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

Fluconazole Capsules

General Notices

Action and use

Antifungal.

DEFINITION

Fluconazole Capsules contain Fluconazole.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of fluconazole, $C_{13}H_{12}F_2N_6O$

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.
(1) Shake a quantity of the powdered capsule contents containing 100 mg of Fluconazole with 10 mL of *methanol*. Filter and use the filtrate.
(2) 1.0% w/v of *fluconazole BPCRS* in *methanol*.
(3) 0.2% w/v of *fluconazole BPCRS* and 0.1% w/v of *ketoconazole BPCRS* in *methanol*.

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, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

1 volume of 13.5M *ammonia*, 20 volumes of *methanol* and 80 volumes of *dichloromethane*.

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 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.

TEST CONDITIONS

(a) Use Apparatus 1, and rotate the basket at 100 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 and measure the *absorbance* of the filtered sample, diluted with the dissolution medium, if necessary, to produce a solution containing 0.0056% w/v of Fluconazole, at 261 nm, Appendix II B using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.0056% w/v solution of *fluconazole BPCRS* in dissolution medium at 261 nm using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of fluconazole, $C_{13}H_{12}F_2N_6O$, in the medium from the absorbances obtained and using the declared content of $C_{13}H_{12}F_2N_6O$ in *fluconazole BPCRS*.

LIMITS

The amount of fluconazole 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 in the mobile phase.

(1) To a quantity of powdered capsule contents containing 0.5 g of Fluconazole, add 25 mL and mix with the aid of ultrasound. Dilute to produce 50 mL, filter and use the filtrate.
(2) Dilute 1 volume of solution (1) to 100 volumes and further dilute 1 volume to 10 volumes.
(3) 0.1% w/v of *fluconazole impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Waters Symmetry C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 260 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 3.5 times the retention time of fluconazole.

MOBILE PHASE

14 volumes of *acetonitrile* and 86 volumes of 0.01M *ammonium formate*.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to fluconazole (retention time about 11 minutes) are: impurity B, about 0.4; impurity A, about 0.5 and impurity C, about 0.8.

SYSTEM SUITABILITY

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

LIMITS

Identify any peaks corresponding to impurities B and C in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the areas of these peaks by correction factors of 0.15 and 0.05, respectively.

In the chromatogram obtained with solution (1):

the area of any peak due to impurity A is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of any peak due to impurity B is not greater than 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 twice the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the total content of impurities is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder the content of 20 capsules. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) To a quantity of powdered capsule contents containing 0.5 g of Fluconazole add 50 mL, mix with the aid of ultrasound and dilute to produce 100 mL. Dilute 1 volume to 10 volumes, filter and use the filtrate.
(2) 0.05% w/v of *fluconazole BPCRS*.
(3) 0.1% w/v of *fluconazole impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances 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 impurity C and fluconazole is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{12}F_2N_6O$ in the capsules using the declared content of $C_{13}H_{12}F_2N_6O$ in *fluconazole BPCRS*.

IMPURITIES

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