Verapamil Hydrochloride Extended-Release Capsules

DEFINITION
Verapamil Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of verapamil hydrochloride (C_{27}H_{38}N_{2}O_{4} · HCl).

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
Solution A: 0.01 N sodium acetate in water containing 33 mL/L of glacial acetic acid
Mobile phase: Acetonitrile, 2-aminoheptane, and Solution A (60:1:140)
System suitability solution: 0.12 mg/mL of USP Verapamil Hydrochloride RS and 0.1 mg/mL of USP Verapamil Related Compound B RS in Mobile phase
Standard solution: 0.12 mg/mL of USP Verapamil Hydrochloride RS in Mobile phase
Sample stock solution: Nominally 1.2 mg/mL of verapamil hydrochloride prepared as follows. Transfer an equivalent to 240 mg of verapamil hydrochloride, from the pool of Capsule contents (NLT 20), to a 200-mL volumetric flask. Add about 150 mL of Mobile phase (prewarm the Mobile phase to 45 °C). While sonicating, stir for 1 h, cool to room temperature, dilute with Mobile phase to volume, and mix. Centrifuge a portion for 20 min, and use the supernatant.
Sample solution: Nominally 0.12 mg/mL of verapamil hydrochloride in Mobile phase from the Sample stock solution

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 278 nm
Column: 4.6-mm × 25-cm; 5-μm packing L1
Flow rate: 1.2 mL/min
Injection volume: 20 μL

System suitability
Samples: System suitability solution and Standard solution
Suitability requirements
Resolution: NLT 1.5 between verapamil and verapamil related compound B
Relative standard deviation: NMT 2.0%, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of verapamil hydrochloride (C_{27}H_{38}N_{2}O_{4} · HCl) dissolved at each time point:
\[ Q_2 = (r_0/r_3) \times (C_4/L) \times V \times 100 \]
\[ Q_4 = (Q_2 \times V_{51}/V) + [(r_6/r_3) \times (C_4/L) \times (V - V_{51}) \times 100] \]
\[ Q_6 = (Q_4 \times V_{52}/V) + [(r_6/r_3) \times (C_4/L) \times (V - V_{52} - V_{51}) + [(r_6/r_3) \times (C_4/L) \times (V - V_{51} - V_{52} - V_{53})] \times 100] \]
\[ Q_{24} = (Q_2 \times V_{51}/V) + [(r_6/r_3) \times (C_4/L) \times (V - V_{51} - V_{52} - V_{53})] + [(r_6/r_3) \times (C_4/L) \times (V - V_{51} + V_{52} + V_{53})] \times 100] \]

Acceptance criteria: 90.0%–110.0%

CHANGE TO READ:

• DISSOLUTION (711)
  • Test 1: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 1.
    • ND 1-Jun-2013

Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 2: 100 rpm
Use a wire helix as necessary.
Times: 2, 4, 8, and 24 h
Solution A and Mobile phase: Proceed as directed in the Assay.
System suitability solution: 0.25 mg/mL of USP Verapamil Hydrochloride RS and 0.2 mg/mL of USP Verapamil Related Compound B RS in Medium
Standard solution: 0.267 mg/mL of USP Verapamil Hydrochloride RS in Medium
Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 278 nm
Column: 4.6-mm × 25-cm; 5-μm packing L1
Flow rate: 1.2 mL/min
Injection volume: 30 μL

System suitability
Samples: System suitability solution and Standard solution
Suitability requirements
Resolution: NLT 1.5 between verapamil and verapamil related compound B
Relative standard deviation: NMT 2.0%, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of verapamil hydrochloride (C_{27}H_{38}N_{2}O_{4} · HCl) dissolved at each time point:
\[ Q_2 = (r_0/r_3) \times (C_4/L) \times V \times 100 \]
\[ Q_4 = (Q_2 \times V_{51}/V) + [(r_6/r_3) \times (C_4/L) \times (V - V_{51}) \times 100] \]
\[ Q_6 = (Q_4 \times V_{52}/V) + [(r_6/r_3) \times (C_4/L) \times (V - V_{52} - V_{51}) + [(r_6/r_3) \times (C_4/L) \times (V - V_{51} - V_{52} - V_{53})] \times 100] \]
\[ Q_{24} = (Q_2 \times V_{51}/V) + [(r_6/r_3) \times (C_4/L) \times (V - V_{51} - V_{52} - V_{53})] + [(r_6/r_3) \times (C_4/L) \times (V - V_{51} + V_{52} + V_{53})] \times 100] \]

\[ r_0 \] = peak response of verapamil hydrochloride from the Sample solution
\[ r_3 \] = peak response of verapamil hydrochloride from the Standard solution
\[ C_4 \] = concentration of USP Verapamil Hydrochloride RS in the Standard solution
\[ L \] = label claim (mg/Capsule)
\[ V \] = initial volume of Medium, 900 mL
\[ V_{60} \] = volume of Medium taken at each time point (mL)
Tolerances: See Table 1.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>10%–25%</td>
</tr>
<tr>
<td>4</td>
<td>15%–40%</td>
</tr>
<tr>
<td>8</td>
<td>40%–65%</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of verapamil hydrochloride (C_{27}H_{38}N_{2}O_{4} · HCl) released at the times specified conform to Acceptance Table 2 in (711).

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


Tolerances: See Table 2.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>NMT 25%</td>
</tr>
<tr>
<td>4</td>
<td>15%–40%</td>
</tr>
<tr>
<td>8</td>
<td>40%–65%</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80%</td>
</tr>
</tbody>
</table>

**Add the following:**

- **LABELING:** When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used. (RB 1-Jun-2013)
- **USP REFERENCE STANDARDS (11)**
  - USP Verapamil Hydrochloride RS
  - USP Verapamil Related Compound B RS
  - Benzenacetonitrile, α-[2-[(3,4-dimethoxyphenyl)-ethyl]methylamino]ethyl]-3,4-dimethoxy-α-(1-methylethyl)-, monohydrochloride. C_{26}H_{36}N_{2}O_{4} · HCl 477.05