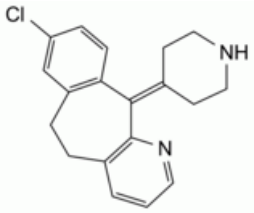
Edition: BP 2025 (Ph. Eur. 11.6 update)

Desloratadine

General Notices

(Ph. Eur. monograph 2570)



$C_{19}H_{19}ClN_2$ 310.8 *100643-71-8*

Action and use

Histamine H1, receptor antagonist; antihistamine.

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DEFINITION

8-Chloro-11-(piperidin-4-ylidene)-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine.

Content

98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white powder.

Solubility

Very slightly soluble or practically insoluble in water, freely soluble in ethanol (96 per cent), slightly soluble or very slightly soluble in heptane.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison desloratadine CRS.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in methyl isobutyl ketone R, evaporate to dryness and record new spectra using the residues.

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 20.0 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase. Dilute 5.0 mL of the solution to 50.0 mL with the mobile phase.

Reference solution (a) Dissolve 20.0 mg of desloratadine CRS in the mobile phase and dilute to 25.0 mL with the mobile phase. Dilute 5.0 mL of the solution to 50.0 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 4 mg of desloratadine for system suitability CRS (containing impurities A and B) in the mobile phase and dilute to 5.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (4 µm);

— *temperature*: 35 °C.

Mobile phase Dissolve 0.865 g of sodium dodecyl sulfate R in water R, add 0.5 mL of trifluoroacetic acid R and dilute to 1000 mL with water R; mix 57 volumes of this solution and 43 volumes of acetonitrile R.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 280 nm.

Injection 100 µL of the test solution and reference solutions (b) and (c).

Run time 2.5 times the retention time of desloratadine.

Identification of impurities Use the chromatogram supplied with desloratadine for system suitability CRS and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities A and B.

Relative retention With reference to desloratadine (retention time = about 21 min): impurity A = about 0.8; impurity B = about 0.9.

System suitability Reference solution (c):

— resolution: minimum 2.0 between the peaks due to impurity B and desloratadine.

Calculation of percentage contents:

— *correction factors*: multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 1.6; impurity B = 1.6;

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

Limits:

— *impurity B*: maximum 0.3 per cent;

— *impurity A*: maximum 0.2 per cent;

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

— *total*: maximum 0.4 per cent;

— *reporting threshold*: 0.05 per cent.

Water (*2.5.32*)

Maximum 0.5 per cent, determined on 0.250 g.

Sulfated ash (*2.4.14*)

Maximum 0.2 per cent, determined on 0.5 g.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Injection Test solution and reference solution (a).

System suitability Reference solution (a):

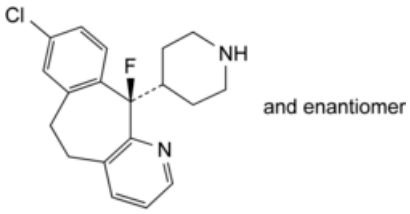
— *symmetry factor*: 0.5 to 1.5 for the peak due to desloratadine.

Calculate the percentage content of $C_{19}H_{19}ClN_2$ taking into account the assigned content of *desloratadine CRS*.

IMPURITIES

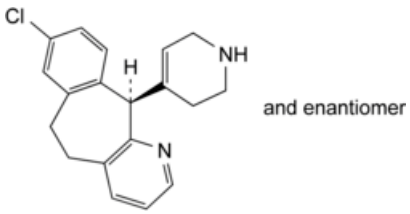
Specified impurities *A, B*.

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) *C.*



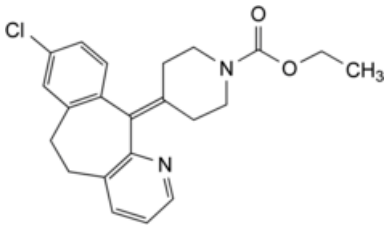
and enantiomer

A. (11*RS*)-8-chloro-11-fluoro-11-(piperidin-4-yl)-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine,



and enantiomer

B. (11*RS*)-8-chloro-11-(1,2,3,6-tetrahydropyridin-4-yl)-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine,



C. ethyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (loratadine).

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