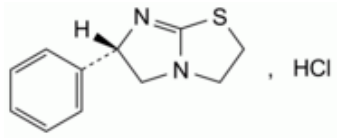
Edition: BP 2025 (Ph. Eur. 11.6 update)

Levamisole Hydrochloride

General Notices

(Ph. Eur. monograph 0726)



$C_{11}H_{13}ClN_2S$ 240.8 *16595-80-5*

Action and use

Immunostimulant; antihelminthic.

Ph Eur

DEFINITION

(6*S*)-6-Phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole hydrochloride.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water, soluble in ethanol (96 per cent), slightly soluble in methylene chloride.

IDENTIFICATION

A. Specific optical rotation (see Tests).
B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison *levamisole hydrochloride CRS*.

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

TESTS

Solution S

Dissolve 2.50 g in *carbon dioxide-free water R* and dilute to 50.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

pH (*2.2.3*)

3.0 to 4.5 for solution S.

Specific optical rotation (*2.2.7*)

-128 to -121 (dried substance), determined on solution S.

Related substances

Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use, protect from light and keep below 25 °C.*

Test solution Dissolve 0.100 g of the substance to be examined in *methanol R*, add 1.0 mL of *concentrated ammonia R* and dilute to 10.0 mL with *methanol R*.

Reference solution (a) Dissolve 10 mg of *levamisole hydrochloride for system suitability CRS* (containing impurities A, B, C, D and E) in *methanol R*, add 0.1 mL of *concentrated ammonia R* and dilute to 1.0 mL with *methanol R*.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with *methanol R*. Dilute 5.0 mL of this solution to 25.0 mL with *methanol R*.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

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

Mobile phase:

— *mobile phase A*: dissolve 0.5 g of *ammonium dihydrogen phosphate R* in 90 mL of *water R*, adjust to pH 6.5 with a 40 g/L solution of *sodium hydroxide R* and dilute to 100 mL with *water R*;

— *mobile phase B*: *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 8	90 → 30	10 → 70
8 - 10	30	70

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 215 nm.

Equilibration At least 4 min with the mobile phase at the initial composition.

Injection 10 µL.

Identification of impurities Use the chromatogram supplied with *levamisole hydrochloride for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A, B, C, D and E.

Relative retention With reference to levamisole (retention time = about 3 min): impurity A = about 0.9; impurity B = about 1.4; impurity C = about 1.5; impurity D = about 1.6; impurity E = about 2.0.

System suitability:

— the chromatogram obtained with reference solution (a) is similar to the chromatogram supplied with *levamisole hydrochloride for system suitability CRS*;

— *symmetry factor*: maximum 3.5 for the principal peak in the chromatogram obtained with reference solution (b).

Limits:

— *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 2.0; impurity B = 1.7; impurity C = 2.9; impurity D = 1.3; impurity E = 2.7;

— *impurities A, B, C, D, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

— *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

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 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 30 mL of *ethanol (96 per cent) R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

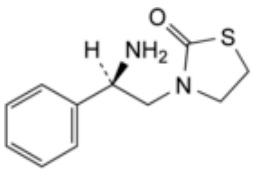
1 mL of *0.1 M sodium hydroxide* is equivalent to 24.08 mg of $C_{11}H_{13}ClN_2S$.

STORAGE

Protected from light.

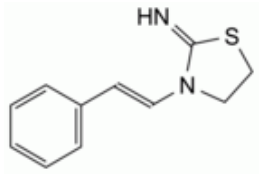
IMPURITIES

Specified impurities *A, B, C, D, E.*

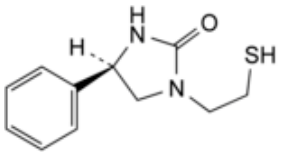


and enantiomer

A. 3-[(2*RS*)-2-amino-2-phenylethyl]thiazolidin-2-one,

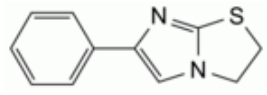


B. 3-[(*E*)-2-phenylethenyl]thiazolidin-2-imine,

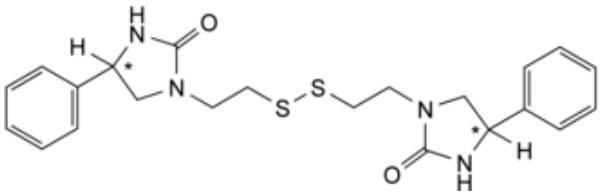


and enantiomer

C. (4*RS*)-4-phenyl-1-(2-sulfanylethyl)imidazolidin-2-one,



D. 6-phenyl-2,3-dihydroimidazo[2,1-*b*]thiazole,



E. 1,1′-[(disulfane-1,2-diyl)bis(ethylene)]bis[(4*RS*)-4-phenylimidazolidin-2-one].

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