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Leflunomide Tablets

DEFINITION
Leflunomide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of leflunomide ($C_{12}H_9F_3N_2O_2$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Wavelength range: 220–360 nm

Sample solution: 0.01 mg/mL in methanol

• **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, triethylamine, and water (70:1:130). Adjust with phosphoric acid to a pH of 4.0.

System suitability solution A: 10 µg/mL of USP Leflunomide Related Compound A RS, 1 mg/mL of USP Leflunomide Related Compound B RS, and 100 µg/mL of USP Leflunomide Related Compound C RS in a minimum amount of acetonitrile, and diluted with *Mobile phase*

System suitability solution B: Transfer 100.0 mg of USP Leflunomide RS to a 100-mL volumetric flask. Dissolve in 2 mL of acetonitrile, add 1 mL of *System suitability solution A* and 80 mL of *Mobile phase*, and shake by mechanical means for 10 min. Dilute with *Mobile phase* to volume.

Standard solution: 1 mg/mL of USP Leflunomide RS in a minimum volume of acetonitrile, and diluted with *Mobile phase*

Sample solution: Transfer equivalent to 100 mg of leflunomide, from finely powdered Tablets (NLT 20), to a 100-mL volumetric flask. Add 20 mL of acetonitrile, dilute with *Mobile phase* to volume, and shake by mechanical means for 10 min. Pass through a membrane filter.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.0-mm × 12.5-cm; packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

[Note—The relative retention times for leflunomide related compound B, leflunomide related compound A, leflunomide related compound C, and leflunomide are 0.2, 0.4, 0.9, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between leflunomide related compound C and leflunomide, *System suitability solution B*

Tailing factor: NMT 3.0 for leflunomide, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of leflunomide ($C_{12}H_9F_3N_2O_2$) 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 Leflunomide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium

For Tablets labeled to contain 10 or 20 mg: Water, 1000 mL, deaerated

For Tablets labeled to contain 100 mg: Water containing 0.6% of polyoxyethylene (23) lauryl ether; 1000 mL, deaerated

Apparatus 2: 100 rpm

Time: 30 min

Determine the amount of leflunomide ($C_{12}H_9F_3N_2O_2$) dissolved by using one of the following methods.

Spectrometric method

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 262 nm

Standard solution: USP Leflunomide RS in *Medium*. [Note—A volume of methanol not exceeding 2% of the final volume of the *Standard solution* may be used to dissolve leflunomide.]

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*, if necessary.

Chromatographic method

Mobile phase: Acetonitrile and water (1:1)

Standard solution: Transfer 22 mg of USP Leflunomide RS to a 100-mL volumetric flask. Add 40 mL of acetonitrile, and sonicate until dissolved. Add 40 mL of water, and cool to room temperature. Dilute with water to volume. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, and dilute with water to volume.

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 leflunomide ($C_{12}H_9F_3N_2O_2$) 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 = label claim (mg/Tablet)

V = volume of *Medium*, 1000 mL

Tolerances: NLT 80% (Q) of the labeled amount of leflunomide ($C_{12}H_9F_3N_2O_2$) 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 leflunomide ($C_{12}H_9F_3N_2O_2$) is dissolved.

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

Procedure for content uniformity

Mobile phase, System suitability solution A, System suitability solution B, Standard solution, Chromatographic system, and **Analysis:** Proceed 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.

IMPURITIES

• **Procedure**

Mobile phase, System suitability solution A, System suitability solution B, 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

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

Topic/Question	Contact	Expert Committee
LEFLUNOMIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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