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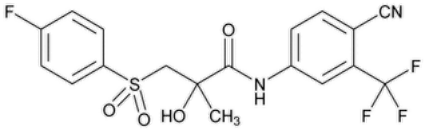
Bicalutamide



$C_{18}H_{14}F_4N_2O_4S$ 430.37

Propanamide, *N*-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (±)-;

(±)-4'-Cyano-α,α,α-trifluoro-3-[(*p*-fluorophenyl)sulfonyl]-2-methyl-*m*-lactotoluidide CAS RN®: 90357-06-5; UNII: A0Z3NAU9DP.

DEFINITION

Bicalutamide contains NLT 98.0% and NMT 102.0% of $C_{18}H_{14}F_4N_2O_4S$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (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**

Solution A: 0.01% (v/v) of trifluoroacetic acid in water

Solution B: 0.01% (v/v) of trifluoroacetic acid in acetonitrile

Mobile phase: *Solution A* and *Solution B* (52:48)

Diluent: *Solution A* and *Solution B* (1:2)

System suitability solution: 5 µg/mL of USP Bicalutamide Related Compound A RS and 50 µg/mL of USP Bicalutamide RS in *Diluent*

Standard solution: 0.05 mg/mL of USP Bicalutamide RS in *Diluent*

Sample solution: 0.05 mg/mL of Bicalutamide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 270 nm

Column: 4.0-mm × 10-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

[Note—The relative retention times for bicalutamide related compound A isomer A and bicalutamide related compound A isomer B are 0.75 and 0.78, respectively.]

Suitability requirements

Resolution: NLT 2.0 between bicalutamide related compound A isomer B and bicalutamide, *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{18}H_{14}F_4N_2O_4S$ in the portion of Bicalutamide taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.1%

Organic Impurities

- **Procedure**

Solution A, Solution B, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	67	33
16.5	67	33
26.5	40	60
32.5	5	95
32.6	67	33
35	67	33

Standard solution: 1 µg/mL of USP Bicalutamide RS in *Diluent*

Sample solution: 1 mg/mL of Bicalutamide in *Diluent*

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution 1: NLT 0.8 between bicalutamide related compound A isomer A and bicalutamide related compound A isomer B

Resolution 2: NLT 8.5 between bicalutamide related compound A isomer B and bicalutamide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Bicalutamide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak area of each impurity from the *Sample solution*

r_S = peak area of bicalutamide from the *Standard solution*

C_S = concentration of bicalutamide in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Impurity Table 1*)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.5%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Bicalutamide aminobenzonitrile[a]	0.30	1.4	0.1
Bicalutamide related compound A isomer A[b]	0.64	1.0	0.1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Bicalutamide related compound A isomer B[b]	0.67	1.0	0.1
Desfluoro bicalutamide[c]	0.83	1.1	0.2
2-Fluoro bicalutamide[d]	0.94	1.0	0.2
Bicalutamide	1.00	—	—
Deoxybicalutamide[e]	1.33	1.0	0.2
Bicalutamide sulfide[f]	1.56	1.0	0.1
Any unspecified impurity	—	1.0	0.1

[a] 4-Amino-2-(trifluoromethyl)benzonitrile.

[b] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfinyl]-2-hydroxy-2-methylpropanamide.

[c] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-2-hydroxy-2-methyl-3-(phenylsulfonyl)propanamide.

[d] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-(2-fluorophenylsulfonyl)-2-hydroxy-2-methylpropanamide.

[e] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-(4-fluorophenylsulfonyl)-2-methylpropanamide.

[f] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-(4-fluorophenylthio)-2-hydroxy-2-methylpropanamide.

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩**:** NMT 0.2%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Bicalutamide RS

USP Bicalutamide Related Compound A RS

[*N*-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4- fluorophenyl)sulfinyl]-2-hydroxy-2-methylpropanamide]
($C_{18}H_{14}F_4N_2O_3S$ 414.37)

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

Topic/Question	Contact	Expert Committee
BICALUTAMIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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