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Letrozole Tablets

DEFINITION
Letrozole Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of letrozole ($C_{17}H_{11}N_5$).

IDENTIFICATION

- **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

  Sample solution: Equivalent to 2 mg/mL of letrozole from powdered Tablets in methanol. [Note—Shake thoroughly, sonicate for 10 min, and centrifuge.]

  Application volume: 5 µL

  Developing solvent system: Ethyl acetate and methanol (9:1)

  Acceptance criteria: Meet the requirements

- **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**

  Mobile phase: Acetonitrile and water (48:52)

  Diluent: Acetonitrile and water (30:70)

  Standard stock solution: 0.2 mg/mL of USP Letrozole RS in *Diluent*. [Note—Dissolve letrozole in acetonitrile, and then dilute with water.]

  Standard solution: 10 µg/mL of USP Letrozole RS in *Mobile phase* from the *Standard stock solution*

  Sample stock solution: Equivalent to 50 mg of letrozole from Tablets in a 250-mL volumetric flask. Add 20 mL of water and shake for 5 min to dissolve the Tablets. Add 75 mL of acetonitrile, shake for 30 min, and dilute with water to volume. Centrifuge a portion of the solution.

  Sample solution: 10 µg/mL of letrozole in *Mobile phase* from the *Sample stock solution*

  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 volume: 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 the labeled amount of letrozole ($C_{17}H_{11}N_5$) in the portion of Tablets 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* (µg/mL)

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 100 rpm

Time: 30 min

Standard solution: Transfer USP Letrozole RS to a suitable volumetric flask, dissolve in acetonitrile equivalent to 10% of the final volume, and dilute with *Medium* to volume to obtain a solution of 0.05 mg/mL of letrozole. Dilute this solution with *Medium* to obtain a solution of 0.005 mg/mL of letrozole.

Sample solution: Centrifuge a portion of the solution under test at 4000 rpm for 5 min.

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*, except use an injection volume of 200 µL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of letrozole ($C_{17}H_{11}N_5$) dissolved:

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

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)

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of letrozole ($C_{17}H_{11}N_5$) is dissolved.

Test 2

Medium: 0.1 N hydrochloric acid solution adjusted with 50% sodium hydroxide (NaOH) to a pH of 1.2; 900 mL, deaerated

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Acetonitrile and water (45:55)

Standard stock solution: 0.3 mg/mL of USP Letrozole RS in *Mobile phase*

Standard solution: 3.0 µg/mL of USP Letrozole RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 35-µm pore size.

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 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of letrozole ($C_{17}H_{11}N_5$) dissolved:

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

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)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of letrozole ($C_{17}H_{11}N_5$) is dissolved.

Test 3

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Acetonitrile and water (48:52)

Standard stock solution: 0.25 mg/mL of USP Letrozole RS in *Mobile phase*

Standard solution: 0.005 mg/mL of USP Letrozole RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first few mL of the filtrate.

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 mL/min

Injection volume: 50 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 the labeled amount of letrozole ($C_{17}H_{11}N_5$) dissolved:

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

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)

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of letrozole ($C_{17}H_{11}N_5$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Solution A: Water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

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

Diluent: Prepare as directed in the *Assay*.

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

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

Sample solution: Nominally 0.1 mg/mL of letrozole in *Diluent*. Shake the whole Tablets (NLT 10) for about 15 min in a portion of *Diluent* to aid in dissolution. Centrifuge, and use the supernatant.

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 volume: 50 µL

System suitability

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

Suitability requirements

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets 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 = nominal concentration of letrozole in the *Sample solution* (mg/mL)

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

Table 2

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

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

[NOTE—Letrozole related compound A and 4,4',4"-Methanetriyltribenzonitrile are process impurities and are controlled in the drug substance monograph.]

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers at controlled room temperature.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **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 TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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