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Gabapentin Capsules

General Notices

Action and use

Antiepileptic

DEFINITION

Gabapentin Capsules contain Gabapentin.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of gabapentin, $C_9H_{17}NO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

The *infrared absorption spectrum* of the content of the capsules collected in ATR mode, Appendix II A, is concordant with the *reference spectrum* obtained with *gabapentin EPCRS*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, *Appendix XII B1*.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium, filter and dilute the filtrate with dissolution medium, if necessary, to produce a solution expected to contain 0.011% w/v of Gabapentin.
(2) 0.011% w/v of *gabapentin EPCRS* in the medium.
(3) 0.033% w/v of *gabapentin EPCRS* and 0.0016% w/v of *gabapentin impurity A EPCRS* in the medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel* (5 µm) (Hypersil ODS is suitable).
(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 210 nm.
(f) Inject 25 µL of each solution.

MOBILE PHASE

1 volume of *orthophosphoric acid*, 22 volumes of *acetonitrile R1*, 78 volumes of *methanol R1* and 115 volumes of a solution containing 1% w/v of *ammonium dihydrogen orthophosphate* and 0.17% w/v of *sodium decanesulfonate* in *water*. Adjust the pH to 4.4 with *triethylamine*.

When the chromatograms are recorded under the prescribed conditions, the retention times of gabapentin and impurity A is about 6 minutes and 8.5 minutes respectively.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gabapentin impurity A and gabapentin is at least 5.0.

DETERMINATION OF CONTENT

Calculate the total content of $C_9H_{17}NO_2$ in the medium from the chromatograms obtained and using the declared content of $C_9H_{17}NO_2$ in *gabapentin EPCRS*.

LIMITS

The amount of gabapentin 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 a mixture of 1 volume of *acetonitrile R1* and 9 volumes of *water* (solvent A).

(1) Dissolve a quantity of the contents of the capsules containing 0.5 g of Gabapentin in 20 mL of solvent A. Add a sufficient volume of the solvent A to produce 25 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes and dilute 1 volume of the resulting solution to 10 volumes.
(3) 0.02% w/v each of *gabapentin EPCRS*, *gabapentin impurity A EPCRS* and *gabapentin impurity B EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *dimethyloctylsilane* (5 µm) (Hypersil MOS-2 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 210 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

Mobile phase A 0.01M *potassium dihydrogen orthophosphate* previously adjusted to pH 6.9 with a 10% w/v solution of *potassium hydroxide*.

Mobile phase B *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0→5	100	0	isocratic
5→15	100→90	0→10	linear gradient
15→45	90→70	10→30	linear gradient
45→55	70→25	30→75	linear gradient
55→60	25	75	isocratic
60→61	25→100	75→0	linear gradient
61→70	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the retention times relative to gabapentin (retention time about 14 minutes) are: impurity B, about 1.1; impurity A, about 2.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gabapentin and gabapentin impurity B is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to gabapentin impurity A is not more than 0.4 times the area of the corresponding peak in the chromatogram obtained with solution (3) (0.4%);

the area of any other *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 peak* is not greater than 10 times the area of the principal peak in 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

Mix and powder the contents of 20 capsules. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) Mix with the aid of ultrasound, a quantity of the powdered contents of the capsules containing 1.25 g of Gabapentin with 150 mL of mobile phase. Add sufficient mobile phase to produce 200 mL and filter.
(2) 0.625% w/v of *gabapentin EPCRS*.
(3) 0.032% w/v each of *gabapentin EPCRS* and *gabapentin impurity A EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 4.6 mm) packed with *octadecylsilyl silica gel* (10 µm) (Lichrosorb RP-18 is suitable).
(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 210 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

10 volumes of *acetonitrile R1*, 35 volumes of *methanol R1*, 55 volumes of *water* and 0.1 volumes of a mixture containing 0.35% w/v of *potassium dihydrogen orthophosphate* and 0.73% w/v of *disodium hydrogen orthophosphate* previously adjusted to pH 7.0 with either *orthophosphoric acid* or a 10% w/v solution of *potassium hydroxide*.

When the chromatograms are recorded under the prescribed conditions, the retention times of gabapentin and impurity A are about 3 minutes and 10 minutes respectively.

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 A is at least 10.0.

DETERMINATION OF CONTENT

Calculate the content of $C_9H_{17}NO_2$ in the capsules using the declared content of gabapentin in *gabapentin EPCRS*.

IMPURITIES

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