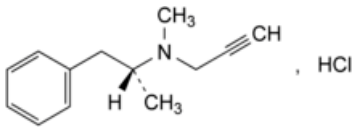
Edition: BP 2025 (Ph. Eur. 11.6 update)

Selegiline Hydrochloride

General Notices

(Ph. Eur. monograph 1260)



$C_{13}H_{18}ClN$ 223.7 *14611-52-0*

Action and use

Monoamine oxidase type B inhibitor; treatment of Parkinson's disease.

Preparations

Selegiline Oral Solution

Selegiline Tablets

Ph Eur

DEFINITION

N-Methyl-*N*-[(1*R*)-1-methyl-2-phenylethyl]prop-2-yn-1-amine hydrochloride.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water and in methanol, slightly soluble in acetone and in ethyl acetate.

mp

About 143 °C.

IDENTIFICATION

Carry out either tests A, B, D or tests B, C, D.

A. Specific optical rotation (2.2.7): -12.0 to -10.0 (dried substance).
Dissolve 2.00 g in carbon dioxide-free water R and dilute to 20.0 mL with the same solvent.

B. Infrared absorption spectrophotometry (2.2.24).

Comparison selegiline hydrochloride CRS.

C. Enantiomeric purity (see Tests).
D. It gives reaction (a) of chlorides (2.3.1).

TESTS

pH (2.2.3)

3.5 to 4.5.

Dissolve 0.20 g in carbon dioxide-free water R and dilute to 10 mL with the same solvent.

Enantiomeric purity

Liquid chromatography (2.2.29).

Test solution Dissolve 20.0 mg of the substance to be examined in a mixture of 10 µL of butylamine R and 1 mL of 2-propanol R and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dissolve 8.0 mg of (RS)-selegiline hydrochloride CRS in a mixture of 10 µL of butylamine R and 1 mL of 2-propanol R and dilute to 10.0 mL with the mobile phase.

Reference solution (b) Dilute 0.5 mL of reference solution (a) to 20.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: cellulose derivative of silica gel for chiral separation R.

Mobile phase 2-propanol R, cyclohexane R (0.2:99.8 *V/V*).

Flow rate 1 mL/min.

Detection Spectrophotometer at 220 nm.

Injection 20 µL.

Relative retention With reference to (*R*)-selegiline (retention time = about 6 min): impurity E = about 0.9.

System suitability Reference solution (a):

— resolution: minimum 1.5 between the peaks due to impurity E and (*R*)-selegiline; if necessary, adjust the concentration of 2-propanol in the mobile phase.

Limit:

— *impurity E*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.5 per cent).

Related substances

Liquid chromatography (2.2.29).

Butylammonium acetate buffer solution Dilute 4 mL of *butylamine R* in 900 mL of *water R*, adjust to pH 6.5 with *acetic acid R* and dilute to 1000.0 mL with *water R*.

Test solution Dissolve 20 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dissolve 50 mg of the substance to be examined and 10 mg of *butyl parahydroxybenzoate R* in the mobile phase and dilute to 50.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 20.0 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase *acetonitrile R1*, butylammonium acetate buffer solution (50:50 *V/V*).

Flow rate 1 mL/min.

Detection Spectrophotometer at 215 nm.

Injection 20 µL.

Run time 1.7 times the retention time of selegiline.

Relative retention With reference to selegiline (retention time = about 14 min): butyl parahydroxybenzoate = about 0.8.

System suitability Reference solution (a):

— *resolution*: minimum 3.0 between the peaks due to butyl parahydroxybenzoate and selegiline.

Limits:

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying at 60 °C at a pressure not exceeding 0.5 kPa for 3 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.180 g in 50 mL of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 22.37 mg of $C_{13}H_{18}ClN$.

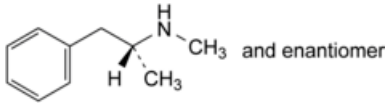
STORAGE

Protected from light.

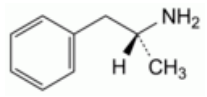
IMPURITIES

Specified impurities *E*.

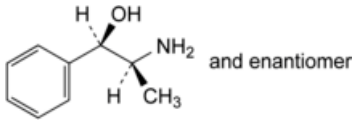
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A, B, C, D, G*.



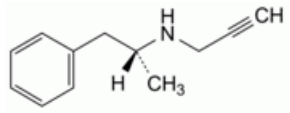
A. (2*RS*)-*N*-methyl-1-phenylpropan-2-amine ((*RS*)-metamfetamine),



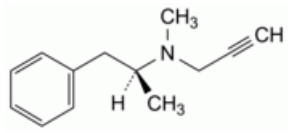
B. (2*R*)-1-phenylpropan-2-amine (amfetamine),



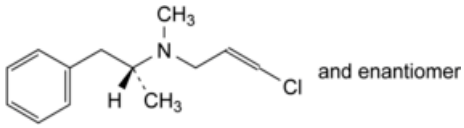
C. (1*RS*,2*SR*)-2-amino-1-phenylpropan-1-ol (phenylpropanolamine),



D. *N*-[(1*R*)-1-methyl-2-phenylethyl]prop-2-yn-1-amine (desmethylselegiline),



E. *N*-methyl-*N*-[(1*S*)-1-methyl-2-phenylethyl]prop-2-yn-1-amine,



G. (2*EZ*)-3-chloro-*N*-methyl-*N*-[(1*RS*)-1-methyl-2-phenylethyl]prop-2-en-1-amine.

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