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

Eplerenone Tablets

General Notices

Action and use

Aldosterone receptor antagonist; antihypertensive.

DEFINITION

Eplerenone Tablets contain Eplerenone.

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

Content of eplerenone, $C_{24}H_{30}O_6$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of powdered tablets containing 50 mg of Eplerenone with 25 mL of *dichloromethane* and filter. Evaporate the filtrate to dryness on a *water-bath*. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the reference spectra of *eplerenone EPCRS* which has been treated in the same manner.

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 1% w/v *sodium dodecyl sulfate* in 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.

Solution B 25 volumes of *acetonitrile*, 25 volumes of *methanol* and 50 volumes of *water*.
(1) After 30 minutes withdraw a sample of the medium and filter. Dilute the filtrate, if necessary, with 0.1M *hydrochloric acid* to produce a solution expected to contain 0.0028% w/v of Eplerenone.
(2) 0.0028% w/v of *eplerenone EPCRS* in 0.1M *hydrochloric acid*.
(3) 0.025% w/v of *eplerenone for system suitability EPCRS* in Solution B.

CHROMATOGRAPHIC CONDITIONS

Solution A 0.1 volume of *orthophosphoric acid*, 40 volumes of *acetonitrile* and 60 volumes of *methanol*
(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (3 µm) (Inertsil ODS-3 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 240 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

46 volumes of solution A and 54 volumes of a 0.1% v/v solution of *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retention with reference to eplerenone (retention time about 9.3 minutes) are: impurity D, about 0.71 and impurity A, about 0.74.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity D and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity A.

DETERMINATION OF CONTENT

Calculate the total content of eplerenone, $C_{24}H_{30}O_6$, in the medium from the chromatograms obtained and using the declared content of $C_{24}H_{30}O_6$ in *eplerenone EPCRS*.

LIMITS

The amount of eplerenone 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.

(1) Shake a quantity of powdered tablets containing 25 mg of Eplerenone with 40 mL of solution B, add sufficient solution B to produce 50mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with Solution B. Further dilute 1 volume of this solution to 5 volumes with the same solvent.
(3) 0.05% w/v of *eplerenone for system suitability EPCRS* in Solution B.
(4) 0.05% w/v of *eplerenone for peak identification EPCRS* in 0.01M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (3 µm) (Inertsil ODS-3 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 30°.
(e) Use a detection wavelength of 240 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.1% v/v solution of *orthophosphoric acid*.

Mobile phase B 0.1 volumes of *orthophosphoric acid*, 40 volumes of *acetonitrile* and 60 volumes of *methanol*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-25	54	46	isocratic
25-32	54→40	46→60	linear gradient
32-45	40	60	isocratic

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
45-46	40→54	60→46	linear gradient
46-55	54	46	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to eplerenone (retention time about 9 minutes) are: impurity D, about 0.71; impurity A, about 0.74 and impurity B, about 1.2.

SYSTEM SUITABILITY

The test is not valid unless:

In the chromatogram obtained with solution (3):

the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity D and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity A.

LIMITS

Identify any peak corresponding to impurities A and D in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and any peak corresponding to impurity B using the chromatogram obtained with solution (4).

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity A or impurity B 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 *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area less than half 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.

Solution B 25 volumes of *acetonitrile*, 25 volumes of *methanol* and 50 volumes of *water*.
(1) Shake a quantity of powdered tablets containing 25 mg of Eplerenone with 40 mL of Solution B, add sufficient Solution B to produce 50mL and filter. Dilute 1 volume of the filtrate to 10 volumes with Solution B.
(2) 0.005% w/v of *eplerenone EPCRS* in Solution B.
(3) 0.05% w/v of *eplerenone for system suitability EPCRS* in Solution B.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity D and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity A.

DETERMINATION OF CONTENT

Calculate the content of eplerenone, $C_{24}H_{30}O_6$, in the tablets from the chromatograms obtained and using the declared content of $C_{24}H_{30}O_6$, in *eplerenone EPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Eplerenone.