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

Lamotrigine Dispersible Tablets

General Notices

Dispersible Lamotrigine Tablets

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

Action and use

Antiepileptic.

DEFINITION

Lamotrigine Dispersible Tablets contain Lamotrigine in a suitable dispersible basis.

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) Shake a quantity of the powdered tablets containing 20 mg of Lamotrigine in 20 mL, dilute to 100 mL, filter and use the filtrate.
(2) 0.02% w/v of *lamotrigine BPCRS*.
(3) 0.02% 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 retention time of the principal peak in thechromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Disintegration

Comply with the requirements for Dispersible Tablets.

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

(1) After 45 minutes withdraw a sample of the medium, filter and dilute 5 mL of the filtrate to 10 mL with 0.3M *sodium hydroxide*. Measure the *absorbance* of the solution at 307 nm, Appendix II B, using 0.1M *sodium hydroxide* in the reference cell. Adjust the concentration with *water* if necessary.
(2) Prepare a suitable solution of *lamotrigine BPCRS* in the dissolution medium, using 0.3M *sodium hydroxide* to produce a solution of the strength expected in solution (1). Measure the *absorbance* of the solution at 307 nm, Appendix II B, using 0.1M *sodium hydroxide* in the reference cell.

DETERMINATION OF CONTENT

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

LIMITS

The amount of lamotrigine released is not less than 80% (Q) of the stated amount.

Related substances

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

(1) Shake a quantity of the powdered tablets containing 20 mg of Lamotrigine with 40 mL of *water* and add 40 mL of *methanol*. Dilute to 100 mL with *methanol (40%)*, filter and use the filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol (40%)* and dilute 1 volume of the resulting solution to 5 volumes with *methanol (40%)*.
(3) 0.02% w/v of *lamotrigine impurity standard BPCRS*in *methanol (40%)*.

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 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 any 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 such 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 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Lamotrigine comply with the requirement stated under Tablets using the following method of analysis.

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

(1) Shake one tablet with 10 mL of *water*, add sufficient *methanol* to produce 25 mL and filter.
(2) 0.008% w/v of *lamotrigine BPCRS* in *methanol (40%)*.
(3) 0.02% w/v of *lamotrigine impurity standard BPCRS* in *methanol (40%)*.

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 content of $C_9H_7Cl_2N_5$ in each tablet using the declared content of $C_9H_7Cl_2N_5$ in *lamotrigine BPCRS*.

ASSAY

For tablets containing less than 2 mg and/or less than 2% w/w of lamotrigine.

Use the average of the individual results determined in the test for Uniformity of content.

For tablets containing 2 mg or more than 2% w/w of lamotrigine.

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the powdered tablets containing 20 mg of Lamotrigine with 60 mL of *water*, add sufficient *methanol* to produce 100 mL and filter.
(2) 0.02% w/v of *lamotrigine BPCRS* in *methanol (40%)*.
(3) 0.02% w/v of *lamotrigine impurity standard BPCRS* in *methanol (40%)*.

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 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.