Nifedipine Extended-Release Tablets

Type of Posting         Revision Bulletin
Posting Date           29–Sep–2017
Official Date          01–Oct–2017
Expert Committee       Chemical Medicines Monographs 2
Reason for Revision    Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Expert Committee 2 has revised the Nifedipine Extended-Release Tablets monograph. The purpose for the revision is to add Dissolution Test 11 and Dissolution Test 12 to accommodate recently approved drug products by the FDA.

Minor editorial changes have been made to update the monograph to the current USP style.

Nifedipine Extended-Release Tablets Revision Bulletin supersedes the currently monograph. The Revision Bulletin will be incorporated in the First Supplement to USP 41–NF 36.

Should you have any questions, please contact Donald Min Ph.D., Senior Scientific Liaison (301–230–7457 or ddm@usp.org).
Nifedipine Extended-Release Tablets

**DEFINITION**
Nifedipine Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of nifedipine (C_{17}H_{18}N_{2}O_{6}). [Note—Nifedipine, when exposed to daylight and certain wavelengths of artificial light, readily converts to a nitrosophenylpyridine derivative. Exposure to UV light leads to the formation of a nitrophenylpyridine derivative. Perform assays and tests in the dark or under golden fluorescent or other low-actinic light. Use low-actinic glassware.]

**IDENTIFICATION**
- **A.** The retention time of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.
- **B. ULTRAVIOLET ABSORPTION (197U)**
  
  **Standard stock solution and Sample stock solution:** Prepare as directed in the Assay.

  **Standard solution:** 0.02 mg/mL of USP Nifedipine RS in Mobile phase from the Standard stock solution

  **Sample solution:** Nominally 0.02 mg/mL of nifedipine in Mobile phase from the Sample stock solution

**ASSAY**

- **PROCEDURE**
  
  [Note—Conduct the Assay promptly after preparation of the Standard solution and the Sample solution.]

  **Mobile phase:** Acetonitrile, methanol, and water (25:25:50)

  **Standard stock solution:** 1 mg/mL of USP Nifedipine RS in methanol

  **Standard solution:** 0.1 mg/mL of USP Nifedipine RS from the Standard stock solution in Mobile phase

  **Sample stock solution:** Dissolve an amount equivalent to 420 mg of nifedipine from powdered Tablets in 130 mL of water in a 250-mL volumetric flask; or transfer the intact Tablets to a 400-mL, high-speed blender cup containing 130 mL of water. Homogenize until a uniform suspension is achieved (about 2 min), and transfer the suspension with the aid of a mixture of acetonitrile and methanol (1:1) to a 250-mL volumetric flask. Dilute with a mixture of acetonitrile and methanol (1:1) to volume, and stir for 30 min. Centrifuge the resulting suspension to obtain a clear supernatant.

  **Sample solution:** Nominally 0.1 mg/mL of nifedipine prepared as follows. Transfer 3.0 mL of the Sample stock solution to a 50-mL volumetric flask, dilute with Mobile phase to volume, and filter. [Note—Reserve a portion of this solution for use as the Sample solution in the test for Organic Impurities.]

  **Chromatographic system**

  (See Chromatography (621), System Suitability.)

**PERFORMANCE TESTS**

**Analysis**

Calculate the percentage of the labeled amount of nifedipine (C_{17}H_{18}N_{2}O_{6}) in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_2}{r_1} \right) \times \left( \frac{C_s}{C_u} \right) \times 100
\]

- **Test 1:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 1.

  **Medium:** Water; 50 mL

  **Apparatus 7:** (See Drug Release (724),) 15–30 cycles/min. Do not use the reciprocating disk; use a 25-cm Plexiglas rod, the perimeter of the Tablets being affixed to the rod with a water-insoluble glue. The solution containers are 25-mm test tubes, 150–200 mm in length, and the water bath is maintained at 37 ± 0.5°C.

  At the end of each specified test interval, the systems are transferred to the next row of new test tubes containing 50 mL of fresh Medium.

  **Times:** 4, 8, 12, 16, 20, and 24 h

  **Diluent:** Methanol and water (1:1)

  **Standard solution:** Transfer 50 mg of USP Nifedipine RS to a 100-mL volumetric flask. Dilute in 50 mL of methanol, and dilute with water to volume. Quantitatively dilute this solution with Diluent to obtain solutions having suitable known concentrations.

  **Sample solution:** Use portions of the solution under test, passed through a suitable filter of 0.4-µm pore size, suitably diluted with methanol, and stepwise if necessary, with Diluent to obtain a final mixture consisting of equal parts of methanol and water.

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

- **Mode:** UV

  - **Analytical wavelength:** 338 nm

  **Cell:** 0.5 cm

  **Analysis:** Determine the amount of nifedipine (C_{17}H_{18}N_{2}O_{6}) released in the Sample solution at each 4-h interval from UV absorbances. [Note—for the 4-h time period, determine the absorbance at 456 nm, and use this determination to correct for excipient interference.]

**Tolerances:** See Table 1.
Nifedipine

The cumulative percentages of the labeled amount of nifedipine \((C_{17}H_{18}N_{2}O_{6})\) released 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.

**Solution A:** Dissolve 330.9 g of dibasic sodium phosphate and 38 g of citric acid in water in a 1-L volumetric flask. Add 10 mL of phosphoric acid, and dilute with water to volume.

**Medium:** Mix 125.0 mL of Solution A and 1 L of 10% sodium lauryl sulfate solution, and dilute to 10 L. Adjust, if necessary, to a pH of 6.8; 900 mL.

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

* **Times:** 3, 6, and 12 h
* **Mobile phase:** Acetonitrile and water (7:3)
* **Standard stock solution:** 1.11 mg/mL of USP Nifedipine RS in methanol
* **Standard solution:** 0.1 mg/mL of USP Nifedipine RS from the Standard stock solution 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 350 nm

**Column:** 4.0-mm × 125-mm; 3-µm packing L1

**Temperature:** 40°

**Flow rate:** 1.5 mL/min

**Injection volume:** 20 µL

**System suitability**

* **Sample:** Standard solution
* **Suitability requirements**
  * **Column efficiency:** NLT 2000 theoretical plates
  * **Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Determine the amount of nifedipine \((C_{17}H_{18}N_{2}O_{6})\) dissolved.

**Tolerances:** See Table 2.

### Table 2

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>10–30</td>
</tr>
<tr>
<td>6</td>
<td>40–65</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine \((C_{17}H_{18}N_{2}O_{6})\) 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.

For Tablets labeled to contain 30 mg of nifedipine:

**Phase 1**

<table>
<thead>
<tr>
<th>Medium</th>
<th>0.05 M phosphate buffer, pH 7.5; 900 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparatus 2</td>
<td>100 rpm</td>
</tr>
<tr>
<td>Time</td>
<td>1 h</td>
</tr>
</tbody>
</table>

**Standard solution:** 0.034 mg/mL of USP Nifedipine RS in Medium. [NOTE—If necessary, a volume of methanol, not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

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

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 238 nm

**Analysis:** [NOTE—After the run, take the Tablet out of the dissolution vessel, adapt a sinker to it, and transfer the Tablet with the sinker to the dissolution vessel containing the Medium for Phase 2.] Determine the amount of nifedipine \((C_{17}H_{18}N_{2}O_{6})\) released in Phase 1, using filtered portions of the Sample solution; in comparison with the Standard solution, using the Medium as the blank.

**For Tablets labeled to contain 30 mg of nifedipine:**

**Phase 2**

**Medium:** 0.5% sodium lauryl sulfate in simulated gastric fluid without enzyme, pH 1.2; 900 mL

**Apparatus 2:** 100 rpm

**Times:** 1, 4, 8, and 12 h

**Standard solution:** 0.034 mg/mL of USP Nifedipine RS in Medium. [NOTE—If necessary, a volume of methanol, not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

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

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 238 nm

**Analysis:** Determine the amount of nifedipine \((C_{17}H_{18}N_{2}O_{6})\) released in Phase 2, using filtered portions of the Sample solution, in comparison with the Standard solution, using Medium as the blank.

**Tolerances:** See Table 3.

### Table 3

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 30</td>
</tr>
<tr>
<td>4</td>
<td>30–55</td>
</tr>
<tr>
<td>8</td>
<td>NLT 60</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

*For each dosage unit, add the amount dissolved in phosphate buffer, pH 7.5 from Phase 1 to the amount dissolved at each time point in Phase 2.*

The cumulative percentages of the labeled amount of nifedipine \((C_{17}H_{18}N_{2}O_{6})\) dissolved at the times specified, conform to Dissolution (711), Acceptance Table 2.

**For Tablets labeled to contain 60 mg of nifedipine:**

**Phase 1**

<table>
<thead>
<tr>
<th>Medium</th>
<th>0.05 M phosphate buffer, pH 7.5; 900 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparatus 2</td>
<td>100 rpm</td>
</tr>
<tr>
<td>Time</td>
<td>25 min</td>
</tr>
</tbody>
</table>

**Standard solution:** 0.067 mg/mL of USP Nifedipine RS in Medium. [NOTE—If necessary, a volume of methanol, not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

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

Instrumental conditions
(See Ultraviolet-Visible Spectroscopy (857).)
Mode: UV
Analytical wavelength: 238 nm
Analysis: [NOTE—After the run, take the Tablet out of the dissolution vessel, adapt a sinker to it, and transfer the Tablet with the sinker to the dissolution vessel containing the Medium for Phase 2.] Determine the amount of nifedipine \( (C_{17}H_{18}N_{2}O_{6}) \) released in Phase 1, using filtered portions of the Sample solution, in comparison with the Standard solution, using the Medium as the blank.

For Tablets labeled to contain 60 mg of nifedipine:

| Phase 2 | Medium: 0.5% sodium lauryl sulfate in simulated gastric fluid without enzyme, pH 1.2; 900 mL | Apparatus 2: 100 rpm | Times: 1, 4, 8, and 12 h | Standard solution: 0.067 mg/mL of USP Nifedipine RS in Medium. [NOTE—If necessary, a volume of methanol, not exceeding 10% of the final volume, can be used to help solubilize nifedipine.] Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions
(See Ultraviolet-Visible Spectroscopy (857).)
Mode: UV
Analytical wavelength: 238 nm
Analysis: Determine the amount of nifedipine \( (C_{17}H_{18}N_{2}O_{6}) \) released in Phase 2, using filtered portions of the Sample solution, in comparison with the Standard solution, using the Medium as the blank.

Tolerances: See Table 4.

### Table 4

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 30</td>
</tr>
<tr>
<td>4</td>
<td>0.70–70</td>
</tr>
<tr>
<td>8</td>
<td>NLT 70</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

*For each dosage unit, add the amount dissolved in phosphate buffer, pH 7.5 from Phase 1 to the amount dissolved at each time point in Phase 2.

The cumulative percentages of the labeled amount of nifedipine \( (C_{17}H_{18}N_{2}O_{6}) \), released in vivo and 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 the product meets USP Dissolution Test 4.

Medium: 0.5% sodium lauryl sulfate in simulated gastric fluid without enzyme, pH 1.2; 900 mL

Apparatus 2: 100 rpm

Times: 1, 4, and 12 h

Standard solution: 0.067 mg/mL of USP Nifedipine RS for Tablets labeled to contain 60 mg, and 0.034 mg/mL of USP Nifedipine RS for Tablets labeled to contain 30 mg, in Medium. [NOTE—If necessary, a volume of methanol, not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

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

Instrumental conditions
(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV
Analytical wavelength: 238 nm
Analysis: Determine the amount of nifedipine \( (C_{17}H_{18}N_{2}O_{6}) \) released, using filtered portions of the Sample solution, in comparison with the Standard solution, using the Medium as the blank.

Tolerances: See Table 5.

### Table 5

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>12–35</td>
</tr>
<tr>
<td>4</td>
<td>44–67</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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

Medium: Water; 50 mL

Apparatus 7: (See Drug Release (724).) Use a 25-cm Plexiglas rod, the perimeter of the Tablets being affixed to the rod with a water-insoluble glue; 30 dips/min. The solution containers are 25-mm test tubes, 150–200 mm in length, and the water bath is maintained at 37 ± 0.5°C. Times: 4, 12, and 24 h

Diluent A: Methanol and acetonitrile (1:1)

Diluent B: Diluent A and water (1:1)

Standard stock solution: 50 mg of USP Nifedipine RS in Diluent A and water (50:50)

Standard solutions: 0.01, 0.05, and 0.20 mg/mL solutions, from the Standard stock solution in Diluent B, that are used at 4-, 12-, and 24-h samplings

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

Instrumental conditions
(See Ultraviolet-Visible Spectroscopy (857).)
Mode: UV
Analytical wavelength: 238 nm
Cell: 0.5 cm

Analysis: [NOTE—For the 4-h time period, filter the solution under test, and determine the absorbance at 456 nm. Use this absorbance value to correct for excipient interference at the other time points.] Determine the amount of nifedipine released at each interval on portions of the Sample solution passed through a suitable filter of 0.45-µm pore size, suitably diluted, if necessary, with Diluent A and water to obtain a final mixture of water, methanol, and acetonitrile (2:1:1), in comparison with the appropriate Standard solution, using Diluent B as the blank.

Tolerances: See Table 6.

### Table 6

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10–30</td>
</tr>
<tr>
<td>4</td>
<td>40–63</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine \( (C_{17}H_{18}N_{2}O_{6}) \), released at the times specified, conform to Dissolution (711), Acceptance Table 2.

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Nifedipine

Table 7

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>NMT 14</td>
</tr>
<tr>
<td>12</td>
<td>39–75</td>
</tr>
<tr>
<td>24</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine, \( \text{C}_{17}\text{H}_{18}\text{N}_{2}\text{O}_{6} \), 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: Simulated gastric fluid without enzyme containing 0.5% of sodium lauryl sulfate, pH 1.2; 900 mL, deaerated

Apparatus 1: 100 rpm

Times: 1, 4, and 12 h

Standard stock solution: 0.33 mg/mL of USP Nifedipine RS in methanol

Standard solution: Quantitatively dilute the Standard stock solution with Medium to obtain a solution having a concentration of about 0.033 mg/mL.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV

Analytical wavelength: 329 nm

Cell: 0.5 cm

Blank: Medium

Tolerances: See Table 8.

Table 8

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>4</td>
<td>20 ± 75 (88-1-Aug-2017)–40</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine (\( \text{C}_{17}\text{H}_{18}\text{N}_{2}\text{O}_{6} \)) 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: Simulated gastric fluid without enzyme containing 0.5% of sodium lauryl sulfate, pH 1.2; 900 mL, deaerated

Apparatus 2: 100 rpm, with three-prong sinker

Times: 1, 4, and 12 h

Standard solution: \((L/900)\) mg/mL of USP Nifedipine RS in Medium, where \( L \) is the label claim, in mg/Tablet, of nifedipine. A small amount of methanol, not exceeding 6%–7% of the final volume of the first dilution, can be used to solubilize nifedipine.

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

Instrumental conditions

(See Ultraviolet-Visible Spectroscopy (857).)

Mode: UV

Analytical wavelength: 238 nm

Cell: 1 mm, flow cell

Blank: Medium

Tolerances: See Table 9.

Table 9

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 15</td>
</tr>
<tr>
<td>4</td>
<td>25–50</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine (\( \text{C}_{17}\text{H}_{18}\text{N}_{2}\text{O}_{6} \)) 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.

Acid stage medium: Simulated gastric fluid without enzyme containing 3% polysorbate 80, pH 1.2; 250 mL

Apparatus 3: 20 dpm, 20-mesh polypropylene screen on the bottom; 1 min drip time. The Tablet is automatically transferred by the apparatus to the next set of vessels for each time point.

Time: 1 h

Buffer stage medium: 0.01 M sodium phosphate buffer, pH 6.8, containing 3% polysorbate 80 (dissolve 8.3 g of monobasic sodium phosphate and 1 g of sodium hydroxide in 6 L of water, adjust with either diluted sodium hydroxide or phosphoric acid to a pH of 6.8 ± 0.05, and add 180 g of polysorbate 80); 250 mL

Times: 2, 8, 12, and 24 h

Mobile phase: Acetonitrile, methanol, and water (35:35:30)

Standard stock solution: 1 mg/mL of USP Nifedipine RS in Buffer stage medium. An amount of methanol, about 40% of the final volume, can be used to dissolve nifedipine.

Standard solution: \((L/1000)\) mg/mL in Buffer stage medium, from the Standard stock solution, where \( L \) is the label claim in mg/Tablet

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 338 nm

Column: 4.6-mm × 25-cm; packing L

Temperature: 30°C

Flow rate: 1.5 mL/min

Injection volume: 10 μL

System suitability

Sample: Standard solution

Suitability requirements

Column efficiency: NLT 4000 theoretical plates

Tailing factor: NMT 1.7

Relative standard deviation: NMT 2.0%

Analysis: Calculate the percentage of the labeled amount of nifedipine dissolved at each time point. At 1 h:

\[
D_1 = (r_0/r_s) \times (C_d/L) \times V \times 100
\]

At 2 h:

\[
D_2 = D_1 + D
\]

At 8 h:

\[
D_8 = D_2 + D
\]
At 12 h:

\[ D = (r_0/r_s) \times (C_i/L) \times V \times 100 \]

\[ D_{12} = D_b + D \]

At 24 h:

\[ D = (r_0/r_s) \times (C_i/L) \times V \times 100 \]

\[ D_{24} = D_{12} + D \]

\[ r_0 = \text{peak response from the Sample solution} \]
\[ r_s = \text{peak response from the Standard solution} \]
\[ C_s = \text{concentration of the Standard solution} \]
\[ L = \text{label claim (mg/Tablet)} \]
\[ V = \text{volume of Medium, 250 mL} \]

**Tolerances**

**Acid stage:** NMT 5% of the labeled amount of nifedipine is dissolved in 1 h.

**Buffer stage:** See Table 10.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 5</td>
</tr>
<tr>
<td>2</td>
<td>0–10</td>
</tr>
<tr>
<td>8</td>
<td>25–60</td>
</tr>
<tr>
<td>12</td>
<td>45–85</td>
</tr>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine \((C_1\cdot H_{18}N_2O_6)\) 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:** 0.03 M phosphate/citrate buffer, pH 6.8 with 1% sodium lauryl sulfate (to a solution of 4.1 g/L of dibasic sodium phosphate and 0.475 g/L of citric acid monohydrate in water, add 10 g/L of sodium lauryl sulfate. Adjust if necessary, with phosphoric acid to a pH of 6.8); 900 mL

**Apparatus 2:** 50 rpm, with a suitable sinker

**Times:** 3, 6, and 12 h

**Standard stock solution:** 0.33 mg/mL of USP Nifedipine RS in methanol

**Standard solution:** Prepare the corresponding USP Nifedipine RS solutions in Medium as directed in Table 11.

**Sample solution:** Pass a portion of the solution under test at each time point through a suitable filter.

**Instrumental conditions**

(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelength:** 346 nm

**Cell:** 1 cm

**Blank:** Medium

**Analysis**

**Samples:** Standard solutions and Sample solution

Calculate the concentration \((C)\) of nifedipine \((C_1\cdot H_{18}N_2O_6)\) in the sample withdrawn from the vessel at each time point \((i)\):

Result = \((A_i/A_0) \times C_i\)

\[ A_i = \text{absorbance of the Sample solution at each time point} \]
\[ A_0 = \text{absorbance of the Standard solution} \]
\[ C_i = \text{concentration of USP Nifedipine RS in the Standard solution (mg/mL)} \]

Calculate the percentage of the labeled amount of nifedipine \((C_1\cdot H_{18}N_2O_6)\) dissolved at each time point \((i)\):

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

\[ \text{Result}_2 = [C_i \times (V - V_3)] + [C_3 - C_i] \times (1/L) \times 100 \]

\[ \text{Result}_3 = [C_i \times (V - (2 \times V_3))] + [C_3 - C_i] \times (1/L) \times 100 \]

\[ C_i = \text{concentration of nifedipine in the Sample solution at the specified time point (i)} \]

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

\[ L = \text{label claim (mg/Tablet)} \]

\[ V_i = \text{volume of the Sample solution withdrawn at each time point (i) (mL)} \]

**Tolerances:** See Table 12.

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Amount Dissolved (% of Tablets Labeled to Contain 30 mg and 60 mg of Nifedipine)</th>
<th>Tablets Labeled to Contain 90 mg of Nifedipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>15–40</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>43–73</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of Nifedipine \((C_1\cdot H_{18}N_2O_6)\) 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 the product meets USP **Dissolution Test 10**.

**Medium:** pH 6.8 phosphate buffer with 0.5% sodium lauryl sulfate (transfer 442.1 g of dibasic sodium phosphate and 38 g of citric acid in a 1-L volumetric flask. Add water to dissolve, add 10 mL of phosphoric acid, and dilute with water to volume. Transfer 60 g of sodium lauryl sulfate to a suitable container. Add 150 mL of the phosphate solution above and 11,850 mL of water. Mix well and adjust with phosphoric acid or sodium hydroxide to a pH of 6.8); 900 mL

**Apparatus 2:** 50 rpm, with sinkers (see Dissolution (711), Figure 2a).
Mobile phase: Methanol and water (60:40)

Standard solution: 0.06 mg/mL of USP Nifedipine RS prepared as follows. Transfer 12 mg of USP Nifedipine RS into a 200-mL volumetric flask. Add 20 mL of methanol, and dilute with Medium to volume. [NOTE—Sonication may be needed to aid dissolution.]

Sample solution: Withdraw a 10-mL aliquot at each time point. Pass a portion of the solution under test through a suitable filter.

Chromatographic system
(See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 380 nm
Column: 4.6-mm × 7.5-mm; 3.5-µm packing L60
Temperature: 45°C
Flow rate: 1 mL/min
Injection volume: 20 µL

System suitability
Sample: Standard solution
Suitability requirements
Column efficiency: NLT 3000 theoretical plates
Tailing factor: NMT 1.5
Relative standard deviation: NMT 3.0%

Analysis
Samples: Standard solution and Sample solution
Calculate the concentration (C) of nifedipine (C₁₇H₁₈N₂O₆) in the sample withdrawn from the vessel at each time point (t):

\[ \text{Result} = \left( \frac{r_{U}}{r_{S}} \right) \times C_{S} \]

where:
- \( r_{U} \) = peak response of nifedipine in the Sample solution at each time point
- \( r_{S} \) = peak response of nifedipine in the Standard solution
- \( C_{S} \) = concentration of USP Nifedipine RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of nifedipine (C₁₇H₁₈N₂O₆) dissolved at each time point (t):

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

\[ \text{Result}_{2} = \left[ \left( C_{2} \times (V - V_{S}) \right) + (C_{1} \times V_{S}) \right] \times \left( \frac{1}{L} \right) \times 100 \]

\[ \text{Result}_{3} = \left[ \left( C_{1} \times (V - (2 \times V_{S})) \right) + \left( C_{2} + C_{3} \times V_{S} \right) \right] \times \left( \frac{1}{L} \right) \times 100 \]

\( C_{L} \) = concentration of nifedipine in the Sample solution at the specified time point (mg/mL)
\( V \) = volume of the Medium, 900 mL
\( L \) = label claim (mg/Tablet)
\( V_{S} \) = volume of the Sample solution withdrawn at each time point (mL)

Tolerances: See Table 13.

### Table 13

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Time (h)</th>
<th>Tablets Labeled to Contain 30 and 60 mg of Nifedipine</th>
<th>Tablets Labeled to Contain 90 mg of Nifedipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>NMT 30</td>
<td>NMT 15</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>53–83</td>
<td>35–58</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>NLT 80</td>
<td>NLT 75</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine (C₁₇H₁₈N₂O₆) 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 the product meets USP Dissolution Test 11.

**Medium:** 1.25% sodium lauryl sulfate in water (transfer 12.5 g of sodium lauryl sulfate to 1 L of water; 900 mL

**Apparatus 2:** 100 rpm

**Times:** 1, 2, 4 and 10 h

**Standard solution:** 0.033 mg/mL of USP Nifedipine RS for Tablets labeled to contain 30 mg prepared as follows. Transfer an appropriate amount of USP Nifedipine RS into a suitable volumetric flask. Add methanol to 1% volume of the flask, and dilute with Medium to volume. [NOTE—Sonication may be needed to aid the dissolution.]

**Sample solution:** A portion of the solution under test at the time points specified

**Instrumental conditions**
(See Ultraviolet-Visible Spectroscopy (857).)

**Mode:** UV

**Analytical wavelengths:** 230–246 nm, from the difference between first derivative values at the wavelengths of maximum and minimum in the wavelength range from 230 to 246 nm

**Cell:** 1 mm

**Blank:** Medium

**Analysis:** Use an automatic dissolution system with an appropriate dissolution software. Determine the amount of nifedipine (C₁₇H₁₈N₂O₆) dissolved, using portions of the Sample solution, in comparison with the Standard solution.

**Tolerances:** See Table 14.

### Table 14

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 25</td>
</tr>
<tr>
<td>2</td>
<td>15–40</td>
</tr>
<tr>
<td>4</td>
<td>35–70</td>
</tr>
<tr>
<td>10</td>
<td>NLT 85</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of nifedipine (C₁₇H₁₈N₂O₆) 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 the product meets USP Dissolution Test 12.

**Medium:** pH 6.8 phosphate buffer with 1.25% sodium lauryl sulfate (transfer 6 g of monobasic sodium phosphate and 112 mL of 0.2 N sodium hydroxide in a 1-L volumetric flask containing 800 mL of water. Mix to dissolve, and dilute with water to volume. Adjust with phosphoric acid or sodium hydroxide to a pH of 6.8. Transfer 12.5 g of sodium lauryl sulfate in 1 L of the phosphate solution); 900 mL

**Apparatus 2:** 50 rpm

**Times:** 2, 6, 8 and 16 h

**Standard solution:** 0.067 mg/mL of USP Nifedipine RS for Tablets labeled to contain 60 mg prepared as follows. Transfer an appropriate amount of USP Nifedipine RS into a suitable volumetric flask. Add methanol to 1% volume of the flask, and dilute with Medium to volume.
ORGANIC IMPURITIES

UNIFORMITY OF DOSAGE UNITS

Sample solution: A portion of the solution under test at the time points specified

Instrumental conditions

Mode: UV

Analytical wavelengths: 230–246 nm, from the difference between first derivative values at the wave-lengths of maximum and minimum in the wave-length range from 230 to 246 nm

Cell: 1 mm

Blank: Medium

Analysis: Use an automatic dissolution system with an appropriate dissolution software. Determine the amount of nifedipine (C₁₇H₁₈N₂O₆) dissolved, using portions of the Sample solution, in comparison with the Standard solution.

Tolerances: See Table 15.

Table 15

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>NMT 20</td>
</tr>
<tr>
<td>6</td>
<td>28–53</td>
</tr>
<tr>
<td>8</td>
<td>43–68</td>
</tr>
<tr>
<td>16</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The cumulative percentages of the labeled amount of nifedipine (C₁₇H₁₈N₂O₆) dissolved at the times specified, conform to Dissolution (711), Acceptance Table 2.

• UNIFORMITY OF DOSAGE UNITS (905): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Sample solution: A portion of the solution under test at the time points specified

Instrumental conditions

Mode: LC

Detector: UV 265 nm

Columns

Guard: 2.1-mm × 3-cm; packing L1

Analytical: 4.6-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Sample: System suitability solution

Suitability requirements

Resolution: NLT 1.5 between the nitrophenylpyridine analog and nitrosophenylpyridine analog peaks; NLT 1.0 between the nitrosophenylpyridine analog and nifedipine peaks

Relative standard deviation: NMT 10% for each analog

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of each analog in the portion of Tablets taken:

Result = \( \frac{r_u}{r_s} \times \left( \frac{C_s}{C_U} \right) \times 100 \)

\( r_u \) = peak response of each analog from the Sample solution

\( r_s \) = peak response of each analog from the Standard solution

\( C_s \) = concentration of the appropriate analog USP Reference Standard in the Standard solution (µg/mL)

\( C_U \) = nominal concentration of nifedipine in the Sample solution (µg/mL)

Acceptance criteria: NMT 2.0% of nifedipine nitrophenylpyridine analog and NMT 0.5% of nifedipine nitrosophenylpyridine analog, both relative to the nifedipine content

ADDITIONAL REQUIREMENTS

• PACKAGING AND STORAGE: Preserve in tight, light-resistant containers, and store at controlled room temperature.

• LABELING: The labeling indicates the Dissolution test with which the product complies.

• USP REFERENCE STANDARDS (11)

USP Nifedipine RS

USP Nifedipine Nitrophenylpyridine Analog RS

Dimethyl 4-(2-nitrophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

C₁₇H₁₆N₂O₆ 344.33

USP Nifedipine Nitrosophenylpyridine Analog RS

Dimethyl 4-(2-nitroso-phenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

C₁₇H₁₆N₂O₆ 328.33