Nifedipine Extended-Release Tablets

Type of Posting	Revision Bulletin
Posting Date	26-Mar-2021
Official Date	1-Apr-2021
Expert Committee	Small Molecules 2

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 2 Expert Committee has revised the Nifedipine Extended-Release Tablets monograph. The purpose for the revision is to add *Dissolution Test 15* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test(s). Existing references to reagents have been updated for consistency with the reagent entry.

- *Dissolution Test 15* was validated using the Agilent Zorbax Bonus-RP brand of 4.6-mm x 7.5-cm, 3.5-µm column with packing L60. The typical retention time for nifedipine is about 2.5 min.

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

Should you have any questions, please contact Robyn Fales, Assistant Scientific Liaison (240-221-2047 or rnp@usp.org).

Revision Bulletin
Official: April 1, 2021

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. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 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	—

Time (h)	Amount Dissolved[a] (%)
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

Time (h)	Amount Dissolved (%)
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

Time (h)	Amount Dissolved[a] (%)
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

Time (h)	Amount Dissolved[a] (%)
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

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*.

▲**Test 15:** If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 15*.

Medium: pH 6.8 phosphate buffer with 0.5% sodium lauryl sulfate (transfer 7.8 g of sodium phosphate monobasic dihydrate and 0.9 g of sodium hydroxide in 1 L of water. Adjust with 1 N sodium hydroxide or phosphoric acid to a pH of 6.8. Transfer 5 g of sodium lauryl sulfate in 1 L of the phosphate solution); 900 mL

Apparatus 2: 50 rpm, with suitable sinkers

Times: 2, 8, 12, and 24 h

Mobile phase: Methanol and water (60:40)

Standard solution: 0.06 mg/mL of USP Nifedipine RS for Tablets labeled to contain 60 or 90 mg, and 0.03 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: At each specified time point, withdraw a 10-mL aliquot. Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 380 nm

Column: 4.6-mm × 7.5-cm, 3.5 µm packing L60

Temperature: 45°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of nifedipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

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):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

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

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

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

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

V = volume of *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 19*.

Table 19

Time (h)	Amount Dissolved (%)
2	NMT 20
8	29–49
12	51–71
24	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-Apr-2021)

- **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

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