Nifedipine Extended-Release Tablets

Type of Posting
Posting Date
Official Date
Expert Committee
Reason for Revision

Revision Bulletin
22–Nov–2019
01–May–2020
Chemical Medicines Monographs 2
Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Nifedipine Extended-Release Tablets monograph. The purpose for the revision is to add Dissolution Test 13 to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution tests.

- Dissolution Test 13 was validated using a Chromachemie Puritas Eximius brand of column with L1 packing. The typical retention time for nifedipine is about 5 min.

The Nifedipine Extended-Release Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Yanyin Yang, Associate Scientific Liaison (301-692-3623 or yanyin.yang@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_{18}H_{17}N_{2}O_{3}). [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 nitrosophenylpyridine 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.

Change to read:
• B. • SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible Spectroscopy: 197Ua, (CN 1-May-2020)

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 in Mobile phase

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

Analysis
Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of nifedipine (C_{18}H_{17}N_{2}O_{3}) in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_o}{r_i} \right) \times \left( \frac{C_3}{C_0} \right) \times 100 \]

- \( r_o \) = peak response from the Sample solution
- \( r_i \) = peak response from the Standard solution
- \( C_3 \) = concentration of USP Nifedipine RS in the Standard solution (mg/mL)
- \( C_0 \) = nominal concentration of nifedipine in the Sample solution (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:
• DISSOLUTION (711)

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. Dissolve 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_{18}H_{17}N_{2}O_{3}) 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.
2 Nifedipine

Table 1 (continued)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

* The amount dissolved is expressed in terms of the labeled Tablet strength rather than in terms of the labeled total contents.

The cumulative percentages of the labeled amount of nifedipine (C\(_7\)H\(_{16}\)N\(_2\)O\(_3\)), 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 sinks (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\(_7\)H\(_{16}\)N\(_2\)O\(_3\)) 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 percentages of the labeled amount of nifedipine (C\(_7\)H\(_{16}\)N\(_2\)O\(_3\)) 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

Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL

Apparatus 2: 100 rpm

Time: 1 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

Cell: 0.5 cm

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\(_7\)H\(_{16}\)N\(_2\)O\(_3\)) 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: 0.034 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\(_7\)H\(_{16}\)N\(_2\)O\(_3\)) 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\(_7\)H\(_{16}\)N\(_2\)O\(_3\)) dissolved at the times specified, conform to Dissolution (711), Acceptance Table 2.

For Tablets labeled to contain 30 mg of nifedipine:

Phase 1

Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL

Apparatus 2: 100 rpm

Time: 25 min

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: [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 \( (C_{16}H_{12}N_2O_2) \) 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 \( (C_{16}H_{12}N_2O_2) \) 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>
<thead>
<tr>
<th>Table 4</th>
<th>Amount Dissolved* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NMT 30</td>
</tr>
<tr>
<td>4</td>
<td>40–70</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 \( (C_{16}H_{12}N_2O_2) \), 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: UV 238 nm

Analysis: Determine the amount of nifedipine \( (C_{16}H_{12}N_2O_2) \) released, using filtered portions of the Sample solution, in comparison with the Standard solution, using the Medium as the blank.

Tolerances: See Table 5 and Table 6.

| Table 5. For Tablets Labeled to Contain 30 mg of Nifedipine |
|-------------|---------------|
| Time (h)    | Amount Dissolved (%) |
| 1           | 12–35         |
| 4           | 44–67         |
| 12          | NLT 80        |

| Table 6. For Tablets Labeled to Contain 60 mg of Nifedipine |
|-------------|---------------|
| Time (h)    | Amount Dissolved (%) |
| 1           | 10–30         |
| 4           | 40–63         |
| 12          | NLT 80        |

The cumulative percentages of the labeled amount of nifedipine \( (C_{16}H_{12}N_2O_2) \), released at the times specified, conform to Dissolution (711), Acceptance Table 2.

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: 0.50 mg/mL of USP Nifedipine RS prepared as follows. Transfer a suitable amount of USP Nifedipine RS to an appropriate volumetric flask. Dissolve in water to volume. In 50% of the flask volume of Diluent A. Dilute with water to volume.
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: 338 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 7.
Nifedipine

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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 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 (C_{17}H_{13}N_{2}O_{4}) 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:** 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 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 (C_{17}H_{13}N_{2}O_{4}) 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

**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.

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The cumulative percentages of the labeled amount of nifedipine 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 rpm, 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 L1

**Temperature:** 30°

**Flow rate:** 1.5 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** Standard solution

**Suitability requirements**

**Column efficiency:** NLT 4000 theoretical plates

**Relative standard deviation:** NMT 2.0%

**Analysis:** Calculate the percentage of the labeled amount of nifedipine dissolved at each time point.

At 1 h:

\[
D_1 = \left(\frac{r_d}{r_t}\right) \times \left(\frac{C_d}{L}\right) \times V \times 100
\]

At 2 h:

\[
D_2 = D_1 + D
\]

At 8 h:

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

\[ D = \left( \frac{r_i}{r} \right) \times \left( \frac{C_l}{L} \right) \times V = 100 \]

\[ D_{12} = D_8 + D \]

At 24 h:

\[ D = \left( \frac{r_i}{r} \right) \times \left( \frac{C_l}{L} \right) \times V = 100 \]

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

\[ r_i = \text{peak response from the Sample solution} \]

\[ r = \text{peak response from the Standard solution} \]

\[ C_l = \text{concentration of the Standard solution (mg/mL)} \]

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

\[ V = \text{volume of Medium, 250 mL} \]

Tolerances

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

**Buffer stage:** See Table 10.

### Table 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\(_{17}\)H\(_{18}\)N\(_2\)O\(_4\)) 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

**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.

### Table 11

<table>
<thead>
<tr>
<th>Tablet Strength (mg)</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>0.033</td>
</tr>
<tr>
<td>60</td>
<td>0.066</td>
</tr>
<tr>
<td>90</td>
<td>0.099</td>
</tr>
</tbody>
</table>

**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\(_{17}\)H\(_{18}\)N\(_2\)O\(_4\)) in the sample withdrawn from the vessel at each time point (i):

\[ \text{Result}_i = \left( \frac{A_i}{A} \right) \times C_i \]

\[ A_i = \text{absorbance of the Sample solution at each time point} \]

\[ A = \text{absorbance of the Standard solution} \]

\[ C_i = \text{concentration of USP Nifedipine RS in the Standard solution (mg/mL)} \]

Calculate the percentage of the labeled amount of nifedipine (C\(_{17}\)H\(_{18}\)N\(_2\)O\(_4\)) dissolved at each time point (i):

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

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

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

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

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

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

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

**Tolerances:** See Table 12.

### Table 12

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Time (h)</th>
<th>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>
<td>10–35</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>43–73</td>
<td>40–65</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>NLT 80</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of nifedipine (C\(_{17}\)H\(_{18}\)N\(_2\)O\(_4\)) 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)

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

**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 x 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%  
  - **Relative standard deviation:** NMT 3.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the concentration (\(C_i\)) of nifedipine (\(C_{17}H_{16}N_2O_4\)) in the sample withdrawn from the vessel at each time point (\(t\)):

\[
\text{Result}_i = \left( \frac{r_i}{r_0} \right) \times C_i
\]

\(r_0\) = peak response of nifedipine in the Sample solution at each time point  
\(r_i\) = peak response of nifedipine in the Sample solution at each time point  
\(C_i\) = concentration of USP Nifedipine RS in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of nifedipine (\(C_{17}H_{16}N_2O_4\)) dissolved at each time point (\(t\)):

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

\[
\text{Result}_2 = \left( \frac{(C_i \times V - V_j) + (C_j \times V_i)}{(1/L) \times 100}
\]

\[
\text{Result}_3 = \left( \frac{(C_i \times (V - 2 \times V_j) + (C_j + C_i) \times V_i)}{(1/L) \times 100}
\]

\(C_i\) = concentration of nifedipine in the Sample solution at the specified time point (\(t\)) (mg/mL)  
\(V\) = volume of the Medium, 900 mL  
\(L\) = label claim (mg/Tablet)  
\(V_j\) = volume of the Sample solution withdrawn at each time point (\(t\)) (mL)

**Tolerances:** See Table 13.

### Table 13

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

The percentages of the labeled amount of nifedipine (\(C_{17}H_{16}N_2O_4\)) 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.  

**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

The cumulative percentages of the labeled amount of nifedipine (\(C_{17}H_{16}N_2O_4\)) 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.  

**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

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Analysis: Use an automatic dissolution system with an appropriate dissolution software. Determine the amount of nifedipine \((C_{17}H_{13}N_{3}O_{2})\) dissolved, using portions of the Sample solution, in comparison with the Standard solution.

Tolerances: See Table 15.

Table 15. For Tablets Labeled to Contain 60 mg of Nifedipine

<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 \((C_{17}H_{13}N_{3}O_{2})\) 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 the product meets USP Dissolution Test 13.

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

Apparatus 2: 100 rpm, with suitable sinkers

Times

For Tablets labeled to contain 30 and 60 mg of nifedipine: 1, 4, 6 and 10 h

For Tablets labeled to contain 90 mg of nifedipine: 1, 4, 6 and 12 h

Mobile phase: Acetonitrile, methanol, water and phosphoric acid (25:30:45:0.1)

Standard stock solution: 1.68 mg/mL of USP Nifedipine RS in methanol

Standard solution: A known concentration of USP Nifedipine RS in Medium from Standard stock solution, prepared as directed in Table 16

Table 16

<table>
<thead>
<tr>
<th>Tablet Strength (mg)</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>0.0336</td>
</tr>
<tr>
<td>60</td>
<td>0.0672</td>
</tr>
<tr>
<td>90</td>
<td>0.1008</td>
</tr>
</tbody>
</table>

Sample solution: At each specified time point, withdraw a 10-mL aliquot and replace with the same volume of Medium. Pass a portion of the solution under test through a suitable filter and discard the first few milliliters of the filtrate.

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 338 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Flow rate: 2.0 mL/min

Injection volume: 20 μL

Run time: NLT 1.6 times the retention time of nifedipine

System suitability

Sample: Standard solution

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the concentration \((C)\) of nifedipine \((C_{17}H_{13}N_{3}O_{2})\) in the sample withdrawn from the vessel at each time point \((t)\):

\[ C = \frac{r_u}{r_s} \times C_s \]

\(r_u\) = 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 nifedipine in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of nifedipine \((C_{17}H_{13}N_{3}O_{2})\) dissolved at each time point \((t)\):

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

\[ \text{Result}_2 = \frac{([C_r \times V] + [C_s \times V_s]) \times (1/L)}{L} \times 100 \]

\[ \text{Result}_3 = \frac{([C_r \times V] + [C_s \times V_s]) \times (1/L)}{L} \times 100 \]

\[ \text{Result}_4 = \frac{([C_r \times V] + [C_s \times V_s]) \times (1/L)}{L} \times 100 \]

\(C_r\) = concentration of nifedipine in the Sample solution at the specified time point \((t)\) (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 \((t)\) (mL)

Tolerances: See Table 17 and Table 18.

Table 17. For Tablets Labeled to Contain 30 and 60 mg of Nifedipine

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3–13</td>
</tr>
<tr>
<td>4</td>
<td>29–54</td>
</tr>
<tr>
<td>6</td>
<td>52–77</td>
</tr>
<tr>
<td>10</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

Table 18. For Tablets Labeled to Contain 90 mg of Nifedipine

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3–13</td>
</tr>
<tr>
<td>4</td>
<td>27–52</td>
</tr>
<tr>
<td>6</td>
<td>45–70</td>
</tr>
<tr>
<td>12</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of nifedipine \((C_{17}H_{13}N_{3}O_{2})\) dissolved at the times specified conform to Dissolution (711), Acceptance Table 2.▲ (RB 1-May-2020)

• Uniformity of Dosage Units (905): Meet the requirements

Impurities

• Organic Impurities

[Note—Conduct this test promptly after preparation of the Standard nifedipine solution and the Sample solution.]

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

Quantitative limit stock solution A: 1 mg/mL of USP Nifedipine Nitrophenylpyridine Analog RS in methanol

Quantitative limit stock solution B: 6 μg/mL of USP Nifedipine Nitrophenylpyridine Analog RS from Quantitative limit stock solution A in Mobile phase

Quantitative limit stock solution C: 1 mg/mL of USP Nifedipine Nitrosophenylpyridine Analog RS in methanol
8 Nifedipine

Quantitative limit solution B: 1.5 µg/mL of USP Nifedipine Nitrophenylpyridine Analog RS from Quantitative limit stock solution B in Mobile phase

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

Standard nifedipine solution: 0.3 mg/mL of USP Nifedipine RS from Standard nifedipine stock solution in Mobile phase


Standard solution: Mobile phase, Quantitative limit solution A, Quantitative limit solution B, and Standard nifedipine solution (1:1:1)

Sample solution: Use a portion of the Sample solution prepared as directed in the Assay.

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

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 nitrophenylpyridine analog peaks; NLT 1.0 between the nitrophenylpyridine 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:

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

\(r_u\) = 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 nitrophenylpyridine 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, \(C_{17}H_{16}N_2O_6\) 344.33
  USP Nifedipine Nitrosophenylpyridine Analog RS
  Dimethyl 4-(2-nitrosophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate, \(C_{17}H_{16}N_2O_5\) 328.33

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