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Nilutamide

$C_{12}H_{10}F_3N_3O_4$ 317.22

2,4-Imidazolidinedione, 5,5-dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]-;

5,5-Dimethyl-3-(α,α,α-trifluoro-4-nitro-*m*-tolyl)hydantoin;

5,5-Dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]-imidazolidine-2,4-dione CAS RN®: 63612-50-0.

DEFINITION

Nilutamide contains NLT 98.0% and NMT 102.0% of nilutamide ($C_{12}H_{10}F_3N_3O_4$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K▲ (CN 1-May-2020)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

[Note—Throughout the following procedures, protect the sample, the Reference Standard, and solutions containing them by conducting the procedures under subdued light or using low-actinic glassware.]

Buffer: 2.0 g/L of monobasic potassium phosphate in water. Adjust with a solution of 1 N sodium hydroxide in water to a pH of 7.5.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Diluent: Acetonitrile and water (35:65)

Standard solution: 0.5 mg/mL of USP Nilutamide RS in *Diluent*

Sample solution: 0.5 mg/mL of Nilutamide in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 267 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 5 times the retention time of nilutamide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nilutamide ($C_{12}H_{10}F_3N_3O_4$) in the portion of Nilutamide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of nilutamide from the *Sample solution*

r_S = peak response of nilutamide from the *Standard solution*

C_S = concentration of USP Nilutamide RS in the *Standard solution* (mg/mL)

C_U = concentration of Nilutamide in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩**

Analysis: Use a platinum crucible.

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

Solution A: 2.0 g/L of monobasic potassium phosphate in water. Adjust with a solution of 1 N sodium hydroxide in water to a pH of 7.5.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	55	45
8	55	45
30	30	70
31	55	45
45	55	45

Diluent: Acetonitrile and water (35:65)

System suitability solution: 0.04 mg/mL each of USP Nilutamide RS and USP Flutamide Related Compound A RS in *Diluent*

Standard solution: 0.002 mg/mL of USP Nilutamide RS in *Diluent*

Sample solution: 1.0 mg/mL of Nilutamide in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between nilutamide and flutamide related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Nilutamide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_S = peak response of nilutamide from the *Standard solution*

C_S = concentration of USP Nilutamide RS in the *Standard solution* (mg/mL)

C_U = concentration of Nilutamide in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
5-Imino nilutamide[a]	0.49	0.10
Flutamide related compound A	0.86	0.10
Nilutamide	1.0	—
3-Oxo nilutamide[b]	2.3	0.10
Nilutamide urea analog[c]	4.6	0.10
Any other individual unspecified impurity	—	0.10
Total impurities	—	0.5

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

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

[c] 1,3-Bis[4-nitro-3-(trifluoromethyl)phenyl]urea.

SPECIFIC TESTS

• **Water Determination ⟨921⟩:** NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Protect from light. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Flutamide Related Compound A RS

4-Nitro-3-(trifluoromethyl)aniline.

$C_7H_5F_3N_2O_2$ 206.12

USP Nilutamide RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
NILUTAMIDE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

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