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

Fluconazole Infusion

General Notices

Action and use

Antifungal.

DEFINITION

Fluconazole Infusion is a sterile solution containing Fluconazole. It is supplied as a ready-to-use solution.

The infusion complies with the requirements stated under Parenteral Preparations 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) Dilute a volume of the infusion with *methanol*, if necessary, to produce a solution containing 0.2% w/v of Fluconazole.
(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 or alkalinity

pH, 4.0 to 8.0, Appendix V L.

Related substances

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

(1) Dilute the infusion, if necessary, to produce a solution containing 0.2% w/v of Fluconazole.
(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

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

(1) Dilute the infusion to produce a solution containing 0.05% w/v of Fluconazole.
(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 infusion using the declared content of $C_{13}H_{12}F_2N_6O$ in *fluconazole BPCRS*.

STORAGE

Fluconazole Infusion should be stored at a temperature not exceeding 30°. It should not be refrigerated or allowed to freeze.

IMPURITIES

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