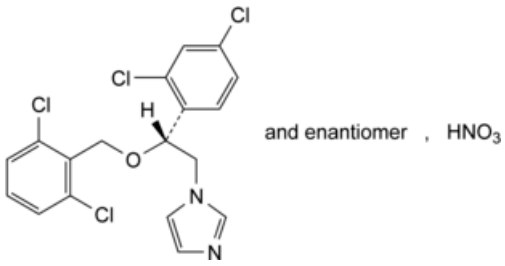
Edition: BP 2025 (Ph. Eur. 11.6 update)

Isoconazole Nitrate

General Notices

(Ph. Eur. monograph 1017)



$C_{18}H_{15}Cl_4N_3O_4$ 479.1 *24168-96-5*

Action and use

Antifungal.

Ph Eur

DEFINITION

1-[(2*RS*)-2-(2,4-Dichlorophenyl)-2-[(2,6-dichlorophenyl)methoxy]ethyl]-1*H*-imidazole nitrate.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white powder.

Solubility

Very slightly soluble in water, soluble in methanol, slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Melting point (*2.2.14*): 178 °C to 182 °C.
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *isoconazole nitrate CRS*.

TESTS

Solution S

Dissolve 0.20 g in *methanol R* and dilute to 20.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

Optical rotation (*2.2.7*)

-0.10° to + 0.10°, determined on solution S.

Related substances

Liquid chromatography (*2.2.29*).

Test solution Dissolve 0.100 g of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a) Dissolve 2.5 mg of *isoconazole nitrate CRS* and 2.5 mg of *miconazole nitrate CRS* (impurity C) in the mobile phase, then dilute to 100 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase Dissolve 6.0 g of *ammonium acetate R* in a mixture of 300 mL of *acetonitrile for chromatography R*, 320 mL of *methanol R1* and 380 mL of *water for chromatography R*.

Flow rate 2 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 10 µL.

Run time Twice the retention time of isoconazole.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peak due to impurity C.

Relative retention With reference to isoconazole (retention time = about 14 min): nitrate = about 0.04; impurity C = about 1.4.

System suitability Reference solution (a):

— *resolution*: minimum 5.0 between the peaks due to isoconazole and impurity C.

Calculation of percentage contents:

— for each impurity, use the concentration of isoconazole nitrate in reference solution (b).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.5 per cent;

— *reporting threshold*: 0.05 per cent; disregard the peak due to the nitrate ion.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.350 g in 75 mL of a mixture of 1 volume of *anhydrous acetic acid R* and 7 volumes of *methyl ethyl ketone R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

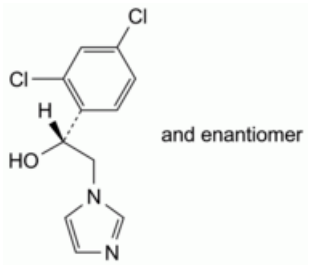
1 mL of *0.1 M perchloric acid* is equivalent to 47.91 mg of $C_{18}H_{15}Cl_4N_3O_4$.

STORAGE

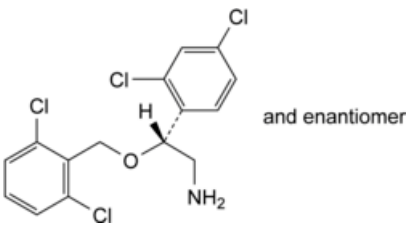
Protected from light.

IMPURITIES

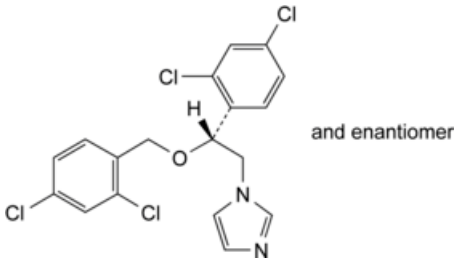
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C.



A. (1*RS*)-1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethan-1-ol,



B. (2*RS*)-2-(2,4-dichlorophenyl)-2-[(2,6-dichlorophenyl)methoxy]ethan-1-amine,



and enantiomer

C. 1-[(2*RS*)-2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methoxy]ethyl]-1*H*-imidazole (miconazole).

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