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

Lamotrigine Tablets

General Notices

Lamotrigine Tablets from different manufacturers, whilst complying with the requirements of the monograph, may not be interchangeable.

Action and use

Antiepileptic.

DEFINITION

Lamotrigine Tablets contain Lamotrigine.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of lamotrigine, $C_9H_7Cl_2N_5$

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) To a quantity of the powdered tablets containing 0.1 g of Lamotrigine add 20 mL of *methanol*, shake well, dilute to 100 mL with *methanol*, filter and use the filtrate.
(2) 0.1% w/v of *lamotrigine BPCRS*.
(3) 0.1% w/v each of *lamotrigine BPCRS* and *carbamazepine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air and immediately examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

5 volumes of *concentrated ammonia*, 10 volumes of *methanol* and 85 volumes of *ethyl acetate*.

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

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2 and rotate 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

(1) After 45 minutes withdraw a 10 mL sample of the medium and filter. Measure the *absorbance* of the filtrate, Appendix II B, diluted with the dissolution medium if necessary, at the maximum at 267 nm using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *lamotrigine BPCRS* in the dissolution medium.

DETERMINATION OF CONTENT

Calculate the total content of lamotrigine, $C_9H_7Cl_2N_5$, in the medium from the absorbances obtained and using the declared content of $C_9H_7Cl_2N_5$ in *lamotrigine BPCRS*.

LIMITS

The amount of Lamotrigine 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 20 volumes of *methanol* and 80 volumes of *0.1M hydrochloric acid* (solution A).

(1) Shake a quantity of the powdered tablets containing 0.20 g of Lamotrigine with 20 mL of *methanol*, dilute to 100 mL with 0.1M *hydrochloric acid*, filter and use the filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes with 0.1M *hydrochloric acid* and dilute 2 volumes of the resulting solution to 10 volumes with solution A.
(3) 0.2% w/v of *lamotrigine impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS1 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 275 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

0.5 volumes of *octylamine*, 20 volumes of *glacial acetic acid*, 100 volumes of *acetonitrile*, 100 volumes of *methanol* and 700 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the chromatogram supplied with *lamotrigine impurity standard BPCRS* and the *resolution* between the peaks due to lamotrigine and saccharin sodium is at least 5.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of the peak corresponding to impurity A is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

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

the sum of the areas of all the *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.5 of the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in solution A described under Related substances.

(1) Shake a quantity of the powdered tablets containing 0.2 g of Lamotrigine with 20 mL of *methanol*, add sufficient 0.1M *hydrochloric acid* to produce 100 mL and filter. Dilute 1 volume of the filtrate to 10 volumes with solution A.
(2) Shake 50 mg of *lamotrigine BPCRS* with 20 mL of *methanol* and add sufficient 0.1M *hydrochloric acid* to produce 100 mL.Dilute 2 volumes to 5 volumes with solution A.
(3) 0.2% w/v of *lamotrigine impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the chromatogram supplied with *lamotrigine impurity standard BPCRS* and the *resolution* between the peaks due to lamotrigine and saccharin sodium is at least 5.0.

DETERMINATION OF CONTENT

Calculate the total content of $C_9H_7Cl_2N_5$ in the tablets using the declared content of $C_9H_7Cl_2N_5$ in *lamotrigine BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity A listed under Lamotrigine.