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

Doxazosin Tablets

General Notices

Action and use

Alpha$_1$-adrenoceptor antagonist.

DEFINITION

Doxazosin Tablets contain Doxazosin Mesilate.

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

PRODUCTION

Risk assessment should be used to evaluate the potential for mutagenic methanesulfonate esters to be formed in the presence of low molecular weight alcohols. If a risk of methanesulfonate ester formation is identified through risk assessment, these impurities should not exceed the threshold of toxicological concern.

Content of doxazosin, $C_{23}H_{25}N_5O_5$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the 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, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.01M hydrochloric acid, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution containing the equivalent of 0.00011% w/v of doxazosin, at the maximum at 246 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.00013% w/v solution of *doxazosin mesilate BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of doxazosin, $C_{23}H_{25}N_5O_5$, in the medium from the absorbances obtained and using the declared content of $C_{23}H_{25}N_5O_5,CH_4O_3S$ in *doxazosin mesilate BPCRS*.

Each mg of $C_{23}H_{25}N_5O_5,CH_4O_3S$ is equivalent to 0.8245 mg of $C_{23}H_{25}N_5O_5$.

LIMITS

The amount of doxazosin 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 prepared in solution A.

Solution A 1 volume of mobile phase B and 9 volumes of mobile phase A.

(1) Shake a quantity of powdered tablets containing the equivalent of 20 mg of doxazosin in 150 mL and mix with the aid of ultrasound. Dilute to produce 250 mL and filter (a 0.45-µm regenerated cellulose membrane filter is suitable).
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.008% w/v of *doxazosin impurity standard BPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (5 µm) (Lichrospher RP-Select B is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 0.8 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 210 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 0.15% w/v of *orthophosphoric acid*.

Mobile phase B 0.15% w/v of *orthophosphoric acid* in *acetonitrile R1* .

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-5	90	10	isocratic
5-40	90→50	10→50	linear gradient
40-45	50	50	isocratic
45-46	50→90	50→10	linear gradient
46-50	90	10	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity D and impurity F is at least 4.5.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of doxazosin in solution (2).

For the reporting threshold, use the concentration of doxazosin in solution (4).

Doxazosin retention time: about 32 minutes.

Relative retention: impurity G, about 0.2; impurity D, about 0.5; impurity F, about 0.7.

LIMITS

— impurity G: not more than 0.5%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 1.0%;

— reporting threshold: 0.1%.

Uniformity of content

Tablets containing the equivalent of less than 2 mg and/or less than 2% w/w of doxazosin comply with the requirements stated under Tablets using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in solution B.

Solution B 0.15% w/v of *orthophosphoric acid* in a mixture of 1 volume *acetonitrile* and 9 volumes of *water*.

(1) Add 2 mL to one tablet and allow to disintegrate. Add a further 5 mL, shake and mix with the aid of ultrasound, then dilute to produce 10 mL. Filter (a 0.45-µm regenerated cellulose membrane filter is suitable) and further dilute to produce a solution expected to contain the equivalent of 0.005% w/v of doxazosin.
(2) 0.0061% w/v of *doxazosin mesilate BPCRS*.
(3) 0.008% w/v of *doxazosin impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm x 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 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 40°.
(e) Use a detection wavelength of 246 nm.
(f) Inject 25 µL of each solution.

MOBILE PHASE

30 volumes of *acetonitrile* and 70 volumes of 0.05M *potassium dihydrogen orthophosphate*, previously adjusted to pH 6.0 with *potassium hydroxide*.

When the chromatograms are recorded under the prescribed conditions, the retention time of doxazosin is about 15 minutes; impurities D and G may co-elute (relative retention time, about 0.1).

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity (D+G) and impurity F is at least 4.5.

DETERMINATION OF CONTENT

Calculate the content of doxazosin, $C_{23}H_{25}N_5O_5$, in each tablet from the chromatograms obtained and using the declared content of $C_{23}H_{25}N_5O_5,CH_4O_3S$ in *doxazosin mesilate BPCRS*.

Each mg of $C_{23}H_{25}N_5O_5,CH_4O_3S$ is equivalent to 0.8245 mg of $C_{23}H_{25}N_5O_5$.

ASSAY

For Tablets containing the equivalent of less than 2 mg and/or less than 2% w/w of doxazosin

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

For Tablets containing the equivalent of 2 mg or more and 2% w/w or more of doxazosin

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

Solution B 0.15% w/v of *orthophosphoric acid* in a mixture of 1 volume *acetonitrile* and 9 volumes of *water*.

(1) Shake a quantity of powdered tablets containing the equivalent of 20 mg of doxazosin in 50 mL and mix with the aid of ultrasound. Dilute to produce 250 mL and filter (a 0.45-µm regenerated cellulose membrane filter is suitable).
(2) 0.0097% w/v of *doxazosin mesilate BPCRS*.
(3) 0.008% w/v of *doxazosin impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Uniformity of content may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between doxazosin and impurity F is at least 4.5.

DETERMINATION OF CONTENT

Calculate the content of doxazosin, $C_{23}H_{25}N_5O_5$, in the tablets from the chromatograms obtained and using the declared content of $C_{23}H_{25}N_5O_5,CH_4O_3S$ in *doxazosin mesilate BPCRS*.

Each mg of $C_{23}H_{25}N_5O_5,CH_4O_3S$ is equivalent to 0.8245 mg of $C_{23}H_{25}N_5O_5$.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of doxazosin.

IMPURITIES

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