Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-4E691E3C-CD20-4A86-B50B-28E2EA7D159E_2_en-US
DOI: https://doi.org/10.31003/USPNF_M44260_02_01
DOI Ref: ujs24

Lamotrigine Tablets

DEFINITION

Lamotrigine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$).

IDENTIFICATION

Change to read:

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

Standard solution: 0.02 mg/mL of USP Lamotrigine RS in 0.01 N hydrochloric acid

Sample solution: 0.02 mg/mL of lamotrigine from crushed powdered Tablets in 0.01 N hydrochloric acid

Acceptance criteria: The spectra of the *Standard solution* and *Sample solution* exhibit maxima and minima at the same wavelengths.

• **B.** The retention time of the lamotrigine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 0.8 g/L of ammonium acetate. Adjust with glacial acetic acid to a pH of 4.5.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: 0.05 mg/mL of USP Lamotrigine RS in *Mobile phase*

Sample solution: Transfer an amount equivalent to 100 mg of lamotrigine from a portion of crushed Tablets (NLT 20) to a suitable volumetric flask to obtain a nominal concentration of lamotrigine of 1.0 mg/mL. Dissolve in 70% of the flask volume of *Mobile phase* by sonicating for 20 min. Dilute with *Mobile phase* to volume. Centrifuge the solution. Quantitatively dilute a suitable volume of centrifugate with *Mobile phase* to obtain a nominal concentration of 0.05 mg/mL of lamotrigine.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for lamotrigine

Relative standard deviation: NMT 2.0% for lamotrigine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) 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 Lamotrigine RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Determine the amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved by using one of the following methods.

Spectrometric method

Standard stock solution: 0.15 mg/mL of USP Lamotrigine RS in *Medium* prepared as follows. Dissolve a suitable quantity in 5% of the flask volume of methanol, then dilute with *Medium* to volume.

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of 0.028 mg/mL.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with *Medium* according to *Table 1*.

Table 1

Tablet Label Claim (mg)	Volume of Sample (mL)	Volume of Volumetric Flask	Final Concentration (mg/mL)
25	—	—	0.028
100	5.0	20	0.029
150	4.0	25	0.027
200	3.0	25	0.027

Instrumental conditions

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

Mode: UV

Analytical wavelength: 267 nm

Blank: *Medium*

Analysis

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times D \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

Chromatographic method

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

Standard stock solution: 0.5 mg/mL of USP Lamotrigine RS in *Medium*, prepared as follows. Dissolve a suitable quantity in 15% of the flask volume of methanol, then dilute with *Medium* to volume.

Standard solution: (L/1000) mg/mL of USP Lamotrigine RS from the *Standard stock solution* in *Medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Column: 4.6-mm × 15-cm; 5-µm packing L1

Detector: UV 310 nm

Flow rate: 1 mL/min

Injection size: See *Table 2*.

Table 2

Label Claim (mg/Tablet)	Injection Size (µL)
25	50
100, 150, 200	10

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for lamotrigine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) 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 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 lamotrigine is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus, and **Time:** Proceed as directed for *Test 1*.

Analysis: Determine the amount of lamotrigine dissolved using either the *Spectrometric method* or *Chromatographic method* described in *Test 1*.

Tolerances: NLT 75% (*Q*) of the labeled amount of lamotrigine is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 15 min

Standard solution: (*L*/900) mg/mL of USP Lamotrigine RS in *Medium*, where *L* is the Tablet label claim in mg

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 270 nm

Cell

For Tablets labeled to contain 100, 150, or 200 mg: 0.2-cm flow cell

For Tablets labeled to contain 25 mg: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of 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 lamotrigine is dissolved.

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

IMPURITIES

• **Organic Impurities**

Buffer: Prepare as directed in the *Assay*.

Mobile phase: Acetonitrile, methanol, and *Buffer* (10:30:60)

Diluent: Methanol and *Buffer* (60:40)

System suitability solution: 1 µg/mL of Lamotrigine Related Compound B RS and 0.4 mg/mL of USP Lamotrigine RS in *Diluent*

Standard solution: 1.0 µg/mL of USP Lamotrigine RS in *Diluent*

Sample solution: Transfer an amount equivalent to 100 mg of lamotrigine from a portion of crushed Tablets (NLT 20) to a suitable volumetric flask to obtain a nominal concentration of lamotrigine of about 0.4 mg/mL. Dissolve in 70% of the flask volume of *Mobile phase* by sonicating and shaking intermittently for 30 min. Dilute with *Diluent* to volume. Pass through a membrane filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 5 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between lamotrigine related compound B and lamotrigine, *System suitability solution*

Tailing factor: NMT 2.0 for lamotrigine, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_S = peak response of lamotrigine from the *Standard solution*

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

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

F = relative response factor for the corresponding impurity (see *Table 3*)

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lamotrigine related compound B[a]	0.67	0.75	0.2
Lamotrigine	1.0	—	—
Lamotrigine related compound C[b]	1.5	1.0	0.5
Any individual unspecified degradation impurity	—	1.0	0.2
Total impurities	—	—	0.75

[a] 2,3-Dichlorobenzoic acid.

[b] 3-Amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5(4*H*)-one.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store 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 Lamotrigine RS

USP Lamotrigine Related Compound B RS

2,3-Dichlorobenzoic acid.

$C_7H_4Cl_2O_2$ 191.01

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

Topic/Question	Contact	Expert Committee
LAMOTRIGINE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 36(6)

Current DocID: GUID-4E691E3C-CD20-4A86-B50B-28E2EA7D159E_2_en-US

DOI: https://doi.org/10.31003/USPNF_M44260_02_01

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