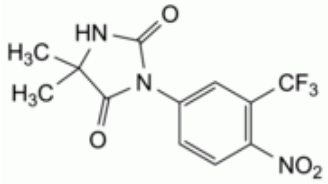
Edition: BP 2025 (Ph. Eur. 11.6 update)

Nilutamide

General Notices

(Ph. Eur. monograph 2256)



$C_{12}H_{10}F_3N_3O_4$ 317.2 *63612-50-0*

Action and use

Cytotoxic.

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DEFINITION

5,5-Dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]imidazolidine-2,4-dione.

Content

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

CHARACTERS

Appearance

White or almost white powder.

Solubility

Very slightly soluble in water, freely soluble in acetone, soluble in anhydrous ethanol.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison nilutamide CRS.

TESTS

Related substances

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

Solvent mixture acetonitrile for chromatography R, water R (35:65 *V/V*).

Test solution Dissolve 0.10 g of the substance to be examined in the solvent mixture and dilute to 100 mL with the solvent mixture.

Reference solution (a) Dilute 20.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 100.0 mL with the solvent mixture.

Reference solution (b) Dissolve 2 mg of the substance to be examined and 2 mg of nilutamide impurity B CRS in the solvent mixture and dilute to 50 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: spherical octadecylsilyl silica gel for chromatography R (5 µm).

Mobile phase:

— *mobile phase A*: 2.0 g/L solution of potassium dihydrogen phosphate R adjusted to pH 7.5 with 1 M sodium hydroxide;

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

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 8	55	45
8 - 30	55 → 30	45 → 70

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 20 µL.

Relative retention With reference to nilutamide (retention time = about 5.3 min): impurity B = about 0.9.

System suitability Reference solution (b):

— resolution: minimum 3.0 between the peaks due to impurity B and nilutamide.

Limits:

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

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

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

Water (*2.5.12*)

Maximum 0.5 per cent, determined on 0.500 g.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Liquid chromatography (*2.2.29*). *The solutions are stable for 24 h at room temperature and in daylight.*

Solvent mixture *acetonitrile for chromatography R*, *water R* (35:65 *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 Dissolve 50.0 mg of *nilutamide CRS* in the solvent mixture and dilute to 100.0 mL with the solvent mixture.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: spherical *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Mix 40 volumes of *acetonitrile R* and 60 volumes of a 2.0 g/L solution of *potassium dihydrogen phosphate R* adjusted to pH 7.5 with *1 M sodium hydroxide*.

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 267 nm.

Injection 20 µL.

Retention time About 9 min.

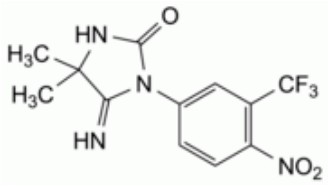
Calculate the percentage content of $C_{12}H_{10}F_3N_3O_4$ from the declared content of *nilutamide CRS*.

STORAGE

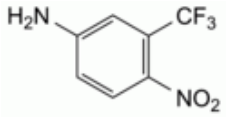
Protected from light.

IMPURITIES

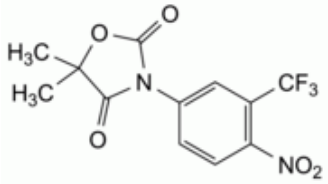
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



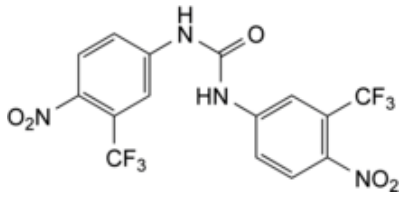
A. 5-imino-4,4-dimethyl-1-[4-nitro-3-(trifluoromethyl)phenyl]imidazolidin-2-one,



B. 4-nitro-3-(trifluoromethyl)aniline (nifeline),



C. 5,5-dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]oxazolidine-2,4-dione,



D. 1,3-bis[4-nitro-3-(trifluoromethyl)phenyl]urea.

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