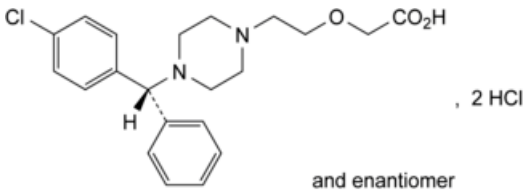
Edition: BP 2025 (Ph. Eur. 11.6 update)

Cetirizine Hydrochloride

General Notices

(Cetirizine Dihydrochloride, Ph. Eur. monograph 1084)



$C_{21}H_{27}Cl_3N_2O_3$ 461.8 *83881-52-1*

Action and use

Histamine H_1 receptor antagonist; antihistamine.

Preparations

Cetirizine Capsules

Cetirizine Oral Solution

Cetirizine Tablets

Ph Eur

DEFINITION

(*RS*)-2-[2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid dihydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white powder.

Solubility

Freely soluble in water, practically insoluble in acetone and in methylene chloride.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (2.2.25).

Test solution Dissolve 20.0 mg in 50 mL of a 10.3 g/L solution of *hydrochloric acid R* and dilute to 100.0 mL with the same acid. Dilute 10.0 mL of this solution to 100.0 mL with a 10.3 g/L solution of *hydrochloric acid R*.

Spectral range 210-350 nm.

Absorption maximum At 231 nm.

Specific absorbance at the absorption maximum 359 to 381.

B. Infrared absorption spectrophotometry (2.2.24).

Comparison *cetirizine dihydrochloride CRS*.

C. Thin-layer chromatography (2.2.27).

Test solution Dissolve 10 mg of the substance to be examined in *water R* and dilute to 5 mL with the same solvent.

Reference solution (a) Dissolve 10 mg of *cetirizine dihydrochloride CRS* in *water R* and dilute to 5 mL with the same solvent.

Reference solution (b) Dissolve 10 mg of *chlorphenamine maleate CRS* in *water R* and dilute to 5 mL with the same solvent. Mix 1 mL of the solution and 1 mL of reference solution (a).

Plate *TLC silica gel GF_{254} plate R*.

Mobile phase *ammonia R*, *methanol R*, *methylene chloride R* (1:10:90 *V/V/V*).

Application 5 µL.

Development Over 2/3 of the plate.

Drying In a current of cold air.

Detection Examine in ultraviolet light at 254 nm.

System suitability Reference solution (b):

— the chromatogram shows 2 clearly separated spots.

Results The principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. It gives reaction (a) of chlorides (2.3.1).

TESTS

Solution S

Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY_7 (2.2.2, *Method II*).

pH (2.2.3)

1.2 to 1.8 for solution S.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 20 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dissolve 2 mg of cetirizine dihydrochloride CRS and 2 mg of cetirizine impurity A CRS in the mobile phase and dilute to 50.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 100.0 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.

Reference solution (c) Dissolve the contents of a vial of cetirizine for peak identification CRS (containing impurities B, C, D, E and F) in 5.0 mL of the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

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

Mobile phase dilute sulfuric acid R, water R, acetonitrile R (0.4:6.6:93 *V/V/V*).

Flow rate 1 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 20 µL.

Run time 3 times the retention time of cetirizine.

Identification of impurities Use the chromatogram supplied with cetirizine for peak identification CRS and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities B, C, D, E and F; use the chromatogram obtained with reference solution (a) to identify the peak due to impurity A.

Relative retention With reference to cetirizine (retention time = about 9 min): impurity D = about 0.6; impurity B = about 0.8; impurity C = about 0.9; impurity E = about 1.2; impurity F = about 1.37; impurity A = about 1.42.

System suitability Reference solution (c):

— peak-to-valley ratio: minimum 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 cetirizine.

Limits:

— *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.7; impurity C = 1.9; impurity D = 0.6; impurity E = 1.3; impurity F = 1.9;

— *impurities A, B, C, D, E, F*: for each impurity, not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.15 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Loss on drying (2.2.32)

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

Sulfated ash (2.4.14)

Maximum 0.2 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.100 g in 70 mL of a mixture of 30 volumes of *water R* and 70 volumes of *acetone R*. Titrate with *0.1 M sodium hydroxide* to the 2nd point of inflexion. Determine the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

1 mL of *0.1 M sodium hydroxide* is equivalent to 15.39 mg of $C_{21}H_{27}Cl_3N_2O_3$.

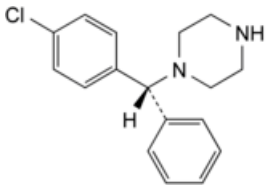
STORAGE

Protected from light.

IMPURITIES

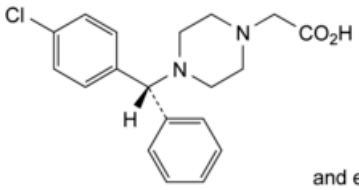
Specified impurities *A, B, C, D, E, F.*

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) *G.*



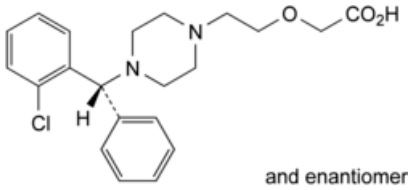
and enantiomer

A. (*RS*)-1-[(4-chlorophenyl)phenylmethyl]piperazine,



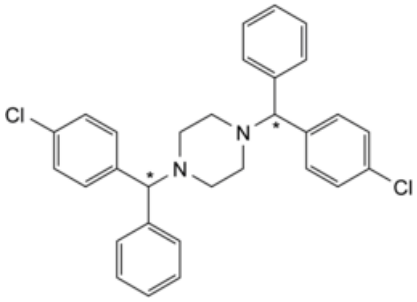
and enantiomer

B. (*RS*)-2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]acetic acid,

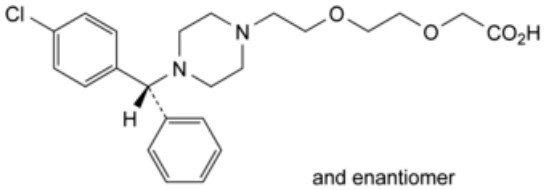


and enantiomer

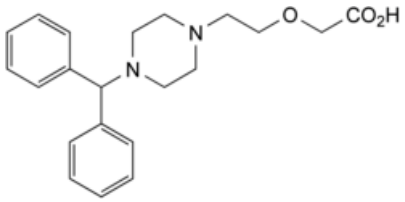
C. (*RS*)-2-[2-[4-[(2-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid,



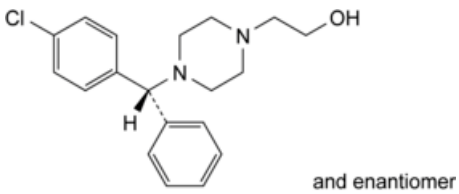
D. 1,4-bis[(4-chlorophenyl)phenylmethyl]piperazine,



E. (*RS*)-2-[2-[2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]ethoxy]acetic acid (ethoxycetirizine),



F. 2-[2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid,



G. (*RS*)-2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethan-1-ol.

Ph Eur