

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

© 2025 USPC
Do not distribute

Lamotrigine Extended-Release Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-lamotrigine-ert-20240628.

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 acid](#) to volume. Pass a portion of the solution through a nylon filter of 0.45- μ m 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 $\times$ 15-cm; 3- μ m packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 5 μ L

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- μ m 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) of lamotrigine ($C_9H_7Cl_2N_3$) 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 ($C_9H_7Cl_2N_3$) 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 ($C_9H_7Cl_2N_3$) dissolved in the *Acid stage medium*:

Result = (r_U/r_S) × C_S × V_A × (1/L) × 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 (C₉H₇Cl₂N₅) in the sample withdrawn from the vessel at each time point (i) during the buffer stage:

Result_i = (r_U/r_S) × 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 (C₉H₇Cl₂N₅) dissolved at each time point (i) during the buffer stage:

Result₁ = [C₁ × V_B × (1/L) × 100] + (Q_A × V_S/V_A)

Result₂ = {[C₂ × V_B + (C₁ × V_S)] × (1/L) × 100} + (Q_A × V_S/V_A)

Result₃ = {[C₃ × V_B + [(C₂ + C₁) × V_S]] × (1/L) × 100} + (Q_A × V_S/V_A)

Result₄ = {[C₄ × V_B + [(C₃ + C₂ + C₁) × V_S]] × (1/L) × 100} + (Q_A × 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*.