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Isosorbide Mononitrate Extended-Release Tablets

DEFINITION

Isosorbide Mononitrate Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$).

IDENTIFICATION

Change to read:

- **A. [THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST \(201\)](#).**

Standard solution: 0.5 mg/mL of isosorbide mononitrate [▲]in [absolute alcohol](#) [▲](USP 1-Dec-2024) from [USP Diluted Isosorbide Mononitrate RS](#) [▲](USP 1-Dec-2024)

Sample stock solution: [▲]Nominally 2.4 mg/mL of isosorbide mononitrate prepared as follows. Finely powder NLT 20 Tablets and transfer a suitable portion of the powder to a suitable container. Add a suitable volume of [absolute alcohol](#), sonicate for 10 min, and centrifuge. Use the supernatant. [▲](USP 1-Dec-2024)

Sample solution: Nominally 0.48 mg/mL of isosorbide mononitrate in [absolute alcohol](#), from [▲]Sample stock solution [▲](USP 1-Dec-2024)

Chromatographic system

[▲]**Adsorbent:** 0.25-mm layer of [chromatographic silica gel mixture](#) [▲](USP 1-Dec-2024)

Application volume: 20 μ L

Developing solvent system: [Chloroform](#) and [methanol](#) (95:5)

Spray reagent: Dissolve 1 g of [soluble starch](#) in 100 mL of boiling [water](#). Cool, and add 0.5 g of [potassium iodide](#).

Analysis

Samples: *Standard solution* and *Sample solution*

Examine the plate under short-wave UV light, marking any observed spots. Visualize nitrates on the plate by spraying with *Spray reagent* and illuminating with short-wave UV light for 10 min.

Acceptance criteria: Isosorbide mononitrate and other nitrates appear as a violet spot on a white-to-light-violet background.

Change to read:

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of *Standard solution* [▲]B, [▲](USP 1-Dec-2024) as obtained in the Assay.

ASSAY

Change to read:

- **PROCEDURE**

Mobile phase: [Methanol](#) and [water](#) [▲](20:80) [▲](USP 1-Dec-2024)

Standard solution A: 0.15 mg/mL of isosorbide mononitrate related compound A [▲]in [water](#), [▲](USP 1-Dec-2024) from [USP Diluted Isosorbide Mononitrate Related Compound A RS](#) [▲](USP 1-Dec-2024)

Standard solution B: [▲]0.12 mg/mL of isosorbide mononitrate prepared as follows. Transfer a suitable amount of [USP Diluted Isosorbide Mononitrate RS](#) to a suitable volumetric flask, dissolve in a suitable volume of [water](#), add [methanol](#) to 20% of the final volume, and dilute with [water](#) to volume. [▲](USP 1-Dec-2024)

System suitability solution: [▲](USP 1-Dec-2024) 0.12 mg/mL of isosorbide mononitrate and 6 μ g/mL of isosorbide mononitrate related compound A prepared as follows. [▲]Transfer a suitable amount of [USP Diluted Isosorbide Mononitrate RS](#) to a suitable volumetric flask, dissolve in a suitable volume of [water](#). Add a suitable amount of *Standard solution A*, add [methanol](#) to 20% of the final volume, [▲](USP 1-Dec-2024) and dilute with [water](#) to volume.

[▲]**Sample stock solution:** Nominally 0.6 mg/mL of isosorbide mononitrate prepared as follows. Finely powder NLT 20 Tablets and transfer a suitable portion of the powder to a suitable volumetric flask. Add [methanol](#) to 50% of the final volume, and sonicate for about 30 min with cooling. Warm to ambient temperature, and dilute with [methanol](#) to volume. Centrifuge a portion of the solution and use the clear supernatant. [▲](USP 1-Dec-2024)

Sample solution: ▲Nominally 0.12 mg/mL of isosorbide mononitrate prepared as follows. Dilute the *Sample stock solution* with [water](#) and pass a portion of the solution through a suitable filter of 0.45-µm pore size.▲ (USP 1-Dec-2024)

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4-mm × 12.5-cm; ▲5-µm▲ (USP 1-Dec-2024) packing [L1](#)

Flow rate: 1.5 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2 times the retention time of isosorbide mononitrate▲ (USP 1-Dec-2024)

System suitability

Samples: *Standard solution B* and *System suitability solution*

▲[NOTE—The relative retention times for isosorbide mononitrate related compound A and isosorbide mononitrate are 0.8 and 1.0, respectively.]▲ (USP 1-Dec-2024)

Suitability requirements

Resolution: NLT 1.5 between isosorbide mononitrate related compound A and isosorbide mononitrate, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution B*

Relative standard deviation: NMT ▲1.0%,▲ (USP 1-Dec-2024) *Standard solution B*

Analysis

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

Calculate the percentage of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) in the portion of Tablets taken:

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

r_U = peak response of isosorbide mononitrate from the *Sample solution*

r_S = peak response of isosorbide mononitrate from *Standard solution B*

C_S = concentration of isosorbide mononitrate in *Standard solution B* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Medium: [Water](#); 900 mL

Apparatus 2: 50 rpm; Tablets are placed in a metal helix prepared by winding 10 in of a 0.8-mm stainless steel wire around a 9/32-in shaft and pulling the coils to form a helix 1 in long.

Times: 1, 2, 4, 8, and 12 h

Mobile phase: [Methanol](#) and [water](#)▲(30:70)▲ (USP 1-Dec-2024)

Standard solution: ($L/1000$) ▲mg/mL of isosorbide mononitrate from▲ (USP 1-Dec-2024) [USP Diluted Isosorbide Mononitrate RS](#) in *Medium*, where L is the label claim in mg/Tablet

Sample solution: ▲Pass a portion of the solution under test▲ (USP 1-Dec-2024) through a suitable nylon filter of 0.45-µm pore size, discarding the first 4–6 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; ▲5-µm▲ (USP 1-Dec-2024) packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 25 µL

▲**Run time:** NLT 1.8 times the retention time of isosorbide mononitrate▲ (USP 1-Dec-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis**Samples:** *Standard solution* and *Sample solution*▲ Calculate the concentration (C_i) of isosorbide mononitrate ($C_6H_9NO_6$) 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 isosorbide mononitrate from the *Sample solution* r_S = peak response of isosorbide mononitrate from the *Standard solution* C_S = concentration of isosorbide mononitrate in the *Standard solution* (mg/mL)Calculate the percentage of the labeled amounts of isosorbide mononitrate ($C_6H_9NO_6$) dissolved at each time point (i):

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

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

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

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

$$\text{Result}_5 = \{[C_5 \times [V - (4 \times V_S)]] + [(C_4 + C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

 C_i = concentration of isosorbide mononitrate in the portion of sample withdrawn at the specified time point (mg/mL) V = volume of *Medium*, 900 mL L = label claim (mg/Tablet) V_S = volume of *Sample solution* withdrawn at each time point (mL) ▲ (USP 1-Dec-2024)**Tolerances:** See [Table 1](#).**Table 1**

▲Time Point (i) ▲ (USP 1-Dec-2024)	Time (h)	Amount Dissolved (%)
▲1 ▲ (USP 1-Dec-2024)	1	15–35
▲2 ▲ (USP 1-Dec-2024)	2	28–48
▲3 ▲ (USP 1-Dec-2024)	4	43–68
▲4 ▲ (USP 1-Dec-2024)	8	65–90
▲5 ▲ (USP 1-Dec-2024)	12	NLT 80

The percentages of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) dissolved at the times specified conform to *Dissolution* (711), [Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.**Medium:** [Simulated gastric fluid](#) (without enzymes); 500 mL**Apparatus 2:** 50 rpm**Times:** 1, 2, 6, and 12 h**Mobile phase:** [Methanol](#) and [water](#) ▲ (40:60) ▲ (USP 1-Dec-2024)**Standard stock solution:** 1.2 mg/mL of isosorbide mononitrate from [USP Diluted Isosorbide Mononitrate RS](#) ▲ (USP 1-Dec-2024) in *Medium***Standard solution****For Tablets labeled to contain 30 mg:** 60 µg/mL of isosorbide mononitrate in *Medium*, from the *Standard stock solution***For Tablets labeled to contain 60 mg:** 120 µg/mL of isosorbide mononitrate in *Medium*, from the *Standard stock solution***Sample solution:** Pass ▲ a portion ▲ (USP 1-Dec-2024) of the solution under test through a suitable filter of 0.45-µm pore size.**Chromatographic system**

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 10-μm packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 μL

▲Run time: NLT 1.6 times the retention time of isosorbide mononitrate▲ (USP 1-Dec-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the concentration (C_i)▲ (USP 1-Dec-2024) of isosorbide mononitrate▲ ($C_6H_9NO_6$) in the sample withdrawn from the vessel▲ (USP 1-Dec-2024) at each time point (i):

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

r_U ▲ (USP 1-Dec-2024) = peak response of isosorbide mononitrate from the *Sample solution*▲ (USP 1-Dec-2024)

r_S = peak response of isosorbide mononitrate from the *Standard solution*

C_S = concentration of isosorbide mononitrate in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) 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 isosorbide mononitrate in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point (mL)▲ (USP 1-Dec-2024)

Tolerances: See [Table 2](#).

Table 2

▲Time Point (i)▲ (USP 1-Dec-2024)	Time (h)	Amount Dissolved (%)
▲1▲ (USP 1-Dec-2024)	1	25–45
▲2▲ (USP 1-Dec-2024)	2	35–60
▲3▲ (USP 1-Dec-2024)	6	65–90
▲4▲ (USP 1-Dec-2024)	12	NLT 80

The percentages of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) 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 the product meets USP *Dissolution Test 3*.

Medium: [Simulated gastric fluid](#) (without enzymes); 500 mL

Apparatus 2: 50 rpm

Times: 1, 2, 6, and 12 h

Buffer: Transfer 15.4 g of [ammonium acetate](#) and 11.5 mL of [glacial acetic acid](#) (USP 1-Dec-2024) to a 1-L volumetric flask containing 500 mL of [water](#). Adjust with [glacial acetic acid](#) (USP 1-Dec-2024) to a pH of 4.7, and dilute with [water](#) to volume.

Mobile phase: [Methanol](#), *Buffer*, and [water](#) (30:10:60) (USP 1-Dec-2024)

Standard stock solution: 0.12 mg/mL of isosorbide mononitrate from [USP Diluted Isosorbide Mononitrate RS](#) in *Medium*

Standard solution

For Tablets labeled to contain 30 mg: 0.06 mg/mL of isosorbide mononitrate in *Medium*, from the *Standard stock solution*

For Tablets labeled to contain 60 mg: Use the *Standard stock solution* with no further dilution.

Sample solution: Pass a portion (USP 1-Dec-2024) of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Flow rate: 1 mL/min

Injection volume: 100 µL

Run time: NLT 1.8 times the retention time of isosorbide mononitrate (USP 1-Dec-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the concentration (C_i) (USP 1-Dec-2024) of isosorbide mononitrate ($C_6H_9NO_6$) in the sample withdrawn from the vessel (USP 1-Dec-2024) at each time point (i):

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

r_U (USP 1-Dec-2024) = peak response of isosorbide mononitrate from the *Sample solution* (USP 1-Dec-2024)

r_S = peak response of isosorbide mononitrate from the *Standard solution*

C_S = concentration of isosorbide mononitrate in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) 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 isosorbide mononitrate in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

V_S = volume of *Sample solution* withdrawn at each time point (mL) (USP 1-Dec-2024)

Tolerances: See [Table 3](#).

Table 3

Time Point (i) (USP 1-Dec-2024)	Time (h)	Amount Dissolved (%)
1 (USP 1-Dec-2024)	1	