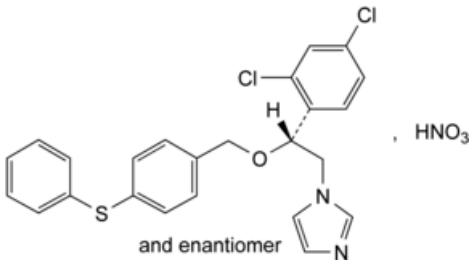
Edition: BP 2025 (Ph. Eur. 11.6 update)

Fenticonazole Nitrate

General Notices

(Ph. Eur. monograph 1211)



$C_{24}H_{21}Cl_2N_3O_4S$ 518.4 *73151-29-8*

Action and use

Antifungal.

Ph Eur

DEFINITION

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

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in dimethylformamide and in methanol, sparingly soluble in anhydrous ethanol.

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D.

A. Melting point (2.2.14): 134 °C to 137 °C.
B. Ultraviolet and visible absorption spectrophotometry (2.2.25).

Test solution Dissolve 20.0 mg in *anhydrous ethanol R* and dilute to 100.0 mL with the same solvent. Dilute 1.0 mL of this solution to 10.0 mL with *anhydrous ethanol R*.

Spectral range 230-350 nm.

Absorption maximum 252 nm.

Shoulder about 270 nm.

Absorption minimum 236 nm.

Specific absorbance at the absorption maximum 260 to 280.

C. Infrared absorption spectrophotometry (2.2.24).

Comparison *fenticonazole nitrate CRS*.

D. It gives the reaction of nitrates (2.3.1).

TESTS

Optical rotation (2.2.7)

-0.10° to + 0.10°.

Dissolve 0.10 g in *methanol R* and dilute to 10.0 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 25.0 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase.

Reference solution (a) Dilute 1.0 mL of the test solution to 200.0 mL with the mobile phase.

Reference solution (b) Dilute 10.0 mL of reference solution (a) to 25.0 mL with the mobile phase.

Reference solution (c) Dilute 1.0 mL of reference solution (a) to 10.0 mL with the mobile phase.

Reference solution (d) Dilute 1 mL of the test solution to 100 mL with the mobile phase. Dissolve the contents of a vial of *fenticonazole impurity D CRS* in 1 mL of this solution.

Reference solution (e) Dissolve the contents of a vial of *fenticonazole impurity E CRS* in 1 mL of the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5-10 µm).

Mobile phase Mix 70 volumes of *acetonitrile R1* and 30 volumes of a phosphate buffer solution prepared by dissolving 3.4 g of *potassium dihydrogen phosphate R* in 900 mL of *water for chromatography R*, adjusting to pH 3.0 with *phosphoric acid R* and diluting to 1000 mL with *water for chromatography R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 229 nm.

Injection 10 µL.

Run time 7.5 times the retention time of fenticonazole.

Identification of impurities Use the chromatogram obtained with reference solution (d) to identify the peak due to impurity D; use the chromatogram obtained with reference solution (e) to identify the peak due to impurity E.

Relative retention With reference to fenticonazole (retention time = about 5.7 min): impurity D = about 0.6; impurity E = about 3.7.

Calculation of percentage contents:

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

System suitability:

— *resolution*: minimum 2.0 between the peaks due to impurity D and fenticonazole in the chromatogram obtained with reference solution (d);

— *signal-to-noise ratio*: minimum 5 for the principal peak in the chromatogram obtained with reference solution (c).

Limits:

— *impurity E*: maximum 0.2 per cent;

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

— *total*: maximum 0.3 per cent;

— *reporting threshold*: maximum 0.05 per cent; disregard the peak due to the nitrate ion (retention time = about 1.5 min).

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.450 g in 50 mL of a mixture of equal volumes of *anhydrous acetic acid R* and *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 51.84 mg of $C_{24}H_{21}Cl_2N_3O_4S$.

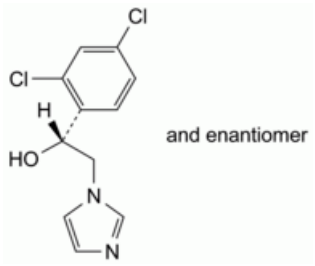
STORAGE

Protected from light.

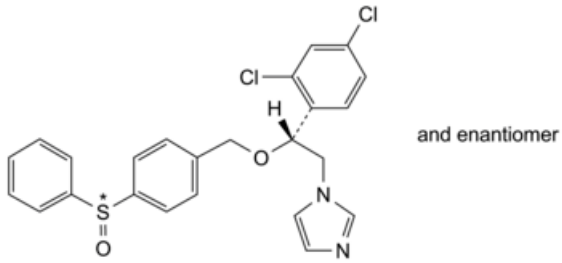
IMPURITIES

Specified impurities *E*.

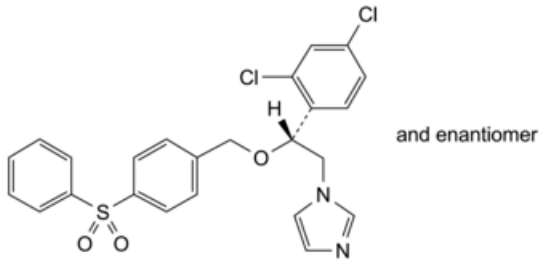
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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, D*.



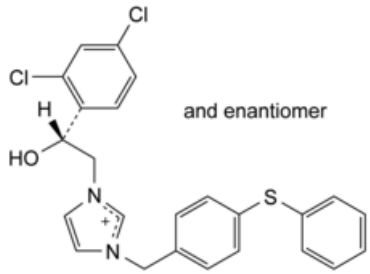
A. (1*RS*)-1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethan-1-ol,



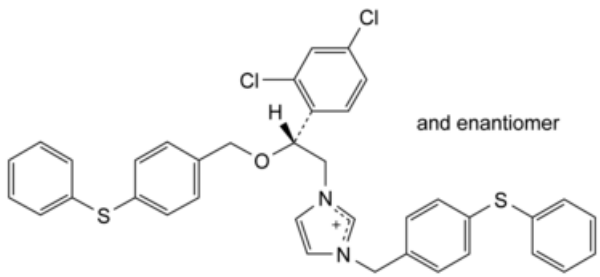
B. 1-[(2*RS*)-2-[[4-[(2Ξ)-benzenesulfinyl]phenyl]methoxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole,



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



D. (7*RS*)-8^{2},8^{4}-dichloro-7-hydroxy-2-thia-5(1,3)-imidazola-1,8(1),3(1,4)-tribenzenaoctaphan-5-ium,



E. (7*RS*)-7-(2,4-dichlorophenyl)-8-oxa-2,11-dithia-5(1,3)-imidazola-1,12(1),3,10(1,4)-tetrabenzenadodecaphan-5-ium.