Nifedipine Extended-Release Tablets

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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 Monographs 2 Expert Committee has revised the Nifedipine Extended-Release Tablets monograph. The purpose for the revision is to add *Dissolution Test 10* 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 *USP41–NF36*.

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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 ($C_{17}H_{18}N_2O_6$). [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*.
- **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*.)
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	—
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 ($C_{17}H_{18}N_2O_6$), ● (RB 1-Aug-2017) 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 ($C_{17}H_{18}N_2O_6$), ● (RB 1-Aug-2017) 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: 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 sampling
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 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, • (RB 1-Aug-2017) 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 • (RB 1-Aug-2017) –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*. ● (RB 1-Aug-2017)

- **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