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%
- **HEAVY METALS,** *Method II* **⟨231⟩:** 10 ppm

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

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)

- **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 (12:13)

Diluent: Acetonitrile and water (3:7)

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 *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 *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 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 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**⟩
Medium: 0.1 N hydrochloric acid; 500 mL
Apparatus 2: 100 rpm
Time: 30 min
Standard solution: Transfer 50 mg of USP Letrozole RS to a 1-L volumetric flask, dissolve in 100 mL of acetonitrile, and dilute with *Medium* to volume. Dilute this solution with *Medium* to obtain a final concentration of 0.005 mg/mL.
Sample solution: Centrifuge a portion of the solution under test at 4000 rpm for 5 min.
Mobile phase and **Chromatographic system:** Prepare as directed in the *Assay*, except to use an injection volume of 200 µL.
Analysis: Inject a filtered portion of the solution under test into the chromatograph, record the chromatogram, and measure the responses for the major peaks.
Calculate the percentage of letrozole 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 the *Standard solution* (mg/mL)
V = volume of *Medium*, 500 mL
Tolerances: NLT 80% (Q) of the labeled amount of $C_{17}H_{11}N_5$ is dissolved.

• **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES

Organic Impurities

• **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: Proceed as directed in the *Assay*.
System suitability solution: 2 µg/mL of USP Letrozole Related Compound A RS, 10 µg/mL of USP Letrozole 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: Equivalent to 0.1 mg/mL of letrozole, from dissolved whole tablets in *Diluent*. [NOTE—Shake Tablets 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 size: 50 µL
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% 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 [NOTE—Disregard any values obtained that are less than 0.05%.]
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	—
Letrozole	1.0	—
4,4′,4″-Methanetriyltribenzonitrile	2.4	—
Any unspecified impurity	—	0.1

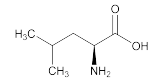
[a] 4,4′-(1*H*-1,3,4-Triazol-1-ylmethylene)dibenzonitrile.[NOTE—Letrozole related compound A and 4,4′,4″-methanetriyltribenzonitrile are process impurities, and are monitored in the drug substance monograph.]

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

Leucine



$C_6H_{13}NO_2$ 131.17
L-Leucine [61-90-5].

DEFINITION

Leucine contains NLT 98.5% and NMT 101.5% of L-leucine ($C_6H_{13}NO_2$), calculated on the dried basis.

IDENTIFICATION

• **A. INFRARED ABSORPTION** ⟨**197K**⟩

ASSAY

• **PROCEDURE**
Sample: 130 mg of Leucine
Blank: Mix 3 mL of formic acid and 50 mL of glacial acetic acid.
Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.1 N perchloric acid VS
Endpoint detection: Potentiometric
Analysis: Dissolve the *Sample* in 3 mL of formic acid and 50 mL of glacial acetic acid. Titrate with the *Titrant*. Perform the *Blank* determination.
Calculate the percentage of leucine ($C_6H_{13}NO_2$) in the *Sample* taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/W\} \times 100$$