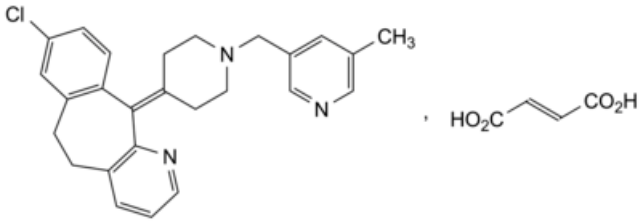
Edition: BP 2025 (Ph. Eur. 11.6 update)

Rupatadine Fumarate

General Notices

(Ph. Eur. monograph 2888)



$C_{30}H_{30}ClN_3O_4$ 532.0 *182349-12-8*

Ph Eur

DEFINITION

8-Chloro-11-[1-[(5-methylpyridin-3-yl)methyl]piperidin-4-ylidene]-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine (2*E*)-but-2-enedioate.

Content

98.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance

White or slightly pinkish powder.

Solubility

Very slightly soluble in water, slightly soluble in anhydrous ethanol, very slightly soluble in heptane.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison *rupatadine fumarate CRS*.

TESTS

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Solvent mixture acetonitrile R, mobile phase A (20:80 *V/V*).

Test solution Dissolve 32.0 mg of the substance to be examined in the solvent mixture and dilute to 50.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (b) Dissolve 3 mg of rupatadine for system suitability CRS (containing impurities A and B) in the solvent mixture and dilute to 5 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 30 °C.

Mobile phase:

— *mobile phase A*: 7.0 g/L solution of sodium dihydrogen phosphate monohydrate R in water for chromatography R;

— *mobile phase B*: acetonitrile R1;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	80	20
2 - 27	80 → 50	20 → 50

Flow rate 1.2 mL/min.

Detection Spectrophotometer at 210 nm.

Injection 50 µL.

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

Relative retention With reference to rupatadine (retention time = about 17 min): fumaric acid = about 0.1; impurity A = about 0.6; impurity B = about 0.7.

System suitability Reference solution (b):

— resolution: minimum 5.0 between the peaks due to impurities A and B.

Calculation of percentage contents:

— *correction factor*: multiply the peak area of impurity A by 1.3;

— for each impurity, use the concentration of rupatadine fumarate in reference solution (a).

Limits:

— *impurity B*: maximum 0.5 per cent;

— *impurity A*: maximum 0.15 per cent;

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

— *total*: maximum 0.7 per cent;

— *reporting threshold*: 0.05 per cent; disregard the peak due to fumaric acid.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* in an oven at 80 °C for 3 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.150 g in 50 mL of *glacial acetic acid 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 17.73 mg of $C_{30}H_{30}ClN_3O_4$.

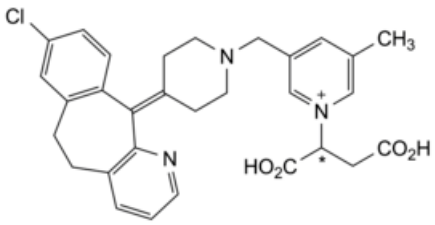
STORAGE

Protected from light.

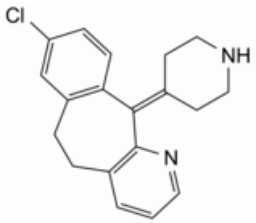
IMPURITIES

Specified impurities A, B.

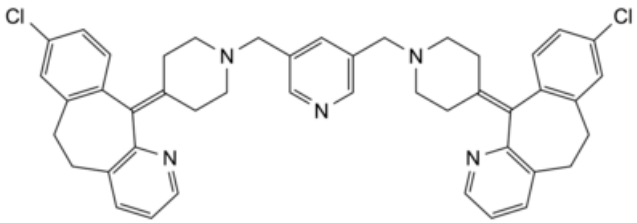
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



A. 3-[[4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidin-1-yl]methyl]-1-(1,2-dicarboxyethyl)-5-methylpyridin-1-ium,



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



C. 11,11′-[pyridine-3,5-diylbis(methylenepiperidin-1-yl-4-ylidene)]bis(8-chloro-6,11-dihydro-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine).

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