



Nicardipine Hydrochloride Injection

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In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 6 Expert Committee has revised the Nicardipine Hydrochloride Injection monograph. The purpose of this revision is to update the *Acceptance criteria* in the *Limit of N-Benzyl-N-methyl-ethanolamine* test from NMT 0.7% to NMT 2.0%. Additionally, the acceptance criteria for the limit of total impurities in *Table 3* of the *Organic Impurities* test has been updated from NMT 3.5% to NMT 4.8% to accommodate the FDA-approved drug product specifications.

The Nicardipine Hydrochloride Injection Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Jasmine Lawrence, Scientist IV (301-230-6363 or jasmine.lawrence@usp.org).

Nicardipine Hydrochloride Injection

DEFINITION

Nicardipine Hydrochloride Injection is a sterile solution of Nicardipine Hydrochloride. It contains NLT 90.0% and NMT 110.0% of the labeled amount of nicardipine hydrochloride ($C_{26}H_{29}N_3O_6 \cdot HCl$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• PROCEDURE

Buffer: 1.36 g/L of [monobasic potassium phosphate](#) in [water](#)

Mobile phase: [Methanol](#) and *Buffer* (80:20)

Diluent: [Acetonitrile](#) and *Buffer* (50:50)

Standard solution: 0.1 mg/mL of [USP Nicardipine Hydrochloride RS](#) in *Diluent*. Sonication may be used to aid in dissolution. Pass through a suitable filter of 0.45- μ m pore size. Discard the first 2–3 mL of the filtrate.

Sample solution: Nominally 0.1 mg/mL of nicardipine hydrochloride in *Diluent* from a suitable volume of Injection. Pass through a suitable filter of 0.45- μ m pore size. Discard the first 2–3 mL of filtrate.

[NOTE—The *Sample solution* is stable for about 26 h.]

Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm \times 25-cm; 5- μ m packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 μ L

Run time: NLT 2 times the retention time of nicardipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of nicardipine hydrochloride ($C_{26}H_{29}N_3O_6 \cdot HCl$) in the portion of Injection taken:

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

r_U = peak response of nicardipine from the *Sample solution*

r_S = peak response of nicardipine from the *Standard solution*

C_S = concentration of [USP Nicardipine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of nicardipine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

Change to read:

● LIMIT OF *N*-BENZYL-*N*-METHYL-ETHANOLAMINE

Solution A: Dissolve 2.80 g of [sodium perchlorate monohydrate](#) in 1 L of [water](#). Adjust with [perchloric acid](#) to a pH of 2.5.

Solution B: [Acetonitrile](#) and [methanol](#) (50:50)

Diluent: [Acetonitrile](#) and [water](#) (20:80)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
10	82	18
12	20	80
22	20	80
24	95	5
32	95	5

Standard solution: 2.5 µg/mL of [USP *N*-Benzyl-*N*-methyl-ethanolamine RS](#) in *Diluent* prepared as follows. To a suitable amount of [USP *N*-Benzyl-*N*-methyl-ethanolamine RS](#), add *Diluent* to 70% of the final volume. Sonicate to dissolve. Cool, and dilute with *Diluent* to volume. Pass the solution through a suitable filter of 0.45-µm pore size.

Sample solution: Nominally 0.5 mg/mL of nicardipine hydrochloride in *Diluent* from a suitable volume of Injection. Pass the solution through a suitable filter of 0.45-µm pore size.

Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

Mode: LC

Detector: UV 205 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L1](#)

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of *N*-benzyl-*N*-methyl-ethanolamine in the portion of Injection taken:

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

r_U = peak response of *N*-benzyl-*N*-methyl-ethanolamine from the *Sample solution*

r_S = peak response of *N*-benzyl-*N*-methyl-ethanolamine from the *Standard solution*

C_S = concentration of [USP *N*-Benzyl-*N*-methyl-ethanolamine RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of nicardipine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: NMT ▲2.0%▲ (RB 1-Apr-2026)

Change to read:

● **ORGANIC IMPURITIES**

Solution A: 3.5 g/L of [sodium perchlorate monohydrate](#) in [water](#). Add 1 mL/L of [triethylamine](#), and adjust with [perchloric acid](#) to a pH of 2.0.

Solution B: [Acetonitrile](#) and [methanol](#) (70:30)

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	70	30
15	70	30
55	35	65
60	35	65
62	70	30
70	70	30

Standard solution: 0.02 mg/mL of [USP Nicardipine Hydrochloride RS](#) in [methanol](#) prepared as follows.

To a suitable amount of [USP Nicardipine Hydrochloride RS](#) add [methanol](#) to 60% of the final volume.

Sonicate to dissolve. Cool, and dilute with [methanol](#) to volume. Pass the solution through a suitable filter of 0.45- μm pore size.

Sensitivity solution: 0.002 mg/mL of [USP Nicardipine Hydrochloride RS](#) in [methanol](#) from *Standard solution*

Sample solution: Nominally 2 mg/mL of nicardipine hydrochloride in [methanol](#) from a suitable volume of Injection. Pass the solution through a suitable filter of 0.45- μm pore size. [NOTE—The *Sample solution* is stable for about 42 h at 10°.]

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 239 nm

Column: 4.6-mm \times 15-cm; 5- μm packing [L1](#)

Temperatures

Autosampler: 10°

Column: 50°

Flow rate: 1 mL/min

Injection volume: 10 μL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity and any unspecified degradation product in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each specified impurity or any unspecified degradation product from the *Sample solution*

r_S = peak response of nicardipine from the *Standard solution*

C_S = concentration of [USP Nicardipine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of nicardipine hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 3](#))

Acceptance criteria: See [Table 3](#).

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Nicardipine monoacid (nicardipine related compound A) ^a	0.72	1.00	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Nicardipine pyridine analog (nicardipine related compound B) ^b	0.94	0.42	2.5
Nicardipine	1.00	1.00	—
Any unspecified degradation product	—	—	0.2
Total impurities ^c	—	—	▲4.8▲ (RB 1-Apr-2026)

^a 5-(Methoxycarbonyl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid.

^b 3-{2-[Benzyl(methyl)amino]ethyl} 5-methyl 2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate.

^c Total impurities include the sum of all organic impurities and *N*-benzyl-*N*-methyl-ethanolamine.

OTHER COMPONENTS

● CONTENT OF SORBITOL (if present)

Buffer: 1 g/L of [tetrabutylammonium hydrogen sulfate](#) in [water](#)

Mobile phase: [Acetonitrile](#) and *Buffer* (70:30)

Standard solution: 4.8 mg/mL of [USP Sorbitol RS](#) in *Mobile phase*. Pass the solution through a suitable filter of 0.45- μ m pore size. Sonication may be necessary to aid in dissolution.

Sample solution: Nominally 4.8 mg/mL of sorbitol in *Mobile phase* from the contents of NLT 3 Injection vials. Pass the solution through a suitable filter of 0.45- μ m pore size. [NOTE—*Sample solution* is stable for about 24 h.]

Chromatographic system

(See [Chromatography](#) (621), [System Suitability](#).)

Mode: LC

Detector: Refractive index

Column: 4.6-mm \times 25-cm; 5- μ m packing [L8](#)

Temperatures

Column: 40°

Detector: 50°

Flow rate: 1 mL/min

Injection volume: 25 μ L

Run time: NLT 2 times the retention time of sorbitol

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sorbitol ($C_6H_{14}O_6$) in the portion of Injection taken:

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

r_U = peak response of sorbitol from the *Sample solution*

r_S = peak response of sorbitol from the *Standard solution*

C_S = concentration of [USP Sorbitol RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of sorbitol in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **BACTERIAL ENDOTOXINS TEST** (85): Meets the requirements
- **STERILITY TESTS** (71): Meets the requirements
- **pH** (791): 3.0–4.2
- **PARTICULATE MATTER IN INJECTIONS** (788): Meets the requirements for small-volume injections
- **OTHER REQUIREMENTS:** Meets the requirements for [Injections and Implanted Drug Products](#) (1).

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose glass vials. Protect from light. Store at controlled room temperature.
- **LABELING:** Label it to indicate that it is to be diluted to the appropriate strength with a suitable intravenous fluid prior to administration.

- **USP REFERENCE STANDARDS** (11).

[USP N-Benzyl-N-methyl-ethanolamine RS](#)

2-[Benzyl(methyl)amino]ethanol.

$C_{10}H_{15}NO$ 165.23

[USP Nicardipine Hydrochloride RS](#)

[USP Sorbitol RS](#)

D-Glucitol.

$C_6H_{14}O_6$ 182.17

Page Information:

Not Applicable

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