



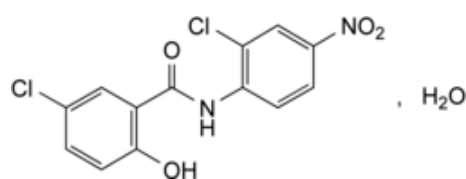
Edition: BP 2025 (Ph. Eur. 11.6 update)

Niclosamide Monohydrate



[General Notices](#)

(Ph. Eur. monograph 0680)



$C_{13}H_8Cl_2N_2O_4 \cdot H_2O$ 345.1

Action and use

Anthelmintic.

Preparation

[Niclosamide Tablets](#)

Ph Eur

DEFINITION

5-Chloro-*N*-(2-chloro-4-nitrophenyl)-2-hydroxybenzamide monohydrate.

Content

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

CHARACTERS

Appearance

Yellowish, fine crystals.

Solubility

IDENTIFICATION

First identification: B, E.

Second identification: A, C, D, E.

A. Melting point ([2.2.14](#)): 227 °C to 232 °C, determined after drying at 100-105 °C for 4 h.

B. Infrared absorption spectrophotometry ([2.2.24](#)).

Preparation Dry the substance to be examined at 100-105 °C for 4 h and examine as discs prepared using about 0.5 mg of substance and 0.3 g of [potassium bromide R](#).

Comparison [anhydrous niclosamide CRS](#).

C. To 50 mg add 5 mL of [1 M hydrochloric acid](#) and 0.1 g of [zinc powder R](#), heat in a water-bath for 10 min, cool and filter. To the filtrate add 1 mL of a 5 g/L solution of [sodium nitrite R](#) and allow to stand for 3 min; add 2 mL of a 20 g/L solution of [ammonium sulfamate R](#), shake, allow to stand for 3 min and add 2 mL of a 5 g/L solution of [naphthylethylenediamine dihydrochloride R](#). A violet colour is produced.

D. Heat the substance on a copper wire in a non-luminous flame. The flame becomes green.

E. Loss on drying (see Tests).

TESTS

Related substances

Liquid chromatography ([2.2.29](#)).

Test solution Dissolve 50 mg of the substance to be examined in [methanol R](#), heating gently, cool and dilute to 50.0 mL with the same solvent.

Reference solution Dilute 1.0 mL of the test solution to 100.0 mL with [acetonitrile R](#). Dilute 1.0 mL of this solution to 20.0 mL with [acetonitrile R](#).

Column:

— *size:* $l = 0.125$ m, $\varnothing = 4$ mm;

— *stationary phase:* [octadecylsilyl silica gel for chromatography R](#) (5 μ m).

Mobile phase Mixture of equal volumes of [acetonitrile R](#) and a solution containing 2 g/L of [potassium dihydrogen phosphate R](#), 1 g/L of [disodium hydrogen phosphate dodecahydrate R](#) and 2 g/L of [tetrabutylammonium hydrogen sulfate R](#).

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 20 μ L.

Run time Twice the retention time of niclosamide.

Limits:

— *total:* not more than 4 times the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent);

— *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with the reference solution (0.005 per cent).

5-Chlorosalicylic acid

Maximum 60 ppm.

Test solution To 1.0 g add 15 mL of [water R](#), boil for 2 min, cool, filter through a membrane filter (nominal pore size 0.45 µm), wash the filter and dilute the combined filtrate and washings to 20.0 mL with [water R](#).

Reference solution Dissolve 30 mg of [5-chlorosalicylic acid R](#) in 20 mL of [methanol R](#) and dilute to 100.0 mL with [water R](#). Dilute 1.0 mL of this solution to 100.0 mL with [water R](#).

To 10.0 mL of the test solution and to 10.0 mL of the reference solution add separately 0.1 mL of [ferric chloride solution R2](#). Any violet colour produced in the test solution is not more intense than that in the reference solution.

2-Chloro-4-nitroaniline

Maximum 100 ppm.

Test solution To 0.250 g add 5 mL of [methanol R](#), heat to boiling, cool, add 45 mL of [1 M hydrochloric acid](#), heat again to boiling, cool, filter and dilute the filtrate to 50.0 mL with [1 M hydrochloric acid](#).

Reference solution Dissolve 50 mg of [2-chloro-4-nitroaniline R](#) in [methanol R](#) and dilute to 100.0 mL with the same solvent. Dilute 1.0 mL of the solution to 100.0 mL with [methanol R](#). Dilute 2.0 mL of this solution to 20.0 mL with [1 M hydrochloric acid](#).

To 10.0 mL of the test solution and to 10.0 mL of the reference solution add separately 0.5 mL of a 5 g/L solution of [sodium nitrite R](#) and allow to stand for 3 min. Add 1 mL of a 20 g/L solution of [ammonium sulfamate R](#), shake, allow to stand for 3 min and add 1 mL of a 5 g/L solution of [naphthylethylenediamine dihydrochloride R](#). Any pinkish-violet colour produced in the test solution is not more intense than that in the reference solution.

Chlorides ([2.4.4](#))

Maximum 500 ppm.

To 2 g add a mixture of 1.2 mL of [acetic acid R](#) and 40 mL of [water R](#), boil for 2 min, cool and filter. Dilute 2 mL of the filtrate to 15 mL with [water R](#).

Loss on drying ([2.2.32](#))

4.5 per cent to 6.0 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 0.3000 g in 80 mL of a mixture of equal volumes of [acetone R](#) and [methanol R](#). Titrate with [0.1 M tetrabutylammonium hydroxide](#), determining the end-point potentiometrically ([2.2.20](#)).

1 mL of [0.1 M tetrabutylammonium hydroxide](#) is equivalent to 32.71 mg of C₁₃H₈Cl₂N₂O₄.

STORAGE

Protected from light.

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