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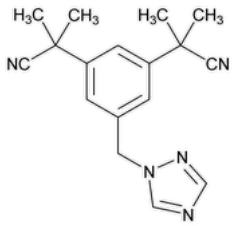
Anastrozole



$C_{17}H_{19}N_5$ 293.37

1,3-Benzenediacetonitrile, α,α,α',α'-tetramethyl-5-(1*H*-1,2,4-triazol-1-ylmethyl)-;

α,α,α',α'-Tetramethyl-5-(1*H*-1,2,4-triazol-1-ylmethyl)-*m*-benzenediacetonitrile CAS RN®: 120511-73-1; UNII: 2Z07MYW1AZ.

DEFINITION

Anastrozole contains NLT 98.0% and NMT 102.0% of anastrozole ($C_{17}H_{19}N_5$), calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

Change to read:

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

Solution A: Acetonitrile, methanol, trifluoroacetic acid, and water (100:300:0.5:600)

Solution B: Acetonitrile, methanol, trifluoroacetic acid, and water (150:450:0.5:400)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
40	0	100
41	100	0
56	100	0

[Note—These gradient elution times are established on an HPLC system with a dwell time of approximately 0 min. The gradient elution times in the table can be adjusted by subtracting the dwell time to achieve the separation described.]

Standard solution: 0.5 mg/mL of USP Anastrozole RS prepared as follows. Transfer USP Anastrozole RS into a suitable volumetric flask. Dissolve in acetonitrile, using 40% of the final volume, and then dilute with *Solution A* to volume.

Sample solution: 0.5 mg/mL of Anastrozole prepared as follows. Transfer 25 mg of Anastrozole to a 50-mL volumetric flask, add 20 mL of acetonitrile to dissolve. Dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 3.2-mm × 10-cm; 5-µm packing L42

Flow rate: 0.75 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: Between 0.9 and 1.4

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of anastrozole ($C_{17}H_{19}N_5$) in the portion of Anastrozole taken:

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

r_U = peak area of anastrozole from the *Sample solution*

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

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

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

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

IMPURITIES

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

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

Standard stock solution: 0.2 mg/mL of USP Anastrozole RS prepared as follows. Dissolve in acetonitrile, using 40% of the final volume, and then dilute with *Solution A* to volume.

Standard solution: 0.02 mg/mL of USP Anastrozole RS in *Solution A* from the *Standard stock solution*

Sample solution: 2 mg/mL of Anastrozole prepared as follows. Transfer 50 mg of Anastrozole to a 25-mL volumetric flask. Add 10 mL of acetonitrile. Dissolve in and dilute with *Solution A* to volume.

Blank solution: Transfer 10 mL of acetonitrile into a 25-mL volumetric flask, and dilute with *Solution A* to volume.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: Between 0.9 and 1.4

Relative standard deviation: NMT 5%

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank solution*. [Note—Adjust the peak areas for any interference from the *Blank solution*.]

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

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

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

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

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

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

Acceptance criteria: See *Table 2*. Disregard any impurity of less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Desmethyl anastrozole[a]	0.6	0.2
Anastrozole	1.0	—
Anastrozole dimer[b]	2.0	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
5-Bromomethyl anastrozole[c]	4.3	0.1
5-Dibromomethyl anastrozole[d]	5.4	0.1
Individual unspecified impurity	—	0.1
Total impurities	—	0.5

[a] 2-(3-(1-Cyanoethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropionitrile.

[b] 2,3-Bis(3-(1-cyano-1-methylethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropionitrile.

[c] 2,2'-(5-(Bromomethyl)-1,3-phenylene)bis(2-methylpropionitrile).

[d] 2,2'-(5-(Dibromomethyl)-1,3-phenylene)bis(2-methylpropionitrile).

SPECIFIC TESTS

• **Water Determination, *Method Ic* (921):** NMT 0.3%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

• **USP Reference Standards (11)**
USP Anastrozole RS

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

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

Chromatographic Database Information: Chromatographic Database

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