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

Fluconazole Oral Suspension

General Notices

Action and use

Antifungal.

DEFINITION

Fluconazole Oral Suspension is a suspension of Fluconazole in a suitable vehicle. It is prepared by dispersing the dry ingredients in the specified volume of Water just before issue for use.

The dry ingredients comply with the requirements for Powders and Granules for Oral Solutions and Suspensions stated under Oral Liquids.

For the following tests prepare the Oral Suspension as directed on the label. The suspension, examined immediately after preparation unless otherwise indicated, complies with the requirements stated under Oral Liquids 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 oral suspension containing 10 mg of Fluconazole with 3 mL of *methanol*. Add sufficient *methanol* to produce 5 mL, filter and use the filtrate.
(2) 0.2% 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 20 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) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Acidity

pH, 3.0 to 5.0, Appendix V L.

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 the oral suspension containing 0.1 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 200 volumes.
(3) 0.1% w/v of *fluconazole impurity standard BPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

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) For solution (1), 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 0.8 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 0.6 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 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the total content of impurities is not greater than twice 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 (4) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) To a weighed quantity of the oral suspension containing 25 mg, add 20 mL and shake. Dilute to 50 mL, 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

Determine the weight per mL of the oral suspension, Appendix V G, and calculate the content of $C_{13}H_{12}F_2N_6O$, weight in volume, using the declared content of $C_{13}H_{12}F_2N_6O$ in *fluconazole BPCRS*.

Repeat the procedure using a portion of the oral suspension that has been stored at the temperature and for the period stated on the label during which it may be expected to be satisfactory for use.

IMPURITIES

The impurities limited by the requirements of this monograph include A, B and C listed under Fluconazole.