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

Griseofulvin Premix

General Notices

Action and use

Antifungal.

DEFINITION

Griseofulvin Premix contains Griseofulvin. The particles of Griseofulvin are generally up to 5 µm in maximum dimension, although larger particles, which may occasionally exceed 30 µm, may be present.

The premix complies with the requirements stated under Premixes and with the following requirements.

Content of griseofulvin, $C_{17}H_{17}ClO_6$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the premix containing 0.1 g of Griseofulvin with 10 mL of *dichloromethane*. Centrifuge, decant the supernatant liquid, dry with *anhydrous sodium sulfate* and evaporate the dichloromethane. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of griseofulvin *(RSV 24)*.

Related substances

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

(1) Disperse a quantity of premix containing 0.25 g of Griseofulvin in mobile phase B and dilute to 500 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.05% w/v of *griseofulvin for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Discovery C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 290 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 20 volumes of 0.1 % v/v *formic acid* adjusted to pH 4.5 with *dilute ammonia R2* and 80 volumes of *water*.

Mobile phase B 15 volumes of *water*, 20 volumes of 0.1 % v/v *formic acid* adjusted to pH 4.5 with *dilute ammonia R2* and 65 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-3	50	50	isocratic
3-13	50→40	50→60	linear gradient
13-16	40→10	60→90	linear gradient
16-24	10	90	isocratic

When the chromatograms are recorded under the prescribed conditions, the relative retention times with reference to griseofulvin (retention time about 16 minutes) are: impurity A, about 0.4; impurity B, about 0.7 and impurity C, about 1.1.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 3.0, where *Hp* is the height above the baseline of the peak due to impurity C and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to griseofulvin.

LIMITS

Identify any peak corresponding to impurity A in the chromatogram obtained with solution (1) and multiply the area of this peak by a correction factor of 0.6.

the area of any peak corresponding to impurity B is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (3.0%);

the area of any peak corresponding to impurity A is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the sum of the areas of all *secondary peaks* is not greater than five times the area of the principal peak in the chromatogram obtained with solution (2) (5.0%).

Disregard any peaks due to excipients and any peak with an area less than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%).

ASSAY

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

(1) Disperse a quantity of premix containing 0.25 g of Griseofulvin in mobile phase B and dilute to 500 mL.
(2) 0.05% w/v of *griseofulvin for LC assay and identification EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{17}H_{17}ClO_6$ in the premix from the chromatograms obtained and using the declared content of $C_{17}H_{17}ClO_6$ in *griseofulvin for LC assay and identification EPCRS*.

IMPURITIES

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