

Venlafaxine Hydrochloride Extended-Release Capsules

Expert Committee: Small Molecules 4

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 4 Expert Committee has revised the Venlafaxine Hydrochloride Extended-Release Capsules monograph. The purpose of this revision is to add *Dissolution Tests 13* and *14* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test(s).

• *Dissolution Test 13* was validated using the InertSustain C8 brand of column with L7 packing. The typical retention time for venlafaxine is about 4.1 min.

• *Dissolution Test 14* was validated using the X-bridge C18 brand of column with L1 packing. The typical retention time for venlafaxine is about 4.1 min.

The Venlafaxine Hydrochloride Extended-Release Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Tsion Biliign, Principal Scientist (301-816-8286 or tb@usp.org).

Venlafaxine Hydrochloride Extended-Release Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-venlafaxine-hcl-erc-20250926.

DEFINITION

Venlafaxine Hydrochloride Extended-Release Capsules contain an amount of Venlafaxine Hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$).

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible Spectroscopy:** 197U

Wavelength range: 250–310 nm

Acceptance criteria: Meet the requirements

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

ASSAY

PROCEDURE

Mobile phase: [Acetonitrile](#), [triethylamine](#), and [water](#) (250:4:750). Adjust with [phosphoric acid](#) to a pH of 3.5.

Standard solution: 0.25 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Mobile phase*

Sample stock solution: Nominally 1.0 mg/mL of venlafaxine (from the contents of NLT 10 Capsules) prepared as follows. Transfer a weighed quantity of Capsule contents to a suitable volumetric flask. Add 8% of the flask volume of [acetonitrile](#), and shake for 40 min. Add 50% of flask volume of *Mobile phase*, and shake for an additional 20 min. Dilute with *Mobile phase* to volume. Pass a portion through a suitable filter of 0.45-µm pore size.

Sample solution: 0.25 mg/mL of venlafaxine (using the filtrate from the *Sample stock solution*) in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: 1.5 times the retention time of venlafaxine

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 venlafaxine ($C_{17}H_{27}NO_2$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#).

Test 1

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 3, 6, 16, and 24 h

Mobile phase: [Acetonitrile](#), [triethylamine](#), and [water](#) (450:4:550). Adjust with [phosphoric acid](#) to a pH of 3.5.

Standard stock solution: 0.1 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in [water](#)

Standard solution: 0.05 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in [acetonitrile](#), from the *Standard stock solution*

Sample stock solution: Pass a portion of the solution under test through a suitable filter.

Sample solution: *Sample stock solution* and [acetonitrile](#) (50:50)

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 274 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 60 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration, C_p , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times D \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution*, 2

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

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

$$\text{Result}_4 = \{[C_4 \times (V - (3 \times V_s))] + [(C_3 + C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

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

V = volume of *Medium*, 900 mL

V_s = volume of the *Sample solution* withdrawn from the *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 1](#).

Table 1

Time Point, i	Time (h)	Amount Dissolved
1	3	NMT 40%
2	6	35%–60%
3	16	60%–85%
4	24	NLT 75%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 2, 4, 8, 12, and 20 h

Capsule correction solution: Dissolve 6 empty Capsule shells in 900 mL of [water](#).

Blank: Dilute 150 mL of *Capsule correction solution* with [water](#) to 900 mL.

Standard solution: ($L/900$) mg/mL of [USP Venlafaxine Hydrochloride RS](#), where L is the label claim, in mg/Capsule, prepared as follows. To a weighed amount of the Standard equivalent to the sample claim, add *Capsule correction solution* to fill 17% of final flask volume. Dilute with [water](#) to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

Mode: UV

Detector: 274 nm

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—If necessary, the volume of *Medium* may be corrected for volumes removed from any previous sample time points.]

Calculate the concentration, C_i of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (A_U/A_S) \times C_S \times (M_{r1}/M_{r2})$$

A_U = absorbance from the *Sample solution*

A_S = absorbance from the *Standard solution*

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

$$\text{Result}_3 = \{[C_3 \times (V - (2 \times V_s))] + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

$$\text{Result}_i = \{[C_i \times (V - ([i - 1] \times V_s))] + [(C_{i-1} + C_{i-2} + \dots + C_1) \times V_s]\} \times (1/L) \times 100$$

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

V = volume of *Medium*, 900 mL

V_s = volume of the *Sample solution* withdrawn from the *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 2](#).

Table 2

Time Point, i	Time (h)	Amount Dissolved
1	2	10%–30%
2	4	33%–53%
3	8	58%–78%
4	12	68%–88%
5	20	NLT 80%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Times: 4, 8, and 16 h

Buffer: Dissolve 1.4 g of [monobasic potassium phosphate](#) in 1 L of [water](#). Add 5 mL of [triethylamine](#), and adjust with [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (35:65)

Standard stock solution: 0.9 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium*

Standard solution: ($L/750$) mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium* from the *Standard stock solution*, where L is the label claim, in mg/Capsule. Pass a portion through a suitable filter of 0.45- μ m pore size.

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of fresh *Medium*. Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L1](#)

Flow rate: 1 mL/min

Column temperature: 30°

Injection volume: 10 μ L

Run time: 2 times the retention time of venlafaxine

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 concentration, C_r , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_s = peak response from the *Standard solution*

C_s = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

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

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

V = volume of *Medium*, 900 mL

V_s = volume of the *Sample solution* withdrawn from the vessel and replaced with *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 3](#).

Table 3

Time Point, i	Time (h)	Amount Dissolved
1	4	35%–55%
2	8	65%–90%
3	16	NLT 85%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 2, 4, 8, 12, and 20 h

Solution A: Dilute 10 mL of [phosphoric acid](#) with [water](#) to 100 mL.

Buffer: 11.4 g/L of [ammonium dihydrogen phosphate](#) in [water](#)

Mobile phase: [Acetonitrile](#) and *Buffer* (35:65). Adjust with *Solution A* to a pH of 4.4.

Standard stock solution: 0.24 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium*. Sonication may be used to aid in dissolution.

Standard solution: See [Table 4](#) for the concentration of [USP Venlafaxine Hydrochloride RS](#) in *Medium* from the *Standard stock solution*. Using a glass syringe, pass a portion through a suitable filter of 0.45- μ m pore size.

Table 4

Label Claim (L)	Standard Solution (mg/mL)
37.5	0.05
75	0.1
150	0.1

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of fresh *Medium*. For Capsules that are labeled to contain 150 mg of venlafaxine, dilute this solution with an equal volume of *Medium*. Using a glass syringe, pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size.

Chromatographic system(See [Chromatography \(621\), System Suitability.](#))**Mode:** LC**Detector:** UV 225 nm**Column:** 4.6-mm × 25-cm; 5-μm packing [L7](#)**Flow rate:** 1.2 mL/min**Injection volume:** 20 μL**Run time:** 2 times the retention time of venlafaxine**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 concentration, C_i , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times D \times (M_{r1}/M_{r2})$$

 r_U = peak response from the *Sample solution* r_S = peak response from the *Standard solution* C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL) D = dilution factor for the *Sample solution*, 2 for Capsules labeled to contain 150 mg of venlafaxine; 1 for Capsules labeled to contain 37.5 or 75 mg of venlafaxine M_{r1} = molecular weight of venlafaxine, 277.40

1

 M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

2

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

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

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

$$\text{Result}_5 = \{[C_5 \times V] + [(C_4 + C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

 C_i = concentration of venlafaxine in *Medium* in the portion of sample withdrawn at time point i (mg/mL) V = volume of *Medium*, 900 mL V_S = volume of the *Sample solution* withdrawn from the vessel and replaced with *Medium* (mL) L = label claim (mg/Capsule)**Tolerances:** See [Table 5](#).**Table 5**

Time Point, i	Time (h)	Amount Dissolved
1	2	10%–30%
2	4	35%–55%
3	8	60%–80%

Time Point, <i>i</i>	Time (h)	Amount Dissolved
4	12	NLT 70%
5	20	NLT 85%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 2, 5, 8, and 20 h

Buffer: 11.4 g/L of [monobasic ammonium phosphate](#) in [water](#). Adjust with dilute [phosphoric acid](#) (1 in 10) or dilute ammonia solution (1 in 10) to a pH of 4.4.

Mobile phase: [Acetonitrile](#) and *Buffer* (25.5: 74.5)

Standard solution: ($L/900$) mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium*, where L is the label claim, in mg/Capsule

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of fresh *Medium*. Pass a portion of the withdrawn sample through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L7](#)

Flow rate: 1 mL/min

Injection volume: 10 μ L

Run time: 1.5 times the retention time of venlafaxine

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 concentration, C_i , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

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

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

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

V = volume of *Medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn from the vessel and replaced with *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 6](#).

Table 6

Time Point, <i>i</i>	Time (h)	Amount Dissolved
1	2	NMT 20%
2	5	35%–55%
3	8	60%–80%
4	20	NLT 80%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: [Water](#); 900 mL, deaerated

Apparatus 1: 100 rpm

Times: 2, 4, 8, 12, and 24 h

Buffer: 10 mL/L of [triethylamine](#) in [water](#) adjusted with [phosphoric acid](#) to a pH of 3.0

Mobile phase: [Acetonitrile](#) and *Buffer* (20:80)

Standard solution: ($L/900$) mg/mL of venlafaxine from [USP Venlafaxine Hydrochloride RS](#) in *Medium*, where L is the label claim, in mg/Capsule

Sample solution: Centrifuge a portion of the solution under test.

Chromatographic system

(See [Chromatography <621>](#), [System Suitability](#).)

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Flow rate: 2.5 mL/min

Injection volume: 20 μL

Run time: 1.5 times the retention time of venlafaxine

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 concentration, C_i , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

$$\text{Result}_3 = \{[C_3 \times (V - (2 \times V_s))] + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{[C_4 \times (V - (3 \times V_s))] + [(C_3 + C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

$$\text{Result}_5 = \{[C_5 \times (V - (4 \times V_s))] + [(C_4 + C_3 + C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

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

V = volume of *Medium*, 900 mL

V_s = volume of the *Sample solution* withdrawn from the *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 7](#).

Table 7

Time Point, i	Time (h)	Amount Dissolved
1	2	NMT 30%
2	4	40%–60%
3	8	60%–80%
4	12	70%–90%
5	24	NLT 85%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 2, 4, 8, 12, and 20 h

Buffer: 1.7 g/L of [dibasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) (1 in 10) to a pH of 7.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (80:20)

Standard solution: ($L/900$) mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium*, where L is the label claim, in mg/Capsule

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of fresh *Medium*. Pass a portion of the withdrawn sample through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L1](#)

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: 2 times the retention time of venlafaxine

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 concentration, C_i of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_s = peak response from the *Standard solution*

C_s = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

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

$$\text{Result}_4 = \{[C_4 \times V] + [(C_3 + C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

$$\text{Result}_5 = \{[C_5 \times V] + [(C_4 + C_3 + C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

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

V = volume of *Medium*, 900 mL

V_s = volume of the *Sample solution* withdrawn from the vessel and replaced with *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 8](#).

Table 8

Time Point, i	Time (h)	Amount Dissolved
1	2	NMT 10%
2	4	NMT 30%
3	8	40%–70%
4	12	60%–90%
5	20	NLT 80%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

Test 8: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 8*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 1, 6, 16, and 24 h

Diluent: [Acetonitrile](#) and [water](#) (30:70)

Buffer: Dissolve 8.9 g of [dibasic sodium phosphate dihydrate](#) and 2.5 g of [sodium 1-octanesulfonate](#) in 1 L of [water](#). Adjust with 10% [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (32:68)

Standard stock solution: 0.9 mg/mL of [USP Venlafaxine Hydrochloride RS](#) prepared as follows. Dissolve the weighed amount of the Standard first in [acetonitrile](#) using 20% of flask volume. Sonicate to dissolve, and dilute with *Diluent* to volume.

Standard solution: (L/900) mg/mL of [USP Venlafaxine Hydrochloride RS](#) from *Standard stock solution* in *Diluent*, where L is the label claim, in mg/Capsule

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of fresh *Medium*. Pass a portion of the withdrawn sample through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography <621>. System Suitability](#).)

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 1.5 mL/min

Injection volume: 20 μL

Run time: 1.7 times the retention time of venlafaxine

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 concentration, C_i , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point i :

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point i :

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

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

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

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

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

V = volume of *Medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn from the vessel and replaced with *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 9](#).

Table 9

Time Point, i	Time (h)	Amount Dissolved
1	1	NMT 25%
2	6	50%–70%
3	16	70%–95%
4	24	NLT 80%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: [Water](#); 900 mL, degassed

Apparatus 1: 100 rpm

Times: 2, 4, 8, 12, and 20 h

Buffer: Dissolve 3.4 g of [monobasic potassium phosphate](#) in 700 mL of [water](#). Add 5 mL of [triethylamine](#). Adjust with [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (30:70)

Standard stock solution: 1.6 mg/mL of [USP Venlafaxine Hydrochloride RS](#) prepared as follows. Dissolve a weighed amount of the Standard first in [methanol](#) using 20% of flask volume. Sonicate to dissolve, and dilute with [water](#) to volume.

Standard solution: (L/900) mg/mL of [USP Venlafaxine Hydrochloride RS](#) from the *Standard stock solution* in *Medium*, where L is the label claim, in mg/Capsule

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace it with an equal volume of fresh *Medium*. Pass a portion of the withdrawn sample through a suitable filter of 0.45-µm pore size.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: 2 times the retention time of venlafaxine

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 concentration, C_p , of venlafaxine ($C_{17}H_{27}NO_2$) in *Medium* (mg/mL) after time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point (i):

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

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

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

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

$$\text{Result}_5 = \{[C_5 \times V] + [(C_4 + C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of venlafaxine in *Medium* in the portion of sample withdrawn at the specified time point i (mg/mL)

V = volume of *Medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn from the vessel and replaced with *Medium* (mL)

L = label claim (mg/Capsule)

Tolerances: See [Table 10](#).

Table 10

Time Point, <i>i</i>	Time (h)	Amount Dissolved
1	2	NMT 25%
2	4	30%–50%
3	8	55%–80%
4	12	65%–90%
5	20	NLT 80%

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 2, 4, and 20 h

Buffer: Add 5 mL of [triethylamine](#) to 1000 mL of [water](#) and mix. Adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (20:80)

Standard stock solution: 1 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in [methanol](#). Sonicate to dissolve, if necessary.

Standard solution: 0.05 mg/mL of [USP Venlafaxine Hydrochloride RS](#) from the *Standard stock solution* in *Medium*

Sample solution: At the specified times, withdraw a known volume of the solution from the dissolution vessel. Dilute with *Medium*, if necessary, to a concentration that is similar to that of the *Standard solution*. Pass a portion of solution through a suitable filter of 0.45- μ m pore size, discarding the first 5 mL of filtrate, and use the filtrate. Replace the portion removed with the same volume of *Medium*.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Column temperature: 50°

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: NLT 2 times the retention time of venlafaxine

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 concentration (C_i) of venlafaxine ($C_{17}H_{27}NO_2$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (r_U/r_S) \times C_S \times D \times (M_{r1}/M_{r2})$$

r_U = peak response of venlafaxine from the *Sample solution*

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

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

D = dilution factor of the *Sample solution*, if applicable

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point (*i*):

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_s = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See [Table 11](#).

Table 11

Time Point (i)	Time (h)	Amount Dissolved (%)
1	2	NMT 30
2	4	37–57
3	20	NLT 80

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) 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*.

Medium: pH 6.8, 0.05 M phosphate buffer (Dissolve 6.8 g of [monobasic potassium phosphate](#) and 0.9 g of [sodium hydroxide](#) in 1 L of [water](#).

Adjust with dilute [phosphoric acid](#) in [water](#) or dilute [sodium hydroxide](#) in [water](#) to a pH of 6.8.; 900 mL

Apparatus 1: 100 rpm

Times: 2, 8, and 24 h

Mobile phase: [Acetonitrile](#) and [water](#) (45:55). Add 4 mL of [triethylamine](#) to each liter of the mixture. Adjust with [phosphoric acid](#) to a pH of 3.5.

Standard stock solution: 0.1 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium*

Standard solution: 0.05 mg/mL of [USP Venlafaxine Hydrochloride RS](#) from *Standard stock solution* in [acetonitrile](#)

Sample solution: At the specified times, withdraw a known volume of the solution from the dissolution vessel. Pass a portion of solution through a suitable filter of 0.45- μ m pore size, discarding the first 2 mL of filtrate. Transfer a suitable volume of the filtrate, equal to one-half of the flask volume, to an appropriate volumetric flask. Dilute with [acetonitrile](#) to volume.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 274 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 60 μ L

Run time: NLT 2 times the retention time of venlafaxine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of venlafaxine ($C_{17}H_{27}NO_2$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times D \times (M_{r1}/M_{r2})$$

r_U = peak response of venlafaxine from the *Sample solution*

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

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

D = dilution factor of the *Sample solution*, 2

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point (i):

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

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

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_s)]] + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_s = volume of the *Sample solution* withdrawn at each time point from the *Medium* (mL)

Tolerances: See [Table 12](#).

Table 12

Time Point (i)	Time (h)	Amount Dissolved (%)
1	2	NMT 25
2	8	50–70
3	24	NLT 80

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 12: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 12*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 2, 8, and 20 h

Mobile phase: [Acetonitrile](#), [water](#), and [triethylamine](#) (25: 75: 0.4). Adjust with [phosphoric acid](#) to a pH of 3.5.

Standard solution: 0.05 mg/mL of [USP Venlafaxine Hydrochloride RS](#) in *Medium*. Sonicate to dissolve, if necessary.

Sample stock solution: At the times specified, withdraw 10 mL of the solution under test and replace with 10 mL of *Medium*. Pass the solution under test through a suitable filter of 0.45- μ m pore size, discarding the first 3 mL of filtrate.

Sample solution

For Capsules labeled to contain 37.5 mg: Use the filtrate.

For Capsules labeled to contain 75 mg: Dilute the filtrate with *Medium* (1:2).

For Capsules labeled to contain 150 mg: Dilute the filtrate with *Medium* (1:4).

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 274 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 30 μ L

Run time: NLT 1.7 times the retention time of venlafaxine

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 concentration (C_i) of venlafaxine ($C_{17}H_{27}NO_2$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times D \times (M_{r1}/M_{r2})$$

r_U = peak response of venlafaxine from the *Sample solution*

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

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution*, 1 for 37.5 mg Capsules, 2 for 75 mg Capsules, or 4 for 150 mg Capsules

M_{r1} = molecular weight of venlafaxine, 277.41

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.87

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point (i):

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

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

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

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See [Table 13](#).

Table 13

Time Point (i)	Time (h)	Amount Dissolved (%)
1	2	NMT 30
2	8	60–80
3	20	NLT 80

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

▲ **Test 13:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 13*.

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Times: 1, 4, and 24 h

Buffer: Dissolve 3.4 g [potassium phosphate, monobasic](#) in 1000 mL of [water](#) and adjust with dilute [phosphoric acid](#) to a pH of 2.7.

Mobile phase: [Acetonitrile](#) and *Buffer* (35:65)

Standard solution: ($L/900$) mg/mL of venlafaxine from [USP Venlafaxine Hydrochloride RS](#) in *Medium*, where L is the label claim of venlafaxine in mg/Capsule. Sonicate to dissolve, if necessary.

Sample solution: At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of *Medium*. Pass a portion of the withdrawn sample through a suitable filter of 0.45- μ m pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

(See [Chromatography <621>](#), [System Suitability](#).)

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm $\times$ 25-cm; 5- μ m packing [L7](#)

Column temperature: 45°

Flow rate: 1.2 mL/min

Injection volume: 10 μ L

Run time: NLT 2.4 times the retention time of venlafaxine

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 concentration (C_i) of venlafaxine ($C_{17}H_{27}NO_2$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

 r_U = peak response of venlafaxine from the *Sample solution* r_S = peak response of venlafaxine from the *Standard solution* C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL) M_{r1} = molecular weight of venlafaxine, 277.41 M_{r2} = molecular weight of venlafaxine hydrochloride, 313.87Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point (i):

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

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

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

 C_i = concentration of venlafaxine in the portion of sample withdrawn at time point i (mg/mL) V = volume of *Medium*, 900 mL L = label claim (mg/Capsule) V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)**Tolerances:** See [Table 14](#).**Table 14**

Time Point (i)	Time (h)	Amount Dissolved (%)
1	1	NMT 20
2	4	33–70
3	24	NLT 80

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

Test 14: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 14*.**Medium:** pH 6.8 phosphate buffer (Combine 250 mL of 0.2 M [potassium phosphate, monobasic](#) solution and 112 mL of 0.2 M [sodium hydroxide](#) solution in a 1000-mL volumetric flask. Dilute with [water](#) to volume.); 500 mL**Apparatus 1:** 75 rpm**Times:** 2, 5, 10, and 24 h**Buffer:** Dissolve 3.4 g of [potassium phosphate, monobasic](#) in 1000 mL of [water](#). Add 5 mL of [triethylamine](#) and adjust with [phosphoric acid](#) to a pH of 3.0.**Mobile phase:** [Acetonitrile](#) and *Buffer* (30:70)**Standard solution:** ($L/500$) mg/mL of venlafaxine from [USP Venlafaxine Hydrochloride RS](#) in *Medium*, where L is the label claim of venlafaxine in mg/Capsule. Sonicate to dissolve, if necessary.**Sample solution:** At the end of the specified time interval, withdraw a known volume of the solution from the dissolution vessel, and replace with an equal volume of *Medium*. Pass a portion of the withdrawn sample through a suitable filter of 0.45- μ m pore size, discarding an

appropriate volume of filtrate so that a consistent result can be obtained. [NOTE—An in-line filter within an autosampler may be a suitable filter.]

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 274 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 1.2 mL/min

Injection volume: 20 μL

Run time: NLT 1.7 times the retention time of venlafaxine

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 concentration (C_i) of venlafaxine ($C_{17}H_{27}NO_2$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response of venlafaxine from the *Sample solution*

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

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of venlafaxine, 277.41

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.87

Calculate the percentage of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at each time point (i):

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

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

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

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

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See [Table 15](#).

Table 15

Time Point (i)	Time (h)	Amount Dissolved (%)
1	2	NMT 30
2	5	42–62
3	10	63–83
4	24	NLT 80

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_2$) dissolved at the times specified conform to [Dissolution \(711\)](#),

[Acceptance Table 2](#). ▲ (RB 1-Oct-2025)

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Mobile phase, Standard solution, and Sample solution: Proceed as directed in the Assay.

System suitability solution: 0.25 µg/mL of [USP Venlafaxine Related Compound A RS](#) in the *Standard solution*

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 226 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: 4 times the retention time of venlafaxine

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for venlafaxine related compound A and venlafaxine are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between venlafaxine related compound A and venlafaxine

Tailing factor: NMT 2.0 for venlafaxine

Relative standard deviation: NMT 5.0% for venlafaxine

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

C_S = concentration of [USP Venlafaxine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of venlafaxine, 277.40

M_{r2} = molecular weight of venlafaxine hydrochloride, 313.86

Acceptance criteria

Individual impurities: NMT 0.2%

Total impurities: NMT 0.5%

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 Venlafaxine Hydrochloride RS](#)

[USP Venlafaxine Related Compound A RS](#)

1-(1-(4-Methoxyphenyl)-2-(methylamino)ethyl)cyclohexanol hydrochloride.

$C_{16}H_{25}NO_2 \cdot HCl$ 299.84

Loading Auxiliary Information...

Chromatographic Database Information: [Chromatographic Database](#)

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