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

Cabergoline Tablets

General Notices

Action and use

Dopamine D_2 receptor agonist.

DEFINITION

Cabergoline Tablets contain Cabergoline.

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

Content of cabergoline, $C_{26}H_{37}N_5O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. The *light absorption*, Appendix II B, in the range 210 to 400 nm of solution (1) in the Assay is concordant with that obtained with solution (2).
B. In the Assay, 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 500 mL of 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.

(1) After 15 minutes withdraw a sample of the medium and filter. Dilute the filtrate with dissolution medium, if necessary, to produce a solution expected to contain 0.0001% w/v of Cabergoline.
(2) 0.0001% w/v of *cabergoline EPCRS* in the dissolution medium.
(3) Suspend 25 mg of *cabergoline EPCRS* in 5 mL of 0.1M sodium hydroxide. Stir for about 15 minutes. To 1 mL of the suspension add 1 mL of 0.1M *hydrochloric acid* and dilute to 10 mL with the mobile phase. Mix with the aid of ultrasound until dissolution is complete and dilute 1 volume of this solution to 5 volumes with the mobile phase (*in-situ* degradation of cabergoline to produce impurity A).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 280 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

0.2 volumes of *triethylamine*, 16 volumes of *acetonitrile* and 84 volumes of a freshly prepared 0.68% w/v solution of *potassium dihydrogen orthophosphate* previously adjusted to pH 2.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to cabergoline (retention time, about 12 minutes) are: impurity D, about 0.3; impurity B, about 0.6; impurity A, about 0.8; impurity C, about 2.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to cabergoline and impurity A is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{37}N_5O_2$ in each tablet from the chromatograms obtained and using the declared content of $C_{26}H_{37}N_5O_2$ in *cabergoline EPCRS*.

LIMITS

The amount of cabergoline 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 2.5 mg of Cabergoline with 7 mL of the mobile phase, add sufficient mobile phase to produce 10 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.
(3) Suspend 25 mg of *cabergoline EPCRS* in 5 mL of 0.1M *sodium hydroxide*. Stir for about 15 minutes. To 1 mL of the suspension add 1 mL of 0.1M *hydrochloric acid* and dilute to 10 mL with the mobile phase. Mix with the aid of ultrasound until dissolution is complete and dilute 1 volume of this solution to 5 volumes with the mobile phase (*in-situ* degradation of cabergoline to produce impurity A).
(4) Dilute 1 volume of solution (2) to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used. For solution (1), allow the chromatography to run for four times the retention time of the peak due to cabergoline.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to cabergoline (retention time, about 12 minutes) are: impurity D, about 0.3; impurity B, about 0.6; impurity A, about 0.8; impurity C, about 2.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to cabergoline and impurity A is at least 3.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A or 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 other *secondary peak* is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

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

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of cabergoline 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.

(1) Disperse one tablet with the aid of ultrasound in 3 mL of the mobile phase. Allow to cool, add sufficient of the mobile phase to produce a solution expected to contain 0.025% w/v of Cabergoline and filter.
(2) 0.025% w/v of *cabergoline EPCRS* in the mobile phase.
(3) Suspend 25 mg of *cabergoline EPCRS* in 5 mL of 0.1M *sodium hydroxide*. Stir for about 15 minutes. To 1 mL of the suspension add 1 mL of 0.1M *hydrochloric acid* and dilute to 10 mL with the mobile phase. Mix with the aid of ultrasound until dissolution is complete and dilute 1 volume of this solution to 5 volumes with the mobile phase (*in-situ* degradation of cabergoline to produce impurity A).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used, with an injection volume of 250 µL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to cabergoline and impurity A is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{37}N_5O_2$ in each tablet from the chromatograms obtained and using the declared content of $C_{26}H_{37}N_5O_2$ in *cabergoline EPCRS*.

ASSAY

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

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

For tablets containing 2 mg or more and 2% w/w or more of cabergoline

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

(1) Shake a quantity of powdered tablets containing 2.5 mg of Cabergoline with 7 mL of the mobile phase, add sufficient mobile phase to produce 10 mL and filter.
(2) 0.025% w/v of *cabergoline EPCRS* in the mobile phase.
(3) Suspend 25 mg of *cabergoline EPCRS* in 5 mL of 0.1M *sodium hydroxide*. Stir for about 15 minutes. To 1 mL of the suspension add 1 mL of 0.1M *hydrochloric acid* and dilute to 10 mL with the mobile phase. Mix with the aid of ultrasound until dissolution is complete and dilute 1 volume of this solution to 5 volumes with the mobile phase (*in-situ* degradation of cabergoline to produce impurity A).

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 *resolution* between the peaks due to cabergoline and impurity A is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{37}N_5O_2$ in the tablets from the chromatograms obtained and using the declared content of $C_{26}H_{37}N_5O_2$ in *cabergoline EPCRS*.

STORAGE

Cabergoline Tablets should be stored in accordance with the manufacturers instruction.

IMPURITIES

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