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

Selegiline Oral Solution

General Notices

Action and use

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

DEFINITION

Selegiline Oral Solution is a solution of Selegiline Hydrochloride in a suitable flavoured vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of selegiline hydrochloride, $C_{13}H_{18}ClN$

90.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (2).
B. In the test for Related substances, the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

TESTS

(*S*)-Selegiline

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

(1) Add to a weighed quantity of the oral solution containing 20 mg of Selegiline Hydrochloride 1 mL of *propan-2-ol* and 10 µL of *butylamine*, dilute to 20 mL with the mobile phase, shake thoroughly, filter and use the filtrate.
(2) Dissolve 8 mg of (RS)-*selegiline hydrochloride EPCRS* in a mixture of 10 µL of *butylamine* and 1 mL of *propan-2-ol* and dilute to 20 mL with the mobile phase.
(3) Dilute 0.5 mL of solution (2) to 20 mL with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *silica gel OD for chiral separation* (Chiralcel OD is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

0.2 volume of *propan-2-ol* and 99.8 volumes of *cyclohexane*

SYSTEM SUITABILITY

When the chromatograms are recorded in the prescribed conditions, the retention time of (*S*)-selegiline is about 10 minutes. Adjust the sensitivity of the system so that the height of the peaks in the chromatogram obtained with solution (3) is about 10% of the full scale of the recorder. The test is not valid unless, in the chromatogram obtained with solution (2), the *resolution factor* between the peaks corresponding to (*S*)-selegiline and (*R*)-selegiline is at least 1.5. If necessary, adjust the concentration of propan-2-ol in the mobile phase.

LIMITS

In the chromatogram obtained with solution (1):

The area of any peak corresponding to (*S*)-selegiline is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.5%).

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Adjust the pH of a quantity of the oral solution containing 10 mg of Selegiline Hydrochloride to 12 with 1M *sodium hydroxide*, add 2 mL of *chloroform*, shake for 30 minutes, allow to separate and use the chloroform layer.
(2) Prepare solution (2) in the same manner as solution (1) but using 4 mL of a 0.25% w/v solution of *selegiline hydrochloride BPCRS* in 0.1M *hydrochloric acid* in place of the oral solution.
(3) Adjust the pH of 1 mL of a 0.025% w/v solution of *selegiline hydrochloride BPCRS* in 0.1M *hydrochloric acid* to 12 with 1M *sodium hydroxide*, add 10 mL of *chloroform*, shake for 30 minutes, allow to separate and use the chloroform layer.
(4) Dilute 2 volumes of solution (3) to 5 volumes with *chloroform*.
(5) Adjust the pH of 2 mL of a 0.025% w/v solution of *methylamphetamine hydrochloride* in 0.1M *hydrochloric acid* to 12 with 1M *sodium hydroxide*, add 10 mL of *chloroform*, shake for 30 minutes, allow to separate and use the chloroform layer.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *TLC silica gel* F_{254} *plate*.
(b) Use the mobile phase as described below.
(c) Apply 50 µL of each solution.
(d) Develop the plate to 155 cm.
(e) After removal of the plate, dry in air, spray with a solution prepared by mixing 2 volumes of a solution in *acetone* containing 10% w/v of *iron*(III) *chloride* and 4% w/v of *iodine* and 1 volume of a 40% w/v solution of (+)-*tartaric acid* in *water* and allowing to stand for 15 minutes before use. Examine the plate in daylight immediately after spraying.

MOBILE PHASE

0.5 volume of 13.5M *ammonia*, 10 volumes of *1,4-dioxan*, 10 volumes of *propan-2-ol*, 10 volumes of *toluene* and 30 volumes of *xylene*. Use an unlined tank and add the mobile phase immediately before placing the plate in the tank.

LIMITS

In the chromatogram obtained with solution (1):

any spot corresponding to methylamphetamine is not more intense than the spot in the chromatogram obtained with solution (5) (1%);

any other *secondary spot* is not more intense than the spot in the chromatogram obtained with solution (3) (0.5%) and not more than two such spots are more intense than the spot in the chromatogram obtained with solution (4) (0.2%).

ASSAY

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

(1) Add 10 mL of a mixture of equal volumes of *acetonitrile* and *methanol* to a weighed quantity of the oral solution containing 10 mg of Selegiline Hydrochloride, mix with the aid of ultrasound for 5 minutes, add 40 mL of a mixture of equal volumes of *acetonitrile* and *methanol* and shake mechanically for 15 minutes. Add sufficient *water* to produce 100 mL and dilute 5 volumes of the resulting solution to 10 volumes with the mobile phase.

(2) 0.005% w/v of *selegiline hydrochloride BPCRS* in the mobile phase.
(3) 0.005% w/v of *selegiline hydrochloride BPCRS* and 0.001% w/v of *nortriptyline hydrochloride BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 215 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Dilute 250 mL of *methanol* and 250 mL of *acetonitrile* to 1000 mL with a solution prepared by dissolving 4 mL of *butylamine* in 900 mL of *water*, adjusting the pH to 6.5 with *acetic acid*, and adding sufficient *water* to produce 1000 mL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the two principal peaks is at least 3.0.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_{13}H_{18}ClN$, weight in volume, using the declared content of $C_{13}H_{18}ClN$ in *selegiline hydrochloride BPCRS*.

STORAGE

Selegiline Oral Solution should not be refrigerated.