



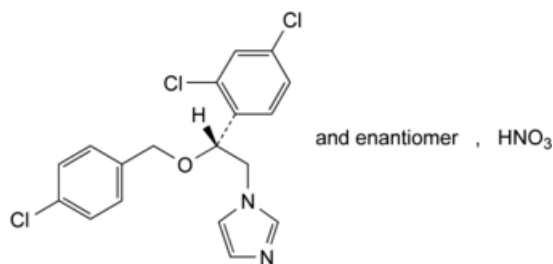
Edition: BP 2025 (Ph. Eur. 11.6 update)

Econazole Nitrate



General Notices

(Ph. Eur. monograph 0665)



C₁₈H₁₆Cl₃N₃O₄ 444.7 24169-02-6

Action and use

Antifungal.

Preparations

[Econazole Cream](#)

[Econazole Pessaries](#)

Ph Eur

DEFINITION

1-[(2*RS*)-2-[(4-Chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)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

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

mp

About 165 °C, with decomposition.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison [econazole nitrate CRS](#).

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.100 g of the substance to be examined in [methanol R](#) and dilute to 10.0 mL with the same solvent.

Reference solution (a) Dissolve 10 mg of [econazole for system suitability CRS](#) (containing impurities A, B and C) in [methanol R](#) and dilute to 1.0 mL with the same solvent.

Reference solution (b) Dilute 1.0 mL of the test solution to 20.0 mL with [methanol R](#). Dilute 1.0 mL of this solution to 25.0 mL with [methanol R](#).

Column:

- *size:* $l = 0.10\text{ m}$, $\varnothing = 4.6\text{ mm}$;
- *stationary phase:* [base-deactivated octadecylsilyl silica gel for chromatography R](#) (3 μm);
- *temperature:* 35 °C.

Mobile phase:

- *mobile phase A:* [methanol R](#), 0.77 g/L solution of [ammonium acetate R](#) (20:80 V/V);
- *mobile phase B:* [methanol R](#), [acetonitrile R](#) (40:60 V/V);

Time (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 - 25	60 → 10	40 → 90
25 - 27	10	90

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 225 nm.

Injection 10 μL .

Identification of impurities Use the chromatogram supplied with [econazole for system suitability CRS](#) and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A, B and C.

Relative retention With reference to econazole (retention time = about 15 min): impurity A = about 0.2; impurity B = about 0.6; impurity C = about 1.1.

System suitability Reference solution (a):

- *peak-to-valley ratio:* minimum 1.5, where H_p = height above the baseline of the peak due to impurity C and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to econazole.

Limits:

- *correction factor*: for the calculation of content, multiply the peak area of impurity A by 1.4;
- *impurities A, B, C*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);
- *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);
- *total*: not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);
- *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard the peak due to the nitrate ion at the beginning of the chromatogram.

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 4 h.

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.400 g in 50 mL of [anhydrous acetic acid R](#). Titrate with [0.1 M perchloric acid](#), determining the end-point potentiometrically ([2.2.20](#)). Carry out a blank titration.

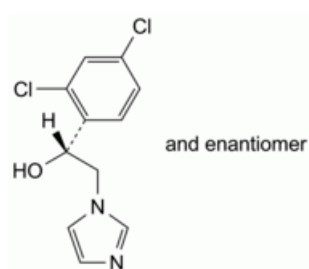
1 mL of [0.1 M perchloric acid](#) is equivalent to 44.47 mg of $C_{18}H_{16}Cl_3N_3O_4$.

STORAGE

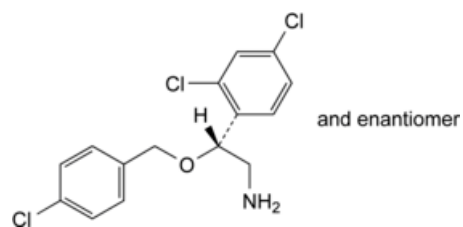
Protected from light.

IMPURITIES

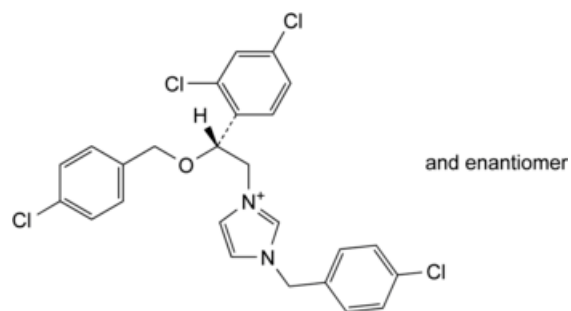
Specified impurities A, B, C.



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



B. (2*RS*)-2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine,



C. 1-(4-chlorobenzyl)-3-[(2*RS*)-2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]imidazolium.

Ph Eur