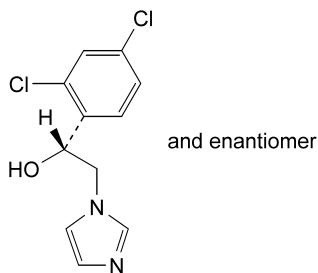
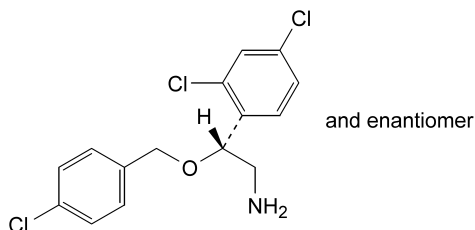


IMPURITIES

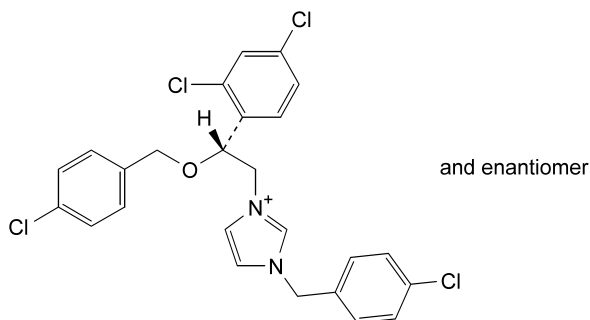
Specified impurities: A, B, C.



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



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

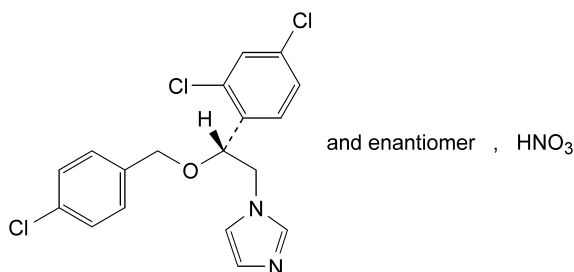


C. 1-(4-chlorobenzyl)-3-[(2RS)-2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]imidazolium.

01/2008:0665
corrected 6.0

ECONAZOLE NITRATE

Econazoli nitras



$C_{18}H_{16}Cl_3N_3O_4$
[68797-31-9]

M_r 444.7

DEFINITION

1-[(2RS)-2-[(4-Chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1H-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 alcohol.

mp: about 165 °C, with decomposition.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison: Ph. Eur. reference spectrum of econazole nitrate.

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 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 the solution to 25.0 ml with methanol R.

Column:

- size: $l = 0.10$ m, $\varnothing = 4.6$ mm,
- stationary phase: base-deactivated octadecylsilyl silica gel for chromatography R (3 μ m),
- temperature: 35 °C.

Mobile phase:

- mobile phase A: mix 20 volumes of methanol R and 80 volumes of a 0.77 g/l solution of ammonium acetate R,
- 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
27 - 28	10 → 60	90 → 40
28 - 33	60	40

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 225 nm.

Injection: 10 μ l.

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 of 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),
- 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.

01/2008:1612

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.

Sulphated 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.

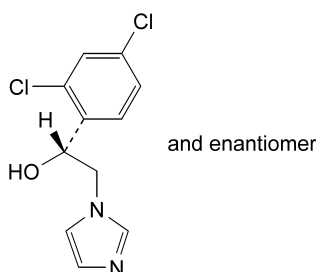
1 ml of 0.1 M *perchloric acid* is equivalent to 44.47 mg of $C_{10}H_{16}Cl_3N_2O_8$.

STORAGE

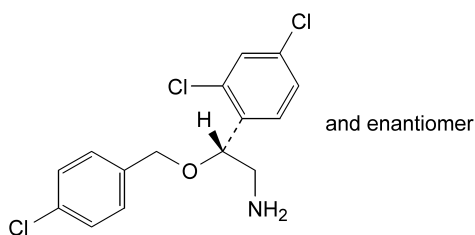
Protected from light.

IMPURITIES

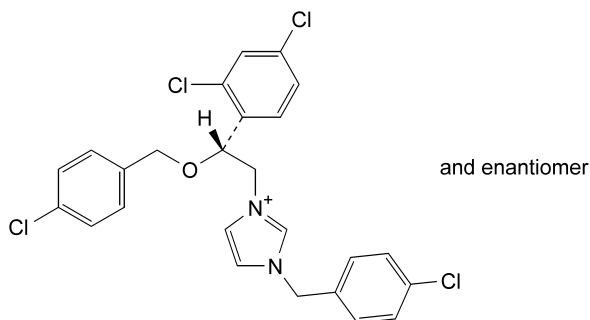
Specified impurities: A, B, C.



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



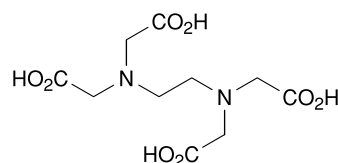
B. (2*RS*)-2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine,



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

EDETIC ACID

Acidum edeticum



$C_{10}H_{16}N_2O_8$
[60-00-4]

M_r 292.2

DEFINITION

(Ethylenedinitrilo)tetraacetic acid.

Content: 98.0 per cent to 101.0 per cent.

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless crystals.

Solubility: practically insoluble in water and in ethanol (96 per cent). It dissolves in dilute solutions of alkali hydroxides.

IDENTIFICATION

First identification: A.

Second identification: B, C.

A. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs, after drying the substance to be examined in an oven at 100-105 °C for 2 h.

Comparison: *sodium edetate R*, treated as follows: dissolve 0.25 g of *sodium edetate R* in 5 ml of *water R*, add 1.0 ml of *dilute hydrochloric acid R*. Filter, wash the residue with 2 quantities, each of 5 ml, of *water R* and dry the residue in an oven at 100-105 °C for 2 h.

B. To 5 ml of *water R* add 0.1 ml of *ammonium thiocyanate solution R* and 0.1 ml of *ferric chloride solution R1* and mix. The solution is red. Add 0.5 ml of solution S (see Tests). The solution becomes yellowish.

C. To 10 ml of solution S add 0.5 ml of *calcium chloride solution R*. Make alkaline to *red litmus paper R* by the addition of *dilute ammonia R2* and add 3 ml of *ammonium oxalate solution R*. No precipitate is formed.

TESTS

Solution S. Dissolve 5.0 g in 20 ml of *dilute sodium hydroxide solution R* and dilute to 100 ml with *water R*.

Appearance of solution. Solution S is clear (2.2.1) and colourless (2.2.2, *Method II*).

Impurity A. Liquid chromatography (2.2.29). Carry out the test protected from light.

Solvent mixture. Dissolve 10.0 g of *ferric sulphate pentahydrate R* in 20 ml of 0.5 M *sulphuric acid* and add 780 ml of *water R*. Adjust to pH 2.0 with 1 M *sodium hydroxide* and dilute to 1000 ml with *water R*.

Test solution. Dissolve 0.100 g of the substance to be examined in 1.0 ml of 1 M *sodium hydroxide* and dilute to 25.0 ml with the solvent mixture.

Reference solution. Dissolve 40.0 mg of *nitrilotriacetic acid R* in the solvent mixture and dilute to 100.0 ml with the solvent mixture. To 1.0 ml of the solution add 0.1 ml of the test solution and dilute to 100.0 ml with the solvent mixture.