Sample solution: Use portions of the solution under test passed through a suitable filter of 0.45-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 260 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Flow rate: 1.5 mL/min
Injection size: 40 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the amount of $C_{12}H_9F_3N_2O_2$ 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 Leflunomide RS in the *Standard solution* (mg/mL)
L = Tablet label claim (mg)
V = volume of Medium (mL), 1000
Tolerances: NLT 80% (Q) of the labeled amount of $C_{12}H_9F_3N_2O_2$ is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.
Medium, Apparatus 2, Time, Spectrometric method, and **Chromatographic method:** Proceed as directed for *Test 1*.
Tolerances: NLT 75% (Q) of the labeled amount of $C_{12}H_9F_3N_2O_2$ is dissolved.

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

Procedure for content uniformity
Mobile phase, System suitability solutions, Standard solution, and **Chromatographic system:** Prepare as directed in the *Assay*.
Sample solution: Transfer 1 Tablet to a suitable volumetric flask, and prepare a solution having a concentration of 1 mg/mL of leflunomide. Add *Mobile phase* 50% by volume, and shake to disintegrate the Tablet. After the Tablet is completely disintegrated, add acetonitrile 20% by volume, dilute with *Mobile phase* to volume, and shake again. Pass through a membrane filter.
Analysis: Proceed as directed in the *Assay*.

IMPURITIES

Organic Impurities

- **PROCEDURE**

Mobile phase, System suitability solutions, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each individual impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_T) \times 100$$

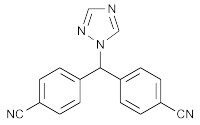
r_U = peak response of each individual impurity from the *Sample solution*
r_T = sum of all the peak responses of the related compounds and leflunomide from the *Sample solution*

Acceptance criteria
Leflunomide related compound A: NMT 0.1%
Leflunomide related compound B: NMT 3.5%
Leflunomide related compound C: NMT 0.2%
Individual impurities: NMT 0.2%
Total impurities: NMT 4.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant, and humidity-resistant containers.
- **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 Leflunomide RS
USP Leflunomide Related Compound A RS
USP Leflunomide Related Compound B RS
USP Leflunomide Related Compound C RS

Letrozole



$C_{17}H_{11}N_5$ 285.31
Benzonitrile, 4,4′-(1*H*-1,2,4-triazol-1-ylmethylene)bis-; 4,4′-(1*H*-1,2,4-Triazol-1-ylmethylene)dibenzonitrile [112809-51-5].

DEFINITION

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

IDENTIFICATION

- **A. INFRARED ABSORPTION ⟨197M⟩**
- **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%
- **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)