## Nifedipine Extended-Release Tablets

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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 ($C_{17}H_{18}N_2O_6$). [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*.

***Change to read:***

• **B. ▲SPECTROSCOPIC IDENTIFICATION TESTS** ⟨197⟩**,** *Ultraviolet-Visible Spectroscopy***:** 197U▲ (CN 1-May-2020)

**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*.)

**Mode:** LC

**Detector:** UV 265 nm

**Columns**

**Guard:** 2.1-mm × 3-cm; packing L1

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

**Flow rate:** 1 mL/min

**Injection volume:** 25 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

**Column efficiency:** NLT 4000 theoretical plates

**Tailing factor:** NMT 1.5

**Relative standard deviation:** NMT 1.0%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) in the portion of Tablets taken:

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

$r_U$ = peak response from the *Sample solution*

$r_S$ = peak response from the *Standard solution*

$C_S$ = concentration of USP Nifedipine RS in the *Standard solution* (mg/mL)

$C_U$ = 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°. 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 ($C_{17}H_{18}N_2O_6$) 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*.

**Table 1**

| Time (h) | Amount Dissolved[a] (%) |
|---|---|
| 4 | 5–17 |
| 8 | — |
| 12 | 43–80 |
| 16 | — |
| 20 | — |

**Table 1** *(continued)*

| Time (h) | Amount Dissolved[a] (%) |
|---|---|
| 24 | NLT 80 |

[a] 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 ($C_{17}H_{18}N_2O_6$), 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
**Tailing factor:** NMT 1.5
**Relative standard deviation:** NMT 2.0%

**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved.

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

**Table 2**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 3 | 10–30 |
| 6 | 40–65 |
| 12 | NLT 80 |

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), 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**
**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 ($C_{17}H_{18}N_2O_6$) 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 ($C_{17}H_{18}N_2O_6$) 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**

| Time (h) | Amount Dissolved[a] (%) |
|---|---|
| 1 | NMT 30 |
| 4 | 30–55 |
| 8 | NLT 60 |
| 12 | NLT 80 |

[a] 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 ($C_{17}H_{18}N_2O_6$), dissolved at the times specified, conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

**For Tablets labeled to contain 60 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 ($C_{17}H_{18}N_2O_6$) 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 ($C_{17}H_{18}N_2O_6$) 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**

| Time (h) | Amount Dissolved[a] (%) |
|---|---|
| 1 | NMT 30 |
| 4 | 40–70 |
| 8 | NLT 70 |
| 12 | NLT 80 |

[a] 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 ($C_{17}H_{18}N_2O_6$), 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:** UV 238 nm
**Cell:** 1 cm
**Analysis:** Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released, using filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using the *Medium* as the blank.
**Tolerances:** See *Table 5* 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 ($C_{17}H_{18}N_2O_6$), 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°.
**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 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*.

**Table 7**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 4 | NMT 14 |
| 12 | 39–75 |
| 24 | NLT 75 |

The cumulative percentages of the labeled amount of nifedipine, 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**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 1 | NMT 15 |
| 4 | 20–40 |
| 12 | NLT 80 |

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) 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% 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*.

**Table 9**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 1 | NMT 15 |
| 4 | 25–50 |
| 12 | NLT 80 |

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) 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 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

**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:

$$D_1 = (r_U/r_S) \times (C_S/L) \times V \times 100$$

At 2 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_2 = D_1 + D$$

At 8 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_8 = D_2 + D$$

At 12 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_{12} = D_8 + D$$

At 24 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$
$$D_{24} = D_{12} + D$$

$r_U$ = peak response from the *Sample solution*
$r_S$ = peak response from the *Standard solution*
$C_S$ = concentration of the *Standard solution* (mg/mL)
$L$ = label claim (mg/Tablet)
$V$ = 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**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 1 | NMT 5 |
| 2 | 0–10 |
| 8 | 25–60 |
| 12 | 45–85 |
| 24 | NLT 80 |

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) 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*.

**Table 11**

| Tablet Strength (mg) | Concentration (mg/mL) |
|---|---|
| 30 | 0.033 |
| 60 | 0.066 |
| 90 | 0.099 |

**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 ($C_i$) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point ($i$):

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

$A_U$ = absorbance of the *Sample solution* at each time point
$A_S$ = absorbance of 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 ($C_{17}H_{18}N_2O_6$) dissolved at each time point ($i$):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$
$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$
$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$C_i$ = concentration of nifedipine in the *Sample solution* at the specified time point ($i$) (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 ($i$) (mL)

**Tolerances:** See *Table 12*.

**Table 12**

| Time Point ($i$) | Time (h) | Amount Dissolved (%) | |
|---|---|---|---|
| | | Tablets Labeled to Contain 30 mg and 60 mg of Nifedipine | Tablets Labeled to Contain 90 mg of Nifedipine |
| 1 | 3 | 15–40 | 10–35 |
| 2 | 6 | 43–73 | 40–65 |
| 3 | 12 | NLT 80 | NLT 80 |

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) 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*)

**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 × 7.5-mm; 3.5-µm packing L60
**Temperature:** 45°
**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 ($C_i$) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (*i*):

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

$r_U$ = 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 USP Nifedipine RS in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$
$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$
$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$C_i$ = concentration of nifedipine in the *Sample solution* at the specified time point (*i*) (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 (*i*) (mL)

**Tolerances:** See *Table 13*.

**Table 13**

| Time Point (*i*) | Time (h) | Amount Dissolved (%) | |
|---|---|---|---|
| | | Tablets Labeled to Contain 30 and 60 mg of Nifedipine | Tablets Labeled to Contain 90 mg of Nifedipine |
| 1 | 2 | NMT 30 | NMT 15 |
| 2 | 8 | 53–83 | 35–58 |
| 3 | 16 | NLT 80 | NLT 75 |

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) 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 ($C_{17}H_{18}N_2O_6$) dissolved, using portions of the *Sample solution*, in comparison with the *Standard solution*.
**Tolerances:** See *Table 14*.

**Table 14. For Tablets Labeled to Contain 30 mg of Nifedipine**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 1 | NMT 25 |
| 2 | 15–40 |
| 4 | 35–70 |
| 10 | NLT 85 |

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), 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. [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 ($C_{17}H_{18}N_2O_6$) 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**

| Time (h) | Amount Dissolved (%) |
|---|---|
| 2 | NMT 20 |
| 6 | 28–53 |
| 8 | 43–68 |
| 16 | NLT 80 |

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), 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**

| Tablet Strength (mg) | Concentration (mg/mL) |
|---|---|
| 30 | 0.0336 |
| 60 | 0.0672 |
| 90 | 0.1008 |

**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 ($C_i$) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (*i*):

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

$r_U$ = 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 USP Nifedipine RS in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$
$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$
$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$
$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$C_i$ = concentration of nifedipine in the *Sample solution* at the specified time point (*i*) (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 (*i*) (mL)

**Tolerances:** See *Table 17* and *Table 18*.

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

| Time (h) | Amount Dissolved (%) |
|---|---|
| 1 | 3–13 |
| 4 | 29–54 |
| 6 | 52–77 |
| 10 | NLT 80 |

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

| Time (h) | Amount Dissolved (%) |
|---|---|
| 1 | 3–13 |
| 4 | 27–52 |
| 6 | 45–70 |
| 12 | NLT 80 |

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) 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 solution A:** 6 µg/mL of USP Nifedipine Nitrophenylpyridine Analog RS from *Quantitative limit stock solution A* in *Mobile phase*
**Quantitative limit stock solution B:** 1 mg/mL of USP Nifedipine Nitrosophenylpyridine Analog RS in methanol

**Quantitative limit solution B:** 1.5 µg/mL of USP Nifedipine Nitrosophenylpyridine 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*
**System suitability solution:** *Quantitative limit solution A*, *Quantitative limit solution B*, and *Standard nifedipine solution* (1:1:1)
**Standard solution:** *Mobile phase*, *Quantitative limit solution A*, and *Quantitative limit solution B* (1:1:1)
[NOTE—Each mL of this solution contains about 2 µg of USP Nifedipine Nitrophenylpyridine Analog RS and 0.5 µg of USP Nifedipine Nitrosophenylpyridine Analog RS.]
**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 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:

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

$r_U$ = 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.
  $C_{17}H_{16}N_2O_6$ 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