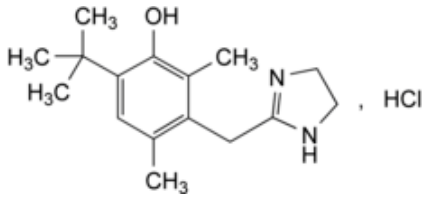
Edition: BP 2025 (Ph. Eur. 11.6 update)

Oxymetazoline Hydrochloride

General Notices

(Ph. Eur. monograph 0943)



$C_{16}H_{25}ClN_2O$ 296.8 *2315-02-8*

Action and use

Alpha-adrenoceptor agonist; decongestant.

Ph Eur

DEFINITION

3-[(4,5-Dihydro-1*H*-imidazol-2-yl)methyl]-6-(1,1-dimethylethyl)-2,4-dimethylphenol hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water and in ethanol (96 per cent).

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Comparison oxymetazoline hydrochloride CRS.

B. Thin-layer chromatography (2.2.27).

Test solution Dissolve 20 mg of the substance to be examined in a mixture of equal volumes of ethyl acetate R and methanol R and dilute to 5 mL with the same mixture of solvents.

Reference solution Dissolve 20 mg of oxymetazoline hydrochloride CRS in a mixture of equal volumes of ethyl acetate R and methanol R and dilute to 5 mL with the same mixture of solvents.

Plate TLC silica gel G plate R.

Mobile phase diethylamine R, cyclohexane R, anhydrous ethanol R (6:15:79 *V/V/V*).

Application 5 µL.

Development Over 2/3 of the plate.

Drying In a current of warm air for 5 min, then allow to cool.

Detection Spray with a freshly prepared 5.0 g/L solution of potassium ferricyanide R in ferric chloride solution R2; examine in daylight.

Results The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. Dissolve about 2 mg in 1 mL of water R, then add 0.2 mL of a 50 g/L solution of sodium nitroprusside R and 0.2 mL of dilute sodium hydroxide solution R. Allow to stand for 10 min. Add 2 mL of sodium hydrogen carbonate solution R. A violet colour develops.

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

TESTS

Appearance of solution

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

Dissolve 2.5 g in water R and dilute to 50 mL with the same solvent.

Acidity or alkalinity

Dissolve 0.25 g in carbon dioxide-free water R and dilute to 25 mL with the same solvent. Add 0.1 mL of methyl red solution R and 0.2 mL of 0.01 M hydrochloric acid. The solution is red. Not more than 0.4 mL of 0.01 M sodium hydroxide is required to change the colour of the indicator to yellow.

Related substances

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

Test solution Dissolve 50.0 mg of the substance to be examined in *water R* and dilute to 50.0 mL with the same solvent.

Reference solution (a) Dilute 5.0 mL of the test solution to 100.0 mL with *water R*. Dilute 2.0 mL of this solution to 100.0 mL with *water R*.

Reference solution (b) Dissolve 5.0 mg of *oxymetazoline impurity A CRS* and 5 mg of the substance to be examined in *water R* and dilute to 50.0 mL with the same solvent. Dilute 10.0 mL of the solution to 50.0 mL with *water R*.

Reference solution (c) Dilute 1.0 mL of reference solution (b) to 20.0 mL with *water R*.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography with embedded polar groups R* (5 µm).

Mobile phase:

— *mobile phase A*: 1.36 g/L solution of *potassium dihydrogen phosphate R* adjusted to pH 3.0 with *phosphoric acid R*;

— *mobile phase B*: *acetonitrile for chromatography R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 5	70	30
5 - 20	70 → 15	30 → 85
20 - 35	15	85

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 220 nm.

Injection 10 µL.

Relative retention With reference to oxymetazoline (retention time = about 5.0 min): impurity A = about 0.9.

System suitability Reference solution (b):

— *resolution*: minimum 4.0 between the peaks due to impurity A and oxymetazoline.

Limits:

— *impurity A*: not more than 1.5 times the area of the corresponding peak in the chromatogram obtained with reference solution (c) (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 (a) (0.10 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

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

Water

(2.5.32): maximum 0.3 per cent, determined on 1.00 g .

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

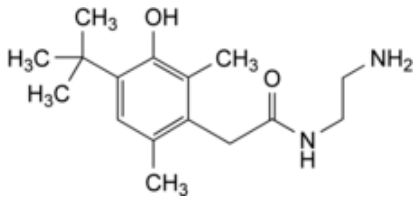
Dissolve 0.200 g in a mixture of 20 mL of *acetic anhydride R* and 20 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (2.2.20).

1 mL of *0.1 M perchloric acid* is equivalent to 29.68 mg of $C_{16}H_{25}ClN_2O$.

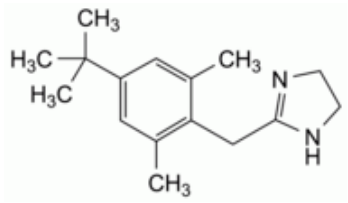
IMPURITIES

Specified impurities A.

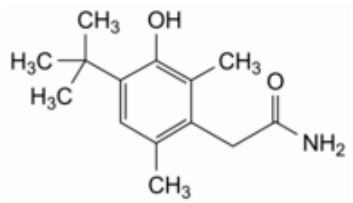
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



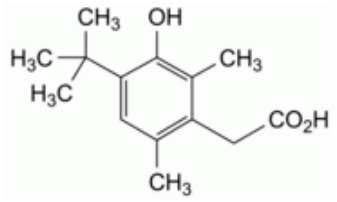
A. *N*-(2-aminoethyl)-2-[4-(1,1-dimethylethyl)-3-hydroxy-2,6-dimethylphenyl]acetamide,



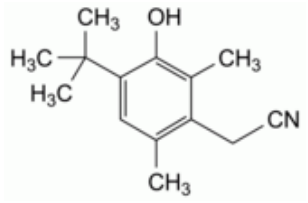
B. 2-[[4-(1,1-dimethylethyl)-2,6-dimethylphenyl]methyl]-4,5-dihydro-1*H*-imidazole (xylometazoline),



C. 2-[4-(1,1-dimethylethyl)-3-hydroxy-2,6-dimethylphenyl]acetamide,



D. 2-[4-(1,1-dimethylethyl)-3-hydroxy-2,6-dimethylphenyl]acetic acid,



E. 2-[4-(1,1-dimethylethyl)-3-hydroxy-2,6-dimethylphenyl]acetonitrile.

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