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

Gabapentin Oral Solution

General Notices

Action and use

Antiepileptic.

DEFINITION

Gabapentin Oral Solution contains Gabapentin.

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

Content of gabapentin, $C_9H_{17}NO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *methanol*.
(1) Dilute a quantity of the oral solution to produce a solution containing 0.025% w/v of Gabapentin.
(2) 0.025% w/v of *gabapentin EPCRS*.
(3) 0.025% w/v each of *gabapentin EPCRS* and *vigabatrin BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel*.
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 8 cm.
(e) After removal of the plate, dry at 105°, spray with *ninhydrin solution R4* and heat at 105° for 2 minutes. Examine in daylight.

MOBILE PHASE

2 volumes of *methanol*, 3 volumes of *acetonitrile* and 15 volumes of 0.05M *potassium dihydrogen orthophosphate*, adjusted to pH 6.3 with *potassium hydroxide solution*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay, the principal peak in the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH, 6.0 to 7.5, Appendix V L.

Gabapentin impurity A

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

(1) Dilute a quantity of the oral solution to produce a solution containing 0.25% w/v of Gabapentin.
(2) 0.001% w/v of *gabapentin impurity A EPCRS*.
(3) 0.05% w/v of each of *methyl 4-hydoxybenzoate* and *gabapentin impurity A EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (5 cm × 2.0 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (1.7 µm) (Kinetex C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.4 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 210 nm.
(f) Inject 1.5 µL of each solution.

MOBILE PHASE

95 volumes of *acetonitrile R1* and 405 volumes of a 0.154% w/v solution of *ammonium acetate* in *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to methyl 4-hydrozybenzoate and gabapentin impurity A is not less than 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.4%).

Related substances

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

(1) Dilute a quantity of the oral solution to produce a solution containing 0.5% w/v of Gabapentin.
(2) Dilute 1 volume of solution (1) to 100 volumes and dilute 1 volume of the resulting solution to 10 volumes.
(3) 0.05% w/v each of *gabapentin EPCRS* and *gabapentin impurity B EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 2.0 mm) packed with *end-capped phenylethyl silica gel for chromatography* (4 µm) (Synergi Polar RP 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 50°.
(e) Use evaporative light scattering detection using a flow rate of 1.3 litres per minute and an evaporator temperature of 60°.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.063% w/v of *ammonium formate* in *water*, adjusted to pH 3.2 with *formic acid*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-1	99	1	isocratic
1-7	99→40	1→60	linear gradient
7-8	40	60	isocratic
8-9	40→99	60→1	linear gradient
9-18	99	1	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gabapentin and impurity B is not less than 6.0.

LIMITS

In the chromatogram obtained with solution (1):

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

the sum of the areas of all the *secondary peaks* is not greater than 10 times the area of the principal peak if the chromatogram obtained with solution (2) (1.0%);

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

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

(1) Dilute a weighed quantity of the oral solution with sufficient *water* to produce a solution containing 0.25% w/v of Gabapentin.
(2) 0.25% w/v of *gabapentin EPCRS* in *water*.
(3) 0.25% w/v of *gabapentin EPCRS* and 0.06% w/v of *methyl parahydroxybenzoate* in *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Eclipse XDB C-18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 211 nm.
(f) Inject 5 µL of each solution.

MOBILE PHASE

2.5 volumes of *orthophosphoric acid*, 200 volumes of *acetonitrile R1* and 800 volumes of 0.006M *sodium heptanesulfonate*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gabapentin and methyl parahydroxybenzoate is at least 10.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_9H_{17}NO_2$, weight in volume, using the declared content of $C_9H_{17}NO_2$ in *gabapentin EPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A and B listed under Gabapentin.