Venlafaxine Hydrochloride Extended-Release Capsules

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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 for the revision is to add *Dissolution Tests 10* and *11* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution tests.

- *Dissolution Test 10* was validated using the Zorbax SB-C18 brand of column with L1 packing. The typical retention time for venlafaxine is about 5 min.

- *Dissolution Test 11* was validated using the Zorbax SB-C18 brand of column with L1 packing. The typical retention time for venlafaxine is about 3 min.

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

Should you have any questions, please contact Nicholas Garito Jr., Sr. Scientific Liaison (301-816-8321 or njg@usp.org).
Venlafaxine Hydrochloride Extended-Release Capsules

**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 (C₁₇H₂₇NO₂).

**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 (C₁₇H₂₇NO₂) in the portion of Capsules taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{M_{r1}}{M_{r2}} \right) \times 100
\]

- \( r_U \) = 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)
\[ M_{r1} \text{ = molecular weight of venlafaxine, } 277.40 \]
\[ M_{r2} \text{ = molecular weight of venlafaxine hydrochloride, } 313.86 \]

**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, \( C_r \), of venlafaxine \((C_{17}H_{27}NO_3)\) in Medium (mg/mL) after time point \( i \):

  \[
  \text{Result}_i = \frac{r_U}{r_S} \times C_S \times D \times \left( \frac{M_{r1}}{M_{r2}} \right)
  \]

  \( r_U \) = 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 \((C_{17}H_{27}NO_3)\) dissolved at each time point \( i \):

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

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

  \[
  \text{Result}_3 = \{(C_3 \times (V - (2 \times V_S))) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100
  \]
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>
<thead>
<tr>
<th>Time Point, $i$</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>NMT 40%</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>35%–60%</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>60%–85%</td>
</tr>
<tr>
<td>4</td>
<td>24</td>
<td>NLT 75%</td>
</tr>
</tbody>
</table>

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

$$ Result_i = \left( \frac{A_U}{A_S} \right) \times C_S \times \left( \frac{M_{r1}}{M_{r2}} \right) $$

- $A_U$ = absorbance (ERR 1-Mar-2021) from the Sample solution
- $A_S$ = absorbance (ERR 1-Mar-2021) 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 \((\text{C}_1\text{H}_2\text{N}_2\text{O}_2)\) dissolved at each time point \(i\):

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

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

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

\[
\text{Result}_i = \left\{ [C_i \times (V - ([i - 1] \times V_S))] + [(C_{i-1} + C_{i-2} + ... + C_1) \times V_S] \right\} \times (1/L) \times 100
\]

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

\(V\) = volume of \(\text{Medium}\), 900 mL

\(V_S\) = volume of the \(\text{Sample solution}\) withdrawn from the \(\text{Medium}\) (mL)

\(L\) = label claim (mg/Capsule)

**Tolerances:** See *Table 2*.

<table>
<thead>
<tr>
<th>Time Point, (i)</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>10%-30%</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>33%-53%</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>58%-78%</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>68%-88%</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of venlafaxine \((\text{C}_1\text{H}_2\text{N}_2\text{O}_2)\) 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-µm 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-µm pore size.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 225 nm

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

**Flow rate:** 1 mL/min
Column temperature: 30°
Injection volume: 10 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 \( i \):

\[
\text{Result}_i = \left( \frac{r_i}{r_S} \right) \times C_S \times \left( \frac{M_{r1}}{M_{r2}} \right)
\]

- \( r_U \) = 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 \( i \):

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

\[
\text{Result}_2 = \left\{ [C_S \times V] + [C_i \times V_S] \right\} \times (1/L) \times 100
\]

\[
\text{Result}_3 = \left\{ [(C_S \times V) + (C_i \times V_S)] + (C_i \times V_S) \right\} \times (1/L) \times 100
\]

- \( C_i \) = 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>
<thead>
<tr>
<th>Time Point, ( i )</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>35%–55%</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>65%–90%</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>NLT 85%</td>
</tr>
</tbody>
</table>

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-µm pore size.

<table>
<thead>
<tr>
<th>Label Claim (L)</th>
<th>Standard Solution (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.5</td>
<td>0.05</td>
</tr>
<tr>
<td>75</td>
<td>0.1</td>
</tr>
<tr>
<td>150</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**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-µm 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 ($C_{17}H_{27}NO_3$) in *Medium* (mg/mL) after time point $i$:

$$\text{Result}_i = \frac{r_U}{r_S} \times C_S \times D \times \frac{M_{1}}{M_{2}}$$

- $r_U$ = 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
- $M_{1}$ = molecular weight of venlafaxine, 277.40
- $M_{2}$ = molecular weight of venlafaxine hydrochloride, 313.86
Calculate the percentage of the labeled amount of venlafaxine \((\text{C}_17\text{H}_{27}\text{NO}_2)\) dissolved at each time point \(i\):

\[
\text{Result}_1 = C_1 \times V \times \left(\frac{1}{L}\right) \times 100
\]

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

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

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

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

\(C_i\) = 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>
<thead>
<tr>
<th>Time Point, (i)</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>10%–30%</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>35%–55%</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>60%–80%</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>NLT 70%</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>NLT 85%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of venlafaxine \((\text{C}_17\text{H}_{27}\text{NO}_2)\) 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-µm pore size.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 225 nm

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

**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 2.0%

Analysis
Samples: Standard solution and Sample solution

Calculate the concentration, $C_i$, of venlafaxine ($C_{17}H_{27}NO_3$) in Medium (mg/mL) after time point $i$:

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

$r_U$ = 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 ($C_{17}H_{27}NO_3$) dissolved at each time point $i$:

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

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

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

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

$C_i$ = 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

<table>
<thead>
<tr>
<th>Time Point, $i$</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 20%</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>35%–55%</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>60%–80%</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of venlafaxine ($C_{17}H_{27}NO_3$) 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 \( (C_{17}H_{27}NO_3) \) in Medium (mg/mL) after time point \( i \):
\[
\text{Result}_i = \left( \frac{r_U}{r_S} \right) \times C_S \times \left( \frac{M_{r1}}{M_{r2}} \right)
\]
\( r_U \) = 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 \( (C_{17}H_{27}NO_3) \) dissolved at each time point \( i \):
\[
\text{Result}_1 = C_i \times V \times (1/L) \times 100
\]
\[
\text{Result}_2 = \left\{ [C_2 \times (V - V_S)] + [C_1 \times V_S] \right\} \times (1/L) \times 100
\]
\[
\text{Result}_3 = \left\{ [C_3 \times (V - (2 \times V_S))] + [(C_2 + C_1) \times V_S] \right\} \times (1/L) \times 100
\]
\[
\text{Result}_4 = \left\{ [C_4 \times (V - (3 \times V_S))] + [(C_3 + C_2 + C_1) \times V_S] \right\} \times (1/L) \times 100
\]
\[
\text{Result}_5 = \left\{ [(C_5 \times (V - (4 \times V_S))] + [(C_4 + C_3 + C_2 + C_1) \times V_S] \right\} \times (1/L) \times 100
\]
\( C_i \) = 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**

<table>
<thead>
<tr>
<th>Time Point, <em>i</em></th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 30%</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>40%–60%</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>60%–80%</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>70%–90%</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>NLT 85%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of venlafaxine (C\textsubscript{17}H\textsubscript{27}NO\textsubscript{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-µm pore size.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 227 nm

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

**Column temperature:** 45°

**Flow rate:** 1.5 mL/min

**Injection volume:** 10 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\textsubscript{17}H\textsubscript{27}NO\textsubscript{2}) in Medium (mg/mL) after time point \( i \):

\[
\text{Result}_i = \left( \frac{r_U}{r_S} \right) \times C_S \times \left( \frac{M_r}{M_i} \right)
\]

- \( r_U \) = 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)
Calculate the percentage of the labeled amount of venlafaxine (C₁₇H₂₇NO₄) dissolved at each time point $i$:

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

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

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

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

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

$C_i$ = 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

<table>
<thead>
<tr>
<th>Time Point, $i$</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 10%</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>NMT 30%</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>40%-70%</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>60%-90%</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of venlafaxine (C₁₇H₂₇NO₄) 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-µm 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 ($C_{17}H_{27}NO_3$) in Medium (mg/mL) after time point $i$:

\[
\text{Result}_i = \left(\frac{r_i}{r_S}\right) \times C_S \times \left(\frac{M_{r1}}{M_{r2}}\right)
\]

- $r_U$ = 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 ($C_{17}H_{27}NO_3$) dissolved at each time point $i$:

\[
\text{Result}_1 = C_I \times V \times (1/L) \times 100
\]

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

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

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

- $C_I$ = 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**

<table>
<thead>
<tr>
<th>Time Point, $i$</th>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>NMT 25%</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>50%–70%</td>
</tr>
</tbody>
</table>
The percentages of the labeled amount of venlafaxine \((C_{17}H_{27}NO_2)\) dissolved at the times specified conform to

\textit{Dissolution (711), Acceptance Table 2.}

**Test 9:** If the product complies with this test, the labeling indicates that it meets USP \textit{Dissolution Test 9}.  
**Medium:** \textit{Water}; 900 mL, degassed  
**Apparatus 1:** 100 rpm  
**Times:** 2, 4, 8, 12, and 20 h  
**Buffer:** Dissolve 3.4 g of \textit{monobasic potassium phosphate} in 700 mL of \textit{water}. Add 5 mL of \textit{triethylamine}. Adjust with \textit{phosphoric acid} to a pH of 3.0.  
**Mobile phase:** \textit{Acetonitrile} and \textit{Buffer} (30:70)  
**Standard stock solution:** 1.6 mg/mL of \textit{USP Venlafaxine Hydrochloride RS} prepared as follows. Dissolve a weighed amount of the Standard first in \textit{methanol} using 20% of flask volume. Sonicate to dissolve, and dilute with \textit{water} to volume.  
**Standard solution:** \((L/900)\) mg/mL of \textit{USP Venlafaxine Hydrochloride RS} from the \textit{Standard stock solution} in \textit{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 \textit{Medium}. Pass a portion of the withdrawn sample through a suitable filter of 0.45-µm pore size.  

**Chromatographic system**  
(See \textit{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:** \textit{Standard solution}  
**Suitability requirements**  
- Tailing factor: NMT 2.0  
- Relative standard deviation: NMT 2.0%  

**Analysis**  
**Samples:** \textit{Standard solution} and \textit{Sample solution}  
Calculate the concentration, \(C_p\) of venlafaxine \((C_{17}H_{27}NO_2)\) in \textit{Medium} (mg/mL) after time point \((i)\):

\[
\text{Result}_i = \left(\frac{r_U}{r_S}\right) \times C_S \times \left(\frac{M_r1}{M_r2}\right)
\]

- \(r_U\) = peak response from the \textit{Sample solution}  
- \(r_S\) = peak response from the \textit{Standard solution}  
- \(C_S\) = concentration of \textit{USP Venlafaxine Hydrochloride RS} in the \textit{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 \((i)\):
Result_1 = C_i \times V \times (1/L) \times 100

Result_2 = [(C_2 \times V) + (C_I \times V_S)] \times (1/L) \times 100

Result_3 = \{[C_3 \times V] + [(C_2 + C_I) \times V_S]\} \times (1/L) \times 100

Result_4 = \{[C_4 \times V] + [(C_3 + C_2 + C_I) \times V_S]\} \times (1/L) \times 100

Result_5 = \{[C_5 \times V] + [(C_4 + C_3 + C_2 + C_I) \times V_S]\} \times (1/L) \times 100

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

V = \text{volume of Medium, 900 mL}

V_S = \text{volume of the Sample solution withdrawn from the vessel and replaced with Medium (mL)}

L = \text{label claim (mg/Capsule)}

**Tolerances:** See Table 10.

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

The percentages of the labeled amount of venlafaxine \( (C_{17}H_{27}NO_2) \) dissolved at the times specified conform to \textit{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-µm 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 × 15-cm; 5-µm packing L1
**Column temperature:** 50°
**Flow rate:** 1.5 mL/min
**Injection volume:** 10 µL
**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 ($i$):

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

- $r_U$ = 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 ($i$):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$
$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$
$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

- $C_i$ = 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>
<thead>
<tr>
<th>Time Point ($i$)</th>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 30</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>37–57</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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-µm 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

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

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) of venlafaxine (C_{17}H_{27}NO_{2}) in the sample withdrawn from the vessel at each time point (i):

\[
\text{Result}_i = \left( \frac{r_i}{r_S} \right) \times C_S \times D \times \left( \frac{M_{r1}}{M_{r2}} \right)
\]

\[r_U\] = 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):

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

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

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

\[C_i\] = concentration of venlafaxine in the portion of sample withdrawn at time point i (mg/mL)
\[ V = \text{volume of } Medium, \ 900 \ mL \]
\[ L = \text{label claim (mg/Capsule)} \]
\[ V_S = \text{volume of the Sample solution withdrawn at each time point from the Medium (mL)} \]

**Tolerances:** See Table 12.

<table>
<thead>
<tr>
<th>Time Point ((i))</th>
<th>Time ((h))</th>
<th>Amount Dissolved ((%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 25</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>50–70</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of venlafaxine \(\text{C}_{17}\text{H}_{27}\text{NO}_2\) dissolved at the times specified conform to *Dissolution (711), Acceptance Table 2.* (RB 1-Mar-2021)

**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:

\[
\text{Result} = \frac{r_U}{r_S} \times \frac{C_S}{C_U} \times \frac{M_1}{M_2} \times 100
\]

- \(r_U\) = 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)
\[ M_{r1} = \text{molecular weight of venlafaxine, 277.40} \]

\[ M_{r2} = \text{molecular weight of venlafaxine hydrochloride, 313.86} \]

**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.

\[ \text{C}_{16} \text{H}_{25} \text{NO}_2 \cdot \text{HCl} \quad 299.84 \]

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**Page Information:**

Not Applicable

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