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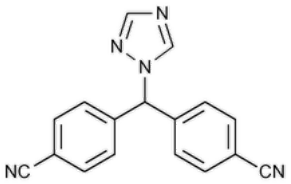
Letrozole



$C_{17}H_{11}N_5$ 285.30

Benzonitrile, 4,4'-(1*H*-1,2,4-triazol-1-ylmethylene)bis-;

4,4'-(1*H*-1,2,4-Triazol-1-ylmethylene)dibenzonitrile CAS RN®: 112809-51-5; UNII: 7LKK855W8I.

DEFINITION

Letrozole contains NLT 98.0% and NMT 102.0% of $C_{17}H_{11}N_5$, calculated on the anhydrous 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: Water

Solution B: Acetonitrile

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	70	30
25	30	70

Diluent: Acetonitrile and water (3:7)

Standard solution: 10 µg/mL of USP Letrozole RS in *Diluent*. [Note—Dissolve USP Letrozole RS in acetonitrile, then dilute with water.]

Sample solution: 10 µg/mL of Letrozole in *Diluent*. [Note—Dissolve Letrozole in acetonitrile, then dilute with water.]

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 12.5-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{17}H_{11}N_5$ in the portion of Letrozole 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 Letrozole RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

Inorganic Impurities

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

Organic Impurities

- **Procedure**

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

System suitability solution: 2 µg/mL of USP Letrozole Related Compound A RS and 10 µg/mL of USP Letrozole RS in *Diluent*. [Note—Dissolve Letrozole and USP Letrozole Related Compound A RS in acetonitrile, then dilute with water.]

Standard solution: 1 µg/mL of USP Letrozole RS in *Diluent*. [Note—Dissolve USP Letrozole RS in acetonitrile, then dilute with water.]

Sample solution: Transfer 25 mg of Letrozole to a 250-mL volumetric flask. Dissolve in 75 mL of acetonitrile, and dilute with water to volume.

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between letrozole related compound A and letrozole, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Letrozole 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 letrozole from the *Standard solution*

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

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

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total unspecified impurities: NMT 0.3%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Letrozole related compound A[a]	0.67	0.3
Letrozole	1.0	—
4,4',4"-Methanetriyl tribenzonitrile	2.4	0.2
Any unspecified impurity	—	0.1

[a] 4,4'-(1*H*-1,3,4-triazol-1-ylmethylene)dibenzonitrile.

[Note—Disregard any impurity peaks less than 0.05%.]

SPECIFIC TESTS

- **Water Determination, *Method I*⟨921⟩:** NMT 0.3%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers at controlled room temperature.
- **USP Reference Standards** (11)

USP Letrozole RS

USP Letrozole Related Compound A RS

4,4'-(1*H*-1,3,4-Triazol-1-ylmethylene)dibenzonitrile.

$C_{17}H_{11}N_5$ 285.31

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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