Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Jul-2024
Document Type: USP Monographs
DocId: GUID-E0FCE04D-38C3-47B6-B9DF-5C6642493D9D_10_en-US
DOI: https://doi.org/10.31003/USPNF_M5924_10_01
DOI Ref: spadw



# Lamotrigine Extended-Release Tablets

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## DEFINITION

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

## IDENTIFICATION

• **A.** 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, water, and trifluoroacetic acid (25: 75: 0.05)

**Diluent:** Acetonitrile, methanol, and water (10:20:70)

**Standard solution:** 0.25 mg/mL of USP Lamotrigine RS in *Diluent*. Sonication may be used to aid dissolution.

**Sample stock solution:** 1.0–3.0 mg/mL of lamotrigine prepared as follows. Transfer Tablets (NLT 5) to a suitable volumetric flask containing 10% of the flask volume of acetonitrile. Allow the Tablets to disperse. Add 20% of the flask volume of methanol. Sonicate for 10 min. Add 30% of the flask volume of 0.1 N hydrochloric acid. Sonicate for 25 min or until a fine, even dispersion is obtained. Allow to cool to room temperature. Dilute with 0.1 N hydrochloric acidto volume. Pass a portion of the solution through a nylon filter of 0.45-µm pore size and use the filtrate.

**Sample solution:** Nominally 0.2–0.3 mg/mL of lamotrigine in 0.1 N hydrochloric acid from a suitable volume of *Sample stock solution*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

**Column:** 4.6-mm × 15-cm; 3-µm packing L1

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 5 µL

**Run time:** NLT 8 times the retention time of lamotrigine

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 1.5%

**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

***Change to read:***

• **Dissolution ⟨711⟩**

**Test 1**

**Medium 1:** 0.01 M hydrochloric acid; 700 mL

**Medium 2:** 7.8 g of tribasic sodium phosphate, and 22.5 g of sodium dodecyl sulfate in 1 L of water. This solution has a pH of about 12.

**Apparatus 2:** 50 rpm with sinkers (see *Dissolution ⟨711⟩*, *Figure 2a*)

**Times**

**For Tablets labeled to contain 25 or 50 mg:** 2, 7, and 15 h

**For Tablets labeled to contain 100, 200, or 250 mg:** 2, 5, and 12 h

**For Tablets labeled to contain 300 mg:** 2, 6, and 13 h

**Procedure:** Run the test with *Medium 1* for 2 h. Add 200 mL of *Medium 2*, preheated at 37°. Within 5 min of the addition of *Medium 2*, withdraw the sample for the 2-h time point. Continue the testing by drawing samples at the time points specified in *Table 1*, *Table 2*, or *Table 3*, depending on the label claim.

**Diluent:** *Medium 1* and *Medium 2* (70:20)

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

**Sample solution:** Pass a suitable portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with *Diluent*, if necessary.

**Blank:** *Diluent*

**Instrumental conditions**

**Mode:** UV

**Analytical wavelength:** 260 nm. [Note—Depending on the label claim, cells with suitable path lengths may be used.]

**Analysis**

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

Calculate the percentage of the labeled amount ($Q_i$) of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point *i*:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

$A_U$ = absorbance of the *Sample solution*

$A_S$ = absorbance of the *Standard solution*

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

$V$ = volume of *Medium*, 900 mL

$D$ = dilution factor, if needed

$L$ = label claim (mg/Tablet)

**Tolerances**

**For Tablets with 25- or 50-mg label claim:** See *Table 1*.

**For Tablets with 100-, 200-, or 250-mg label claim:** See *Table 2*.

**For Tablets with 300-mg label claim:** See *Table 3*.

**Table 1**

| Time Point (*i*) | Time (h) | Amount Dissolved |
|---|---|---|
| 1 | 2 | NMT 10% |
| 2 | 7 | 35%–55% |
| 3 | 15 | NLT 80% |

**Table 2**

| Time Point (*i*) | Time (h) | Amount Dissolved | |
|---|---|---|---|
| | | 100 mg, 200 mg | 250 mg |
| 1 | 2 | NMT 10% | NMT 10% |
| 2 | 5 | 20%–45% | 20%–40% |
| 3 | 12 | NLT 80% | NLT 80% |

**Table 3**

| Time Point (*i*) | Time (h) | Amount Dissolved |
|---|---|---|
| 1 | 2 | NMT 10% |
| 2 | 6 | 25%–45% |
| 3 | 13 | NLT 80% |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

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

**Acid stage medium:** 0.01 M hydrochloric acid; 700 mL

**Buffer stage stock medium:** 2.83 g of sodium phosphate monobasic, 1.72 g of sodium hydroxide, and 22.5 g of sodium dodecyl sulfate in 1 L of water

**Buffer stage medium:** *Acid stage medium* and *Buffer stage stock medium* (70:20); 900 mL. Adjust with solution A (phosphoric acid in water prepared by diluting 1 mL of phosphoric acid with water to 50 mL) or 0.1 N sodium hydroxide, if necessary, to a pH of 6.8. Record the required volume of solution A or 0.1 N sodium hydroxide for adjustment of the pH to 6.8.

**Apparatus 2:** 50 rpm with stationary tablet basket. See Figures *2b* and *2c* in *Dissolution* ⟨711⟩.

**Times**

**For Tablets labeled to contain 25 or 50 mg:** 2 h in *Acid stage medium*; 4, 7, 9, and 15 h in *Buffer stage medium*

**For Tablets labeled to contain 100, 200, or 300 mg:** 2 h in *Acid stage medium*; 3, 5, 7, and 12 h in *Buffer stage medium*

[Note—The times in the *Buffer stage medium* include the time in the *Acid stage medium*.]

**Procedure:** Run the test with *Acid stage medium* for 2 h followed by collecting the *Acid stage medium* sample and replacing it with the same volume of *Acid stage medium*. Add 200 mL of *Buffer stage stock medium* to the above solution. If necessary, add either solution A or 0.1 N sodium hydroxide to the solution to reach a pH of 6.8. Continue the testing by drawing samples at the time points specified in *Table 4* or *Table 5*, depending on the label claim. Replace each of the volumes withdrawn with an equal volume of *Buffer stage medium*.

**Buffer:** Dissolve 2.76 g of sodium phosphate monobasic in 1 L of water. Add 2 mL of triethylamine and adjust with solution A to a pH of 7.0.

**Mobile phase:** Methanol and *Buffer* (55:45)

**Standard stock solution:** 1.4 mg/mL of USP Lamotrigine RS in methanol

**Acid stage standard solution:** (*L*/900) mg/mL of USP Lamotrigine RS from *Standard stock solution*, in *Acid stage medium*, where *L* is the label claim in mg/Tablet

**Buffer stage standard solution:** (*L*/900) mg/mL of USP Lamotrigine RS from *Standard stock solution*, in *Buffer stage medium*, where *L* is the label claim in mg/Tablet

**Acid stage sample solution:** Withdraw a 10.0-mL aliquot, and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Replace the 10.0-mL aliquot withdrawn for analysis with a 10.0-mL aliquot of *Acid stage medium*.

**Buffer stage sample solution:** Withdraw a 10.0-mL aliquot, and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Replace the 10.0-mL aliquot withdrawn for analysis with a 10.0-mL aliquot of *Buffer stage medium*.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

**Column:** 4.6-mm × 15-cm; 5-µm packing L7

**Flow rate:** 1 mL/min

**Injection volume**

**For 25-mg Tablets:** 80 µL

**For 50-mg Tablets:** 40 µL

**For 100-mg Tablets:** 20 µL

**For 200- or 300-mg Tablets:** 10 µL

**Run time:** NLT 1.8 times the retention time of lamotrigine

**System suitability**

**Samples:** *Acid stage standard solution* and *Buffer stage standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage ($Q_A$) of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved in the *Acid stage medium*:

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

$r_U$ = peak response from the *Acid stage sample solution*

$r_S$ = peak response from the *Acid stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Acid stage standard solution* (mg/mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

$L$ = label claim (mg/Tablet)

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point ($i$) during the buffer stage:

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

$r_U$ = peak response from the *Buffer stage sample solution* at time point *i*

$r_S$ = peak response from the *Buffer stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point ($i$) during the buffer stage:

$$\text{Result}_1 = [C_1 \times V_B \times (1/L) \times 100] + (Q_A \times V_S/V_A)$$

$$\text{Result}_2 = \{[(C_2 \times V_B) + (C_1 \times V_S)] \times (1/L) \times 100\} + (Q_A \times V_S/V_A)$$

$$\text{Result}_3 = (\{(C_3 \times V_B) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100) + (Q_A \times V_S/V_A)$$

$$\text{Result}_4 = (\{(C_4 \times V_B) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100) + (Q_A \times V_S/V_A)$$

$C_i$ = concentration of lamotrigine in the *Buffer stage sample solution* withdrawn at time point *i* (mg/mL)

$V_B$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$Q_A$ = the percentage of the labeled amount of lamotrigine dissolved in the *Acid stage medium*

$V_S$ = volume of the sample solution withdrawn at each time point ($i$) during the acid stage or buffer stage (mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

**Tolerances**

**For Tablets labeled to contain 25 or 50 mg:** See *Table 4*.

**For Tablets labeled to contain 100, 200, or 300 mg:** See *Table 5*.

**Table 4**

| Time Point (*i*) | Time (h) | Amount Dissolved |
|---|---|---|
| 1 | 2 | NMT 10% |
| 2 | 4 | 5%–25% |
| 3 | 7 | 30%–50% |
| 4 | 9 | 50%–70% |
| 5 | 15 | NLT 80% |

**Table 5**

| Time Point (*i*) | Time (h) | Amount Dissolved |
|---|---|---|
| 1 | 2 | NMT 10% |
| 2 | 3 | 5%–20% |
| 3 | 5 | 25%–50% |
| 4 | 7 | 50%–70% |
| 5 | 12 | NLT 80% |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

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

**Acid stage medium:** 0.01 M hydrochloric acid; 700 mL

**Buffer stage stock medium:** 7.8 g of sodium phosphate tribasic and 22.5 g of sodium dodecyl sulfate in 1 L of water

**Buffer stage medium:** *Acid stage medium* and *Buffer stage stock medium* (70:20); 900 mL. Adjust with 2 N hydrochloric acid TS or 2 N sodium hydroxide TS, if necessary, to a pH of 6.8.

**Apparatus 2:** 50 rpm with stationary tablet basket. See Figures *2b* and *2c* in *Dissolution* ⟨711⟩.

**Times**

**For Tablets labeled to contain 25, 50, 100, or 200 mg:** 2 h in *Acid stage medium*; 4, 7, and 14 h in *Buffer stage medium*

[Note—The times in the *Buffer stage medium* include the time in the *Acid stage medium*.]

**Procedure:** Run the test with *Acid stage medium* for 2 h followed by collecting the *Acid stage medium* sample and replacing it with the same volume of *Acid stage medium*. Add 200 mL of *Buffer stage stock medium* to the above solution. Continue the testing by drawing samples at the time points specified in *Table 6*. Replace each of the volumes withdrawn with an equal volume of the *Buffer stage medium*.

**Buffer:** Dissolve 2.72 g of potassium phosphate monobasic in 1 L of water and adjust with dilute phosphoric acid to a pH of 3.7.

**Mobile phase:** Methanol, acetonitrile, and *Buffer* (50:15:35)

**Standard stock solution:** 0.6 mg/mL of USP Lamotrigine RS in methanol. Sonicate to dissolve as needed.

**Acid stage standard solution:** 0.036 mg/mL of USP Lamotrigine RS from *Standard stock solution*, in *Acid stage medium*

**Buffer stage standard solution:** (*L*/900) mg/mL of USP Lamotrigine RS from *Standard stock solution*, in *Buffer stage medium*, where *L* is the label claim in mg/Tablet

**Acid stage sample solution:** Withdraw a 10.0-mL aliquot and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 5 mL of the filtrate. Replace the 10.0-mL aliquot withdrawn for analysis with a 10.0-mL aliquot of *Acid stage medium*.

**Buffer stage sample solution:** Withdraw a 10.0-mL aliquot and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Replace the 10.0-mL aliquot withdrawn for analysis with a 10.0-mL aliquot of *Buffer stage medium*.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

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

**Column temperature:** 35°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 1.7 times the retention time of lamotrigine

**System suitability**

**Samples:** *Acid stage standard solution* and *Buffer stage standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage ($Q_A$) of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved in the *Acid stage medium*:

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

$r_U$ = peak response from the *Acid stage sample solution*

$r_S$ = peak response from the *Acid stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Acid stage standard solution* (mg/mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

$L$ = label claim (mg/Tablet)

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point ($i$) during the buffer stage:

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

$r_U$ = peak response from the *Buffer stage sample solution* at time point $i$

$r_S$ = peak response from the *Buffer stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point ($i$) during the buffer stage:

$$\text{Result}_1 = [C_1 \times V_B \times (1/L) \times 100] + (Q_A \times V_S/V_A)$$

$$\text{Result}_2 = \{[(C_2 \times V_B) + (C_1 \times V_S)] \times (1/L) \times 100\} + (Q_A \times V_S/V_A)$$

$$\text{Result}_3 = (\{(C_3 \times V_B) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100) + (Q_A \times V_S/V_A)$$

$C_i$ = concentration of lamotrigine in the *Buffer stage sample solution* withdrawn at time point $i$ (mg/mL)

$V_B$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$Q_A$ = the percentage of the labeled amount of lamotrigine dissolved in the *Acid stage medium*

$V_S$ = volume of the sample solution withdrawn at each time point ($i$) during the acid stage or buffer stage (mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

**Tolerances**

**For Tablets labeled to contain 25, 50, 100, or 200 mg:** See *Table 6*.

**Table 6**

| Time Point ($i$) | Time (h) | Amount Dissolved (%) |
|---|---|---|
| 1 | 2 | NMT 10 |
| 2 | 4 | NMT 25 |
| 3 | 7 | 36–61 |
| 4 | 14 | NLT 85 |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

**Test 4:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

**Acid stage medium:** 0.01 M hydrochloric acid; 700 mL

**Buffer stage stock medium:** 7.8 g of sodium phosphate tribasic and 22.5 g of sodium dodecyl sulfate in 1 L of water

**Buffer stage medium:** *Acid stage medium* and *Buffer stage stock medium* (70:20); 900 mL

**Apparatus 2:** 50 rpm with sinkers

**Times**

**For Tablets labeled to contain 25, 50, 100, 200, or 300 mg:** 2 h in *Acid stage medium*; 9 and 17 h in *Buffer stage medium*

[NOTE—The times in the *Buffer stage medium* include the time in the *Acid stage medium*.]

**Procedure:** Run the test with *Acid stage medium* for 2 h followed by collecting the *Acid stage medium* sample and replacing it with the same volume of *Acid stage medium*. Add 200 mL of *Buffer stage stock medium* to the above solution. Continue the testing by drawing samples at the time points specified in *Table 7*. Replace each of the volumes withdrawn with an equal volume of the *Buffer stage medium*.

**Buffer:** Dissolve 4.1 g of potassium phosphate monobasic in 900 mL of water and adjust with dilute phosphoric acid to a pH of 2.0, and then dilute with water to 1 L. Add 1.25 g of sodium 1-hexanesulfonate to the solution and mix.

**Mobile phase:** Acetonitrile and *Buffer* (25:75)

**Acid stage standard stock solution 1:** 0.07 mg/mL of USP Lamotrigine RS prepared as follows. Transfer an appropriate amount of USP Lamotrigine RS to a suitable volumetric flask and add 20% of the flask volume of methanol. Sonicate to dissolve and dilute with *Acid stage medium* to volume. Further dilute this solution with *Acid stage medium* to obtain a final concentration of 0.07 mg/mL.

**Acid stage standard stock solution 2:** 0.14 mg/mL of USP Lamotrigine RS prepared as follows. Transfer an appropriate amount of USP Lamotrigine RS to a suitable volumetric flask and add 20% of the flask volume of methanol. Sonicate to dissolve and dilute with *Acid stage medium* to volume. Further dilute this solution with *Acid stage medium* to obtain a final concentration of 0.14 mg/mL.

**Acid stage standard solution:** 0.1 × (*L*/700) mg/mL of USP Lamotrigine RS either from *Acid stage standard stock solution 1* for Tablets labeled to contain 25, 50, 100, and 200 mg, or from *Acid stage standard stock solution 2* for Tablets labeled to contain 300 mg, in *Acid stage medium*, where *L* is the label claim in mg/Tablet. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

**Buffer stage standard stock solution 1:** 0.55 mg/mL of USP Lamotrigine RS prepared as follows. Transfer an appropriate amount of USP Lamotrigine RS to a suitable volumetric flask and add 10% of the flask volume of methanol. Sonicate to dissolve and dilute with *Buffer stage medium* to volume.

**Buffer stage standard stock solution 2:** 1.1 mg/mL of USP Lamotrigine RS prepared as follows. Transfer an appropriate amount of USP Lamotrigine RS to a suitable volumetric flask and add 20% of the flask volume of methanol. Sonicate to dissolve and dilute with *Buffer stage medium* to volume.

**Buffer stage standard solution:** (*L*/900) mg/mL of USP Lamotrigine RS either from *Buffer stage standard stock solution 1* for Tablets labeled to contain 25, 50, 100, and 200 mg, or from *Buffer stage standard stock solution 2* for Tablets labeled to contain 300 mg, in *Buffer stage medium*, where *L* is the label claim in mg/Tablet. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

**Acid stage sample solution:** Withdraw a 10.0-mL aliquot and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate. Replace the 10.0-mL aliquot withdrawn for analysis with a 10.0-mL aliquot of *Acid stage medium*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

**Buffer stage sample solution:** Withdraw a 10.0-mL aliquot and pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Replace the 10.0-mL aliquot withdrawn for analysis with a 10.0-mL aliquot of *Buffer stage medium*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

**Column:** 4.6-mm × 25-cm; 5-µm packing L7

**Column temperature:** 60°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 2 times the retention time of lamotrigine

**System suitability**

**Samples:** *Acid stage standard solution* and *Buffer stage standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage ($Q_A$) of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved in the *Acid stage medium*:

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

$r_U$ = peak response from the *Acid stage sample solution*

$r_S$ = peak response from the *Acid stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Acid stage standard solution* (mg/mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

$L$ = label claim (mg/Tablet)

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point ($i$) during the buffer stage:

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

$r_U$ = peak response from the *Buffer stage sample solution* at time point *i*

$r_S$ = peak response from the *Buffer stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point (*i*) during the buffer stage:

$$\text{Result}_1 = [C_1 \times V_B \times (1/L) \times 100] + (Q_A \times V_S/V_A)$$

$$\text{Result}_2 = \{[(C_2 \times V_B) + (C_1 \times V_S)] \times (1/L) \times 100\} + (Q_A \times V_S/V_A)$$

$C_i$ = concentration of lamotrigine in the *Buffer stage sample solution* withdrawn at time point *i* (mg/mL)

$V_B$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$Q_A$ = the percentage of the labeled amount of lamotrigine dissolved in the *Acid stage medium*

$V_S$ = volume of the sample solution withdrawn at each time point (*i*) during the acid stage or buffer stage (mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

**Tolerances**

**For Tablets labeled to contain 25, 50, 100, 200, or 300 mg:** See *Table 7*.

**Table 7**

| Time Point (*i*) | Time (h) | Amount Dissolved (%) |
|---|---|---|
| 1 | 2 | NMT 10 |
| 2 | 9 | 35–55 |
| 3 | 17 | NLT 80 |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

**Test 5:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

**Acid stage medium:** 0.01 M hydrochloric acid; 710 mL

**Buffer stage stock medium:** 3.36 g of anhydrous tribasic sodium phosphate and 22.5 g of sodium dodecyl sulfate in 1 L of water

**Buffer stage medium:** *Acid stage medium* and *Buffer stage stock medium* (70:20); 900 mL. Adjust with hydrochloric acid or 5 N sodium hydroxide TS, if necessary, to a pH of 6.8.

**Apparatus 2:** 50 rpm with sinkers

**Times**

**For Tablets labeled to contain 25, 50, 100, or 200 mg:** 2 h in *Acid stage medium*; 4, 7, and 17 h in *Buffer stage medium*

[Note—The times in the *Buffer stage medium* include the time in *Acid stage medium*.]

**Procedure:** Run the test with *Acid stage medium* for 2 h followed by collecting the *Acid stage medium* sample. Add 200 mL of *Buffer stage stock medium* to this solution. Continue the testing by drawing samples at the time points specified in *Table 8*.

**Buffer:** Dissolve 3.45 g of monobasic sodium phosphate in 1 L of water, and adjust with phosphoric acid to a pH of 3.3. To this solution, add 5.77 g of sodium dodecyl sulfate, and mix well.

**Mobile phase:** Acetonitrile and *Buffer* (45:55)

**Standard solution:** 0.22 mg/mL of USP Lamotrigine RS in *Mobile phase*. Sonicate to dissolve as needed.

**Acid stage sample solution:** Withdraw a 10.0-mL aliquot, and pass a portion of the solution under test through a suitable full flow filter of 10-µm pore size.

**Buffer stage sample solution:** Withdraw a 2.5-mL aliquot, and pass a portion of the solution under test through a suitable full flow filter of 10-µm pore size.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 266 nm

**Column:** 4.6-mm × 5-cm; 3.5-µm packing L1

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 1.6 times the retention time of lamotrigine

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 1.5

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage ($Q_A$) of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved in the *Acid stage medium*:

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

$r_U$ = peak response from the *Acid stage sample solution*

$r_S$ = peak response from the *Standard solution*

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

$V_A$ = volume of the *Acid stage medium*, 710 mL

$L$ = label claim (mg/Tablet)

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point ($i$) during the buffer stage:

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

$r_U$ = peak response from the *Buffer stage sample solution* at time point *i*

$r_S$ = peak response from the *Standard solution*

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

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point ($i$) during the buffer stage:

$$\text{Result}_1 = [C_1 \times V_B \times (1/L) \times 100] + (Q_A \times V_S/V_A)$$

$$\text{Result}_2 = \{[C_2 \times (V_B - V_S) + (C_1 \times V_S)] \times (1/L) \times 100\} + (Q_A \times V_S/V_A)$$

$$\text{Result}_3 = (\{[C_3 \times (V_B - 2V_S)] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100) + (Q_A \times V_S/V_A)$$

$C_i$ = concentration of lamotrigine in the *Buffer stage sample solution* withdrawn at time point *i* (mg/mL)

$V_B$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$Q_A$ = the percentage of the labeled amount of lamotrigine dissolved in the *Acid stage medium*

$V_S$ = volume of the *Sample solution* withdrawn at each time point ($i$), 10 mL for acid stage or 2.5 mL for buffer stage

$V_A$ = volume of the *Acid stage medium*, 710 mL

**Tolerances**

**For Tablets labeled to contain 25, 50, 100, or 200 mg:** See *Table 8*.

**Table 8**

| Time Point (*i*) | Time (h) | Amount Dissolved | |
|---|---|---|---|
| | | 25, 50, and 200 mg/Tablet (%) | 100 mg/Tablet (%) |
| 1 | 2 | NMT 10 | NMT 10 |
| 2 | 4 | 10–30 | 10–30 |
| 3 | 7 | 35–60 | 40–65 |

| Time Point (*i*) | Time (h) | Amount Dissolved | |
|---|---|---|---|
| | | 25, 50, and 200 mg/Tablet (%) | 100 mg/Tablet (%) |
| 4 | 17 | NLT 80 | NLT 80 |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

**Test 7:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.

**Acid stage medium:** 0.01 N hydrochloric acid TS; 700 mL, degas by helium sparging before use

**Buffer stage stock medium:** 7.8 g of sodium phosphate tribasic in 1 L of water, add 2 mL of sodium hydroxide TS and degas by helium sparging, then add 22.5 g of sodium dodecyl sulfate and mix well. Degas by warming the solution to NMT 50° and bring back to 37° before use.

**Buffer stage medium:** *Acid stage medium* and *Buffer stage stock medium* (70:20), pH 6.8; 900 mL. Adjust with 1 N hydrochloric acid VS or sodium hydroxide TS, if necessary.

**Apparatus 1:** 75 rpm for Tablets labeled to contain 25, 50, 100, 200, or 300 mg

**Apparatus 2:** 50 rpm for Tablets labeled to contain 250 mg

**Times:** 2 h in *Acid stage medium*; see *Table 9* for times in *Buffer stage medium*. The times in the *Buffer stage medium* include the time in *Acid stage medium*.

**Procedure:** Run the test with *Acid stage medium* for 2 h followed by collecting the *Acid stage medium* sample and replacing it with the same volume of *Acid stage medium*. Add 200 mL of *Buffer stage stock medium* to the above solution. Continue the testing by drawing samples at the time points specified in *Table 9* without replacing the withdrawn volume.

**Buffer:** 3.85 g/L of ammonium acetate in water, adjust with acetic acid to a pH of 5.60 ± 0.05

**Mobile phase:** Acetonitrile and *Buffer* (32:68)

**Standard stock solution:** 2.0 mg/mL of USP Lamotrigine RS prepared as follows. Transfer an appropriate amount of USP Lamotrigine RS to a suitable volumetric flask and add 50% of the flask volume of methanol. Sonicate with occasional swirling for 5 min or until the Reference Standard is completely dissolved. Dilute with *Buffer stage medium* to volume.

**Standard solution:** 0.16 mg/mL of USP Lamotrigine RS from *Standard stock solution* in *Buffer stage medium*

**Acid stage sample solution:** Withdraw a suitable volume of the solution under test and replace the withdrawn aliquot with the same volume of *Acid stage medium*. Pass a portion of the withdrawn solution through a filter of suitable pore size. Discard the first few milliliters of the filtrate.

**Buffer stage sample solution:** Withdraw a suitable volume of the solution under test and pass a portion of the withdrawn solution through a filter of suitable pore size. Discard the first few milliliters of the filtrate.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 306 nm

**Column:** 4.6-mm × 15-cm; 5-µm packing L7

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 1.4 times the retention time of lamotrigine

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage ($Q_A$) of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved in the *Acid stage medium*:

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

$r_U$ = peak response from the *Acid stage sample solution*

$r_S$ = peak response from the *Standard solution*

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

$V_A$ = volume of the *Acid stage medium*, 700 mL

$L$ = label claim (mg/Tablet)

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point (*i*) during the buffer stage:

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

$r_U$ = peak response from the *Buffer stage sample solution* at time point *i*

$r_S$ = peak response from the *Standard solution*

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

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point (*i*) during the buffer stage:

$$\text{Result}_2 = [C_2 \times V_B \times (1/L) \times 100] + (Q_A \times V_S/V_A)$$

$$\text{Result}_3 = \{[C_3 \times (V_B - V_S) + (C_2 \times V_S)] \times (1/L) \times 100\} + (Q_A \times V_S/V_A)$$

$$\text{Result}_4 = (\{[C_4 \times (V_B - 2V_S)] + [(C_3 + C_2) \times V_S]\} \times (1/L) \times 100) + (Q_A \times V_S/V_A)$$

$C_i$ = concentration of lamotrigine in the *Buffer stage sample solution* withdrawn at time point *i* (mg/mL)

$V_B$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$Q_A$ = percentage of the labeled amount of lamotrigine dissolved in the *Acid stage medium*

$V_S$ = volume of the *Sample solution* withdrawn at each time point (*i*)

$V_A$ = volume of the *Acid stage medium*, 700 mL

**Tolerances:** See *Table 9*.

**Table 9**

| Time Point (*i*) | Time (h) | Amount Dissolved | | | | | |
|---|---|---|---|---|---|---|---|
| | | 25 mg/Tablet (%) | 50 mg/Tablet (%) | 100 mg/Tablet (%) | 200 mg/Tablet (%) | 250 mg/Tablet (%) | 300 mg/Tablet (%) |
| 1 | 2 | NMT 10 | NMT 10 | NMT 10 | NMT 10 | NMT 10 | NMT 10 |
| 2 | 4 | 10–30 | 10–30 | 10–30 | 10–30 | 8–25 | 10–28 |
| 3 | 7 | — | — | 53–73 | — | — | — |
| | 8 | 50–70 | — | — | 50–70 | — | 50–70 |
| | 9 | — | 45–65 | — | — | 55–75 | — |
| 4 | 10 | — | — | NLT 80 | — | — | — |
| | 11 | — | — | — | — | — | NLT 80 |
| | 12 | NLT 80 | — | — | NLT 80 | — | — |
| | 14 | — | NLT 80 | — | — | — | — |
| | 15 | — | — | — | — | NLT 85 | — |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

**Test 9:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 9*.

**Acid stage**

**Acid stage medium:** 0.01 N hydrochloric acid; 700 mL

**Apparatus 2:** 50 rpm, with stationary basket. See ⟨711⟩, Figures *2b* and *2c*.

**Time:** 2 h

**Buffer:** 2 mL/L of triethylamine in water. Adjust with phosphoric acid to a pH of 2.5.

**Mobile phase:** Acetonitrile and *Buffer* (30:70)

**Acid stage standard stock solution:** 0.36 mg/mL of USP Lamotrigine RS in methanol. Sonicate to dissolve, if necessary.

**Acid stage standard solution:** (*L*/7000) mg/mL of USP Lamotrigine RS from *Acid stage standard stock solution* in *Acid stage medium*, where *L* is the label claim in mg/Tablet.

**Acid stage sample solution:** At the end of the 2 h *Acid stage*, withdraw 10 mL of the solution under test and replace the withdrawn aliquot with the same volume of *Acid stage medium*. Pass a portion of the solution withdrawn through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of filtrate.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

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

**Column temperature:** 50°

**Flow rate:** 0.7 mL/min

**Injection volume:** 20 µL

**Run time:** NLT 3 times the retention time of lamotrigine

**System suitability**

**Sample:** *Acid stage Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Acid stage standard solution* and *Acid stage sample solution*

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved in the *Acid stage*:

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

$r_U$ = peak response of lamotrigine from the *Acid stage sample solution*

$r_S$ = peak response of lamotrigine from the *Acid stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Acid stage standard solution* (mg/mL)

$V$ = volume of the *Acid stage medium*, 700 mL

$L$ = label claim (mg/Tablet)

**Tolerances:** NMT 10%. The percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the time specified conforms to *Dissolution ⟨711⟩, Acceptance Table 3*.

**Buffer stage**

**Buffer stage stock medium:** 7.8 g/L of sodium phosphate tribasic and 22.3 g/L of sodium dodecyl sulfate in water prepared as follows. Dissolve 7.8 g of sodium phosphate tribasic in 1000 mL of water. Add 22.3 g of sodium dodecyl sulfate and mix well.

**Buffer stage medium:** *Acid stage medium* and *Buffer stage stock medium* (70:20); 900 mL.

**Apparatus 2:** 50 rpm, with stationary basket. See ⟨711⟩, Figures *2b* and *2c*.

**Times:**

**For Tablets labeled to contain 25 and 50 mg:** 2, 7, and 15 h

**For Tablets labeled to contain 100 and 200 mg** ▲▲ (RB 1-Jul-2024) **:** 1, 4, and 11 h

▲**For Tablets labeled to contain 250 and 300 mg:** 1, 5, and 11 h▲ (RB 1-Jul-2024)

**Buffer:** 2 mL/L of triethylamine in water. Adjust with phosphoric acid to a pH of 2.5.

**Mobile phase:** Acetonitrile and *Buffer* (35:65)

**Buffer stage standard stock solution:** 1.11 mg/mL of USP Lamotrigine RS in methanol. Sonicate to dissolve, if necessary.

**Buffer stage standard solution:** (*L*/900) mg/mL of USP Lamotrigine RS from *Buffer stage standard stock solution* in *Buffer stage medium*, where *L* is the label claim in mg/Tablet.

**Buffer stage sample solution:** After the 2 h in the *Acid stage*, add 200 mL of *Buffer stage stock medium* to the vessel containing *Acid stage medium*. At the times specified, withdraw 10 mL of the solution under test and replace the withdrawn aliquot with the same volume of *Buffer stage medium*. Pass a portion of the solution withdrawn through a suitable filter of 0.45-µm pore size, discarding the first 5 mL of filtrate.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

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

**Column temperature:** 50°

**Flow rate:** 1 mL/min

**Injection volume:** 5 µL

**Run time:** NLT 3 times the retention time of lamotrigine

**System suitability**

**Sample:** *Buffer stage standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Buffer stage standard solution* and *Buffer stage sample solution*

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point (*i*) in the *Buffer stage*:

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

$r_U$ = peak response of lamotrigine from the *Buffer stage sample solution*

$r_S$ = peak response of lamotrigine from the *Buffer stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Buffer stage standard solution* (mg/mL)

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point (*i*) in the *Buffer stage*:

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$C_i$ = concentration of lamotrigine in the portion of sample withdrawn at time point *i* (mg/mL)

$V$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$V_S$ = volume of the *Buffer stage sample solution* withdrawn at each time point and replaced with *Buffer stage medium*, 10 mL

**Tolerances:** See *Table 10*.

**Table 10**

| For Tablets Labeled to Contain 25 and 50 mg of Lamotrigine | | | For Tablets Labeled to Contain 100 mg of Lamotrigine | | For Tablets Labeled to Contain 200 mg of Lamotrigine | | For Tablets Labeled to Contain 250 mg of Lamotrigine | | ▲For Tablets Labeled to Contain 300 mg of Lamotrigine▲ (RB 1-Jul-2024) | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Time Point (*i*)** | **Time (h)** | **Amount Dissolved (%)** | **Time (h)** | **Amount Dissolved (%)** | **Time (h)** | **Amount Dissolved (%)** | **Time (h)** | **Amount Dissolved (%)** | **▲Time (h)▲ (RB 1-Jul-2024)** | **▲Amount Dissolved (%)▲ (RB 1-Jul-2024)** |
| 1 | 2 | 5–25 | 1 | NMT 20 | 1 | NMT 20 | 1 | NMT 20 | ▲1▲ (RB 1-Jul-2024) | ▲NMT 20▲ (RB 1-Jul-2024) |
| 2 | 7 | 45–65 | 4 | 30–50 | 4 | 38–58 | ▲5▲ (RB 1-Jul-2024) | ▲46–66▲ (RB 1-Jul-2024) | ▲5▲ (RB 1-Jul-2024) | ▲42–62▲ (RB 1-Jul-2024) |

| For Tablets Labeled to Contain 25 and 50 mg of Lamotrigine | | | For Tablets Labeled to Contain 100 mg of Lamotrigine | | For Tablets Labeled to Contain 200 mg of Lamotrigine | | For Tablets Labeled to Contain 250 mg of Lamotrigine | | ▲For Tablets Labeled to Contain 300 mg of Lamotrigine▲ (RB 1-Jul-2024) | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Time Point (*i*)** | **Time (h)** | **Amount Dissolved (%)** | **Time (h)** | **Amount Dissolved (%)** | **Time (h)** | **Amount Dissolved (%)** | **Time (h)** | **Amount Dissolved (%)** | **▲Time (h)▲** (RB 1-Jul-2024) | **▲Amount Dissolved (%)▲** (RB 1-Jul-2024) |
| 3 | 15 | NLT 80 | 11 | NLT 80 | 11 | NLT 80 | 11 | NLT 80 | ▲11▲ (RB 1-Jul-2024) | ▲NLT 80▲ (RB 1-Jul-2024) |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

▲**Test 10:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 10*.

**Acid stage medium:** 0.01 N hydrochloric acid; 700 mL

**Buffer stage medium:** To 700 mL of *Acid stage medium*, add 200 mL of a pre-warmed solution containing 7.8 g of sodium phosphate, tribasic and 22.5 g of sodium dodecyl sulfate in 1 L of water; 900 mL.

**Apparatus 2:** 50 rpm with sinkers (see *Dissolution* ⟨711⟩, *Figure 2a*)

**Times**

**For Tablets labeled to contain 25 and 50 mg:** 2 h in *Acid stage medium*; 7 and 15 h in *Buffer stage medium*. The times in the *Buffer stage medium* include the time in the *Acid stage medium*.

**For Tablets labeled to contain 100, 200, and 250 mg:** 2 h in *Acid stage medium*; 5 and 14 h in *Buffer stage medium*. The times in the *Buffer stage medium* include the time in the *Acid stage medium*.

**For Tablets labeled to contain 300 mg:** 2 h in *Acid stage medium*; 6 and 13 h in *Buffer stage medium*. The times in the *Buffer stage medium* include the time in the *Acid stage medium*.

**Buffer:** Dissolve 6.8 g of potassium phosphate monobasic in 1 L of water.

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

**Standard stock solution**

**For Tablets labeled to contain 25 mg:** 0.28 mg/mL of USP Lamotrigine RS prepared as follows. Transfer a quantity of USP Lamotrigine RS to an appropriate volumetric flask and add 7.5% of the flask volume of methanol. Sonicate to dissolve, if necessary. Dilute with *Buffer stage medium* to volume.

**For Tablets labeled to contain 50 mg:** 0.56 mg/mL of USP Lamotrigine RS prepared as follows. Transfer a quantity of USP Lamotrigine RS to an appropriate volumetric flask and add 15% of the flask volume of methanol. Sonicate to dissolve, if necessary. Dilute with *Buffer stage medium* to volume.

**Standard solution**

**For Tablets labeled to contain 25 mg:** 0.028 mg/mL of USP Lamotrigine RS from *Standard stock solution* in *Buffer stage medium*

**For Tablets labeled to contain 50 mg:** 0.056 mg/mL of USP Lamotrigine RS from *Standard stock solution* in *Buffer stage medium*

**For Tablets labeled to contain 100, 200, 250, and 300 mg:** (*L*/900) mg/mL of USP Lamotrigine RS, where *L* is the label claim in mg/Tablet, prepared as follows. Transfer a quantity of USP Lamotrigine RS to an appropriate volumetric flask and add 7.5% of the flask volume of methanol. Sonicate to dissolve, if necessary. Dilute with *Buffer stage medium* to volume.

**Sample solution:** At the times specified, pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Replace the portion removed with an equal volume of fresh *Acid stage medium* or *Buffer stage medium* at 37°.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 310 nm

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

**Column temperature:** 30°

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**Run time:** NLT 2 times the retention time of lamotrigine

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 1.5%

**Analysis**

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

Calculate the concentration ($C_i$) of lamotrigine ($C_9H_7Cl_2N_5$) in the sample withdrawn from the vessel at each time point ($i$):

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

$r_U$ = peak response of lamotrigine 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)

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point ($i$):

$$\text{Result}_1 = C_1 \times V_A \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V_B) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V_B) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$C_i$ = concentration of lamotrigine in the portion of sample withdrawn at time point $i$ (mg/mL)

$V_A$ = volume of the *Acid stage medium*, 700 mL

$V_B$ = volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

$V_S$ = volume of the *Sample solution* withdrawn at each time point and replaced with *Acid stage medium* or *Buffer stage medium* (mL)

**Tolerances:** See *Table 11*, *Table 12*, and *Table 13*.

**Table 11**

| Time Point (*i*) | Time (h) | Amount Dissolved (for Tablets labeled to contain 25 mg of lamotrigine) (%) | Amount Dissolved (for Tablets labeled to contain 50 mg of lamotrigine) (%) |
|---|---|---|---|
| 1 | 2 | NMT 10 | NMT 10 |
| 2 | 7 | 35–55 | 31–51 |
| 3 | 15 | NLT 80 | NLT 80 |

**Table 12**

| Time Point (*i*) | Time (h) | Amount Dissolved (for Tablets labeled to contain 100, 200, and 250 mg of lamotrigine) (%) |
|---|---|---|
| 1 | 2 | NMT 10 |
| 2 | 5 | 20–40 |
| 3 | 14 | NLT 80 |

**Table 13**

| Time Point (*i*) | Time (h) | Amount Dissolved (for Tablets labeled to contain 300 mg of lamotrigine) (%) |
|---|---|---|
| 1 | 2 | NMT 10 |
| 2 | 6 | 25–45 |
| 3 | 13 | NLT 80 |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

**Test 11:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 11*.

**Acid stage medium:** 0.01 N hydrochloric acid, deaerated, if necessary; 700 mL

**Buffer stage medium:** To 700 mL of *Acid stage medium*, add 200 mL of a pre-warmed solution containing 2.9 g of sodium phosphate, dibasic, anhydrous, 22.5 g of sodium dodecyl sulfate, and 4 mL of 5 N sodium hydroxide solution in 1 L of water. Adjust with 5 N sodium hydroxide or 5 N hydrochloric acid to a pH of 6.8; 900 mL.

**Apparatus 2:** 50 rpm with suitable sinkers

**Times:** 2 h in *Acid stage medium*; 6, 10, and 16 h in *Buffer stage medium*. The times in the *Buffer stage medium* include the time in the *Acid stage medium*.

**Acid stage standard solution**

**For Tablets labeled to contain 25 and 50 mg:** (*L*/2500) mg/mL of USP Lamotrigine RS in *Acid stage medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve, if necessary.

**For Tablets labeled to contain 100, 200, 250, and 300 mg:** (*L*/2000) mg/mL of USP Lamotrigine RS in *Acid stage medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve, if necessary.

**Buffer stage standard solution**

**For Tablets labeled to contain 25 and 50 mg:** (*L*/950) mg/mL of USP Lamotrigine RS in *Buffer stage medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve, if necessary.

**For Tablets labeled to contain 100, 200, 250, and 300 mg:** (*L*/900) mg/mL of USP Lamotrigine RS in *Buffer stage medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve, if necessary.

**Acid stage sample solution:** Pass through a suitable filter of 2.7-µm or 10-µm pore size.

**Buffer stage sample solution:** Pass through a suitable filter of 2.7-µm or 10-µm pore size.

**Instrumental conditions**

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

**Mode:** UV-Vis

**Analytical wavelength:** 270 nm

**Cell**

**For Tablets labeled to contain 25 and 50 mg:** 0.5-cm flow cell

**For Tablets labeled to contain 100, 200, 250, and 300 mg:** 0.1-cm flow cell

**Blank:** *Acid stage medium* or *Buffer stage medium*

**Analysis**

**Samples:** *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

Calculate the percentage of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at each time point (*i*):

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

$A_U$ = absorbance of the *Acid stage sample solution* or *Buffer stage sample solution*

$A_S$ = absorbance of the *Acid stage standard solution* or *Buffer stage standard solution*

$C_S$ = concentration of USP Lamotrigine RS in the *Acid stage standard solution* or *Buffer stage standard solution* (mg/mL)

$V$ = volume of the *Acid stage medium*, 700 mL or volume of the *Buffer stage medium*, 900 mL

$L$ = label claim (mg/Tablet)

**Tolerances:** See *Table 14*.

**Table 14**

| Time Point (*i*) | Time (h) | Amount Dissolved (for Tablets labeled to contain 25 and 200 mg of lamotrigine) (%) | Amount Dissolved (for Tablets labeled to contain 50 mg of lamotrigine) (%) | Amount Dissolved (for Tablets labeled to contain 100 mg of lamotrigine) (%) | Amount Dissolved (for Tablets labeled to contain 250 mg of lamotrigine) (%) | Amount Dissolved (for Tablets labeled to contain 300 mg of lamotrigine) (%) |
|---|---|---|---|---|---|---|
| 1 | 2 | NMT 30 | NMT 30 | NMT 30 | NMT 35 | NMT 30 |
| 2 | 6 | 38–63 | 38–63 | 38–63 | 40–65 | 34–54 |
| 3 | 10 | 65–90 | 70–95 | 65–95 | 69–94 | 60–83 |
| 4 | 16 | NLT 85 | NLT 85 | NLT 85 | NLT 85 | NLT 85 |

The percentages of the labeled amount of lamotrigine ($C_9H_7Cl_2N_5$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.▲ (RB 1-Jul-2024)

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

**IMPURITIES**

***Change to read:***

• **Organic Impurities**

**Mobile phase, Sample solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**Diluent 1:** Acetonitrile, methanol, and 0.1 N hydrochloric acid (10:20:70)

**Diluent 2:** Acetonitrile, methanol, and water (10:20:70)

**System suitability stock solution:** 0.025 mg/mL of USP Lamotrigine Related Compound C RS in *Diluent 1*

**System suitability solution:** 1.25 µg/mL of USP Lamotrigine Related Compound C RS and 0.25 mg/mL of USP Lamotrigine RS in *Diluent 2* prepared as follows. Transfer a suitable amount of USP Lamotrigine RS to a suitable volumetric flask. Transfer a suitable volume of *System suitability stock solution* to the flask. Dissolve and dilute with *Diluent 2* to volume.

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 10 between the lamotrigine and lamotrigine related compound C peaks

**Signal-to-noise ratio:** NLT 100 for lamotrigine related compound C

**Analysis**

**Sample:** *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

$r_U$ = response of each impurity from the *Sample solution*

$r_T$ = sum of all of the impurity peak responses and the lamotrigine peak response from the *Sample solution*

**Acceptance criteria:** See ▲*Table 15*.▲ (RB 1-Jul-2024) Disregard peaks less than 0.05%.

**▲Table 15▲** (RB 1-Jul-2024)

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Lamotrigine | 1.0 | — |
| Lamotrigine related compound C | 1.7 | 0.3 |
| Lamotrigine dimer[a] | 6.0 | 0.2 |
| Any individual unspecified degradation product | — | 0.2 |
| Total impurities | — | 0.5 |

[a] This is either lamotrigine *o*-dimer [$N^5$,$N^{5'}$-methylenebis(6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine)] or lamotrigine *p*-dimer [$N^3$,$N^{3'}$-methylenebis(6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine)].

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed containers. 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 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 EXTENDED-RELEASE TABLETS | Documentary Standards Support | SM42020 Small Molecules 4 |

**Chromatographic Database Information:** Chromatographic Database

**Most Recently Appeared In:**
Pharmacopeial Forum: Volume No. 46(6)

**Current DocID: GUID-E0FCE04D-38C3-47B6-B9DF-5C6642493D9D_10_en-US**

**DOI: https://doi.org/10.31003/USPNF_M5924_10_01**

**DOI ref: spadw**