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

Enalapril Tablets

General Notices

Action and use

Angiotensin converting enzyme inhibitor.

DEFINITION

Enalapril Tablets contain Enalapril Maleate.

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

Content of enalapril maleate, $C_{20}H_{28}N_2O_5,C_4H_4O_4$

93.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the powdered tablets containing 20 mg of Enalapril Maleate with 10 mL of *ethanol (90%)* for 10 minutes, centrifuge and use the clear supernatant liquid (if necessary, filter through a 0.45-µm membrane filter).
(2) 0.2% w/v of *enalapril maleate BPCRS* in *ethanol (90%)*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a *TLC silica gel plate* (Merck silica gel 60 HPTLC plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with a solution prepared by mixing equal volumes of a 40% w/v solution of *potassium iodide* in *water* and a solution prepared by dissolving 0.85 g of *bismuth oxynitrate* in a mixture of 10 mL of *glacial acetic acid* and 40 mL of *water* and diluting 10 volumes of the mixture with 20 volumes of *glacial acetic acid* and 70 volumes of *water* immediately before use, then spray with *dilute hydrogen peroxide solution*.

MOBILE PHASE

15 volumes of *glacial acetic acid*, 25 volumes of *water* and 60 volumes of *butan-1-ol*.

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 the chromatogram obtained with solution (1) corresponds to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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

Solution A 0.01M *sodium dihydrogen orthophosphate monohydrate*, adjusted to pH to 2.2 with *orthophosphoric acid*.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of *water*, 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 30 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with *water* if necessary, to produce a solution expected to contain 0.00028% w/v of Enalapril Maleate.
(2) 0.00028% w/v of *enalapril maleate BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Alltech Platinum EPS C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 50°.
(e) Use a detection wavelength of 215 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

25 volumes of *acetonitrile R1* and 75 volumes of solution A.

When the chromatograms are recorded under the prescribed conditions, the retention time of enalapril is about 5 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to enalapril is between 0.8 and 2.0.

DETERMINATION OF CONTENT

Calculate the total content of enalapril maleate, $C_{20}H_{28}N_2O_5,C_4H_4O_4$, in the medium from the chromatograms obtained and using the declared content of $C_{20}H_{28}N_2O_5,C_4H_4O_4$ in *enalapril maleate BPCRS*.

LIMITS

The amount of enalapril maleate 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 prepared in solution A described under Dissolution.

(1) Shake a quantity of the powdered tablets containing 20 mg of Enalapril Maleate with 80 mL of solution A and then mix with the aid of ultrasound. Dilute to produce 100 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes.

(3) 0.02% w/v of *enalapril maleate BPCRS* and 0.001% w/v each of *enalapril diketopiperazine BPCRS* (impurity D), *enalaprilat BPCRS* (impurity C) and *3-phenylpropanoic acid* (impurity 1).
(4) 0.002% w/v of *L-alanyl-L-proline*.
(5) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to enalapril (retention time about 5 minutes) are: maleic acid, about 0.2; L-alanyl-L-proline, about 0.3; impurity C, about 0.4; impurity 1, about 0.5 and impurity D, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to maleic acid and impurity C is at least 2.0.

LIMITS

Identify any peaks due to impurities C, D, 1 and maleic acid in the chromatogram obtained with solution (1) using the chromatogram obtained with solution (3). Multiply the area of any peak corresponding to impurity C by a correction factor of 0.7 and any peak corresponding to impurity 1 by a correction factor of 0.6.

Identify any peak due to L-alanyl-L-proline in the chromatogram obtained with solution (1) using the chromatogram obtained with solution (4).

In the chromatogram obtained with solution (1):

the area of the peak corresponding to impurity C is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);

the area of the peak corresponding to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any peak corresponding to impurity 1 is not greater than 0.3 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 0.2 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any other *secondary peaks*, excluding impurities C, D and 1, is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

Disregard any peaks due to maleic acid and L-alanyl-L-proline and any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

ASSAY

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

(1) Shake a quantity of the powdered tablets containing 20 mg of Enalapril Maleate with 80 mL of solution A and then mix with the aid of ultrasound. Dilute to produce 100 mL and filter.
(2) 0.02% w/v of *enalapril maleate BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under the Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to enalapril is between 0.8 and 2.0.

DETERMINATION OF CONTENT

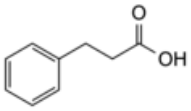
Calculate the content of $C_{20}H_{28}N_2O_5,C_4H_4O_4$ in the tablets using the declared content of $C_{20}H_{28}N_2O_5,C_4H_4O_4$ in *enalapril maleate BPCRS*.

STORAGE

Enalapril Tablets should be protected from light and moisture.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Enalapril Maleate and the following:



1. 3-Phenylpropanoic acid (dihydrocinnamic acid)