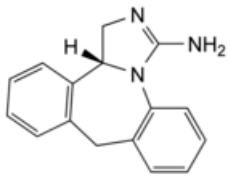
Edition: BP 2025 (Ph. Eur. 11.6 update)

Epinastine Hydrochloride

General Notices

(Ph. Eur. monograph 2411)



and enantiomer , HCl

$C_{16}H_{16}ClN_3$ 285.8 *108929-04-0*

Action and use

Antihistamine.

Ph Eur

DEFINITION

(13b*RS*)-9,13b-Dihydro-1*H*-dibenzo[*c,f*]imidazo[1,5-*a*]azepin-3-amine hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, hygroscopic, crystalline powder.

Solubility

Freely soluble in water and in methanol, sparingly soluble in methylene chloride, slightly soluble in acetonitrile.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *epinastine hydrochloride CRS*.

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

TESTS

Acidity or alkalinity

Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 10 mL with the same solvent. Add 0.1 mL of *methyl red mixed solution R* and 0.25 mL of *0.01 M sodium hydroxide*. The solution is green. Add 0.5 mL of *0.01 M hydrochloric acid*. The solution is reddish-violet.

Related substances

Liquid chromatography (*2.2.29*).

Buffer solution pH 4.4 Dissolve 3.8 g of *sodium pentanesulfonate monohydrate R* and 4.0 g of *potassium dihydrogen phosphate R* in 900 mL of *water for chromatography R*, adjust to pH 4.4 with *phosphoric acid R* and dilute to 1000 mL with *water for chromatography R*.

Solvent mixture Mobile phase B, mobile phase A (25:75 *V/V*).

Test solution Dissolve 50.0 mg of the substance to be examined in the solvent mixture and dilute to 100.0 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 5 mg of *epinastine for system suitability A CRS* (containing impurity A) in 10 mL of the solvent mixture.

Column:

— *size*: *l* = 0.10 m, Ø = 3.0 mm;

— *stationary phase*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (3 µm);

— *temperature*: 50 °C.

Mobile phase :

— *mobile phase A*: *methanol R1*, buffer solution pH 4.4 (15:85 *V/V*);

— *mobile phase B*: *methanol R1*, *acetonitrile for chromatography R* (15:85 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 4	80	20
4 - 13	80 → 30	20 → 70

Flow rate 1.4 mL/min.

Detection Spectrophotometer at 220 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram supplied with *epinastine for system suitability A CRS* and the chromatogram obtained with reference solution (b) to identify the peak due to impurity A.

Relative retention With reference to epinastine (retention time = about 4 min): impurity A = about 1.2.

System suitability Reference solution (b):

— *peak-to-valley ratio*: minimum 2.0, where H_p = height above the baseline of the peak due to impurity A and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to epinastine.

Calculation of percentage contents:

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

Limits:

— *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.

Loss on drying (*2.2.32*)

Maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 100 mL of a mixture of 1 volume of *anhydrous acetic acid R* and 2 volumes of *acetic anhydride 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 28.58 mg of $C_{16}H_{16}ClN_3$.

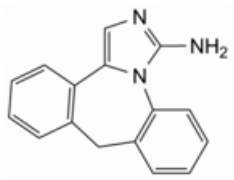
STORAGE

In an airtight container.

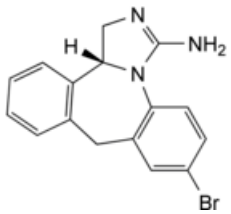
IMPURITIES

Specified impurities A.

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) B.



A. 9*H*-dibenzo[*c,f*]imidazo[1,5-*a*]azepin-3-amine,



and enantiomer

B. (13b*RS*)-7-bromo-9,13b-dihydro-1*H*-dibenzo[*c,f*]imidazo[1,5-*a*]azepin-3-amine.