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# Lamotrigine Tablets for Oral Suspension

## DEFINITION

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

## IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **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**

**Buffer:** 0.77 g/L of ammonium acetate in water; adjusted with glacial acetic acid to a pH of 4.5

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

**Diluent:** Acetonitrile, methanol, and *Buffer* (30:30:40)

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

**Sample solution:** Nominally 0.05 mg/mL of lamotrigine prepared as follows. Transfer NLT 6 Tablets for Oral Suspension to a suitable volumetric flask. Sonicate in 70% of the flask volume of *Diluent* for 30 min with intermittent shaking. Dilute with *Diluent* to final volume, and pass a portion through a suitable membrane filter.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 210 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

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

**Flow rate:** 1.5 mL/min

**Injection volume:** 10 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 percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) in the portion of Tablets for Oral Suspension 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⟩**

**Medium:** 0.1 N hydrochloric acid; 900 mL, degassed

**Apparatus 2:** 50 rpm

**Time:** 15 min. [Note—The *Sample solution* may be analyzed using either *Chromatographic procedure 1* or *Chromatographic procedure 2*.]

**Standard stock solution:** 0.5 mg/mL of USP Lamotrigine RS in methanol

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

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

Determine the amount of lamotrigine dissolved by employing one of the following chromatographic procedures.

**Chromatographic procedure 1**

**Buffer:** To 1 L of 0.77 g/L of ammonium acetate in water add 2 mL of triethylamine, and adjust with glacial acetic acid to a pH of 7.5.

**Mobile phase:** Acetonitrile, methanol, and *Buffer* (20:15:65)

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 310 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 2.0

**Relative standard deviation:** NMT 2.0%

**Chromatographic procedure 2**

**Mobile phase:** Acetonitrile, water, glacial acetic acid, and triethylamine (47:148:4:1). [Note—The *Mobile phase* is stable for 48 h at room temperature.]

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

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

**Flow rate:** 1 mL/min

**Injection volume:** 10 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 percentage of the labeled amount of lamotrigine 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 Lamotrigine RS in the *Standard solution* (mg/mL)

$L$ = label claim of lamotrigine (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**

[Note—*Procedure 1* is recommended if lamotrigine related compound B is a potential organic impurity. *Procedure 2* is recommended if lamotrigine related compound C is a potential organic impurity.]

- **Organic Impurities, Procedure 1**

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

**Standard solution:** 0.8 µg/mL of USP Lamotrigine RS in *Diluent*

**Sample solution:** Nominally 0.25 mg/mL of lamotrigine prepared as follows. From NLT 20 Tablets for Oral Suspension ground to a fine powder, transfer an amount of powder to a suitable flask to obtain a nominal concentration of 0.25 mg/mL of lamotrigine in *Diluent*. Sonicate for 15 min to dissolve the contents. Filter a portion, and discard the first 1 mL of the filtrate.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 210 nm

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

**Flow rate:** 1 mL/min

**Injection volume:** 20 µL

**System suitability**

**Sample:** *Standard solution*

[Note—See *Table 1* for relative retention times.]

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 10%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets for Oral Suspension taken:

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

$r_U$ = peak response of each 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 each impurity (see *Table 1*)

**Acceptance criteria:** See *Table 1*.

**Table 1**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Lamotrigine | 1.0 | — | — |
| Lamotrigine related compound B[a] | 1.59 | 0.69 | 0.1 |
| Any other individual impurity | — | 1.0 | 0.2 |
| Total impurities | — | — | 0.4 |

[a] 2,3-Dichlorobenzoic acid.

• **Organic Impurities, Procedure 2**

**Mobile phase** and **Chromatographic system:** Proceed as directed in *Chromatographic procedure 2* in the *Dissolution* test.

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

**Standard solution:** 0.2 mg/mL of USP Lamotrigine RS and 0.002 mg/mL of USP Lamotrigine Related Compound C RS prepared as follows. Transfer suitable amounts of USP Lamotrigine RS and USP Lamotrigine Related Compound C RS to a suitable volumetric flask. Add 40% of the flask volume of methanol, and sonicate until dissolved. Allow to cool to room temperature, and dilute with water to volume.

**Sample solution:** Nominally 0.2 mg/mL of lamotrigine. Use 10 Tablets for Oral Suspension for a label claim of 25 mg or less and 5 Tablets for Oral Suspension for a label claim of 50 mg or more prepared as follows. Transfer the appropriate number of Tablets for Oral Suspension to a suitable volumetric flask. Add 40% of the flask volume of water. Swirl until the tablets have disintegrated. Allow the effervescence to stop, and then add an additional 40% of the flask volume of methanol. Sonicate the flask for 10 min, and cool to room temperature. Dilute with water to volume. [Note—For Tablets for Oral Suspension with a 50 mg or higher label claim, a suitable intermediate concentration may be chosen. The final dilution to arrive at the nominal concentration is made using *Diluent*.]

**System suitability**

**Sample:** *Standard solution*

[Note—See *Table 2* for relative retention times.]

**Suitability requirements**

**Resolution:** NLT 2.0 between lamotrigine and lamotrigine related compound C

**Tailing factor:** NMT 2.0 for lamotrigine and lamotrigine related compound C

**Relative standard deviation:** NMT 5.0% for lamotrigine related compound C and NMT 1.5% for lamotrigine

**Analysis**

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**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of lamotrigine related compound C in the portion of Tablets for Oral Suspension taken:

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

$r_U$ = peak response of lamotrigine related compound C from the *Sample solution*

$r_S$ = peak response of lamotrigine related compound C from the *Standard solution*

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

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

Calculate the percentage of any other individual unspecified impurity in the portion of Tablets for Oral Suspension taken:

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

$r_U$ = peak response of any other 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)

**Acceptance criteria:** See *Table 2*.

**Table 2**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Lamotrigine | 1.0 | — |
| Lamotrigine related compound C[a] | 1.3 | 0.3 |
| Any other individual unspecified impurity | — | 0.2 |
| Total impurities | — | 0.5 |

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

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store in tight, light-resistant containers, at controlled room temperature.

• **Labeling:** If a procedure for *Organic Impurities* other than *Procedure 1* is used, then the labeling states with which *Organic Impurities* procedure the article complies. The label states that the Tablets for Oral Suspension may be swallowed whole, chewed, or dispersed in water or diluted fruit juice.

• **USP Reference Standards** ⟨11⟩

USP Lamotrigine RS

1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl).

$C_9H_7Cl_2N_5$ 256.09

USP Lamotrigine Related Compound C RS

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

$C_9H_6Cl_2N_4O$ 257.08

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| LAMOTRIGINE TABLETS FOR ORAL SUSPENSION | Documentary Standards Support | SM42020 Small Molecules 4 |

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