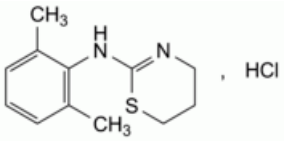
Edition: BP 2025 (Ph. Eur. 11.6 update)

Xylazine Hydrochloride

General Notices

(Xylazine Hydrochloride for Veterinary Use, Ph. Eur. monograph 1481)



$C_{12}H_{17}ClN_2S$ 256.8 *23076-35-9*

Action and use

Analgesic.

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DEFINITION

N-(2,6-Dimethylphenyl)-5,6-dihydro-4*H*-1,3-thiazin-2-amine hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder, hygroscopic.

Solubility

Freely soluble in water, very soluble in methanol, freely soluble in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *xylazine hydrochloride CRS*.

If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in the minimum volume of *water R*, evaporate to dryness at 60 °C at a pressure of 10-20 kPa, and record new spectra using the residues.

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

TESTS

Solution S

Dissolve 5.0 g in *carbon dioxide-free water R*, heating at 60 °C if necessary; allow to cool and dilute to 50.0 mL with the same solvent.

Appearance of solution

Solution S is not more opalescent than reference suspension II (*2.2.1*) and is colourless (*2.2.2, Method II*).

pH (*2.2.3*)

4.0 to 5.5 for solution S.

Related substances

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

Solvent mixture Mix 8 volumes of *acetonitrile R*, 30 volumes of *methanol R* and 62 volumes of a 2.72 g/L solution of *potassium dihydrogen phosphate R* previously adjusted to pH 7.2 with *dilute sodium hydroxide solution R*.

Test solution Dissolve 0.100 g of the substance to be examined in the solvent mixture and dilute to 20.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 50.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Reference solution (b) Dissolve 5.0 mg of *bupivacaine impurity F CRS* (xylazine impurity A) in *acetonitrile R* and dilute to 100.0 mL with the same solvent.

Reference solution (c) Dilute 1.0 mL of reference solution (b) to 100.0 mL with the solvent mixture.

Reference solution (d) Dilute 1 mL of the test solution to 100 mL with the solvent mixture. Mix 10 mL of this solution with 10 mL of reference solution (b). Dilute 1 mL of this solution to 5 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 3.9 mm;

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

— *temperature*: 40 °C.

Mobile phase:

— *mobile phase A*: mix 30 volumes of *methanol R1* and 70 volumes of a 2.72 g/L solution of *potassium dihydrogen phosphate R* previously adjusted to pH 7.2 with *dilute sodium hydroxide solution R*;

— *mobile phase B*: *methanol R1*, *acetonitrile for chromatography R* (30:70 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 15	89 → 28	11 → 72
15 - 21	28	72

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 20 µL of the test solution and reference solutions (a), (c) and (d).

Identification of impurities Use the chromatogram obtained with reference solution (c) to identify the peak due to impurity A.

Relative retention With reference to xylazine (retention time = about 8 min): impurity A = about 0.8.

System suitability Reference solution (d):

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

Calculation of percentage contents:

— for impurity A, use the concentration of impurity A in reference solution (c);

— for impurities other than A, use the concentration of xylazine hydrochloride in reference solution (a).

Limits:

— *impurity A*: maximum 0.01 per cent;

— *unspecified impurities*: for each impurity, maximum 0.20 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.10 per cent, except for impurity A.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 25 mL of *ethanol (96 per cent) R*. Add 25 mL of *water R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M sodium hydroxide* is equivalent to 25.68 mg of $C_{12}H_{17}ClN_2S$.

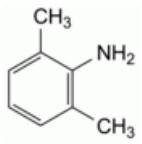
STORAGE

In an airtight container, protected from light.

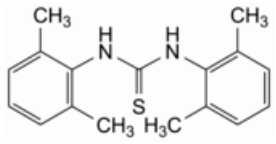
IMPURITIES

Specified impurities *A*.

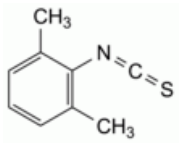
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



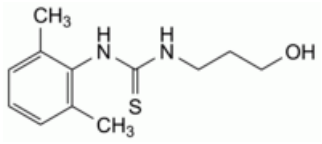
A. 2,6-dimethylaniline (2,6-xylidine),



B. *N*,*N*′-bis(2,6-dimethylphenyl)thiourea,



C. 1-isothiocyanato-2,6-dimethylbenzene,



D. *N*-(2,6-dimethylphenyl)-*N*′-(3-hydroxypropyl)thiourea.

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