Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2024
Document Type: USP Monographs
DocId: GUID-2CBE0A8C-0B02-46A9-B279-61C2F5306845_4_en-US
DOI: https://doi.org/10.31003/USPNF_M43615_04_01
DOI Ref: auqes

Isosorbide Mononitrate Tablets

DEFINITION
Isosorbide Mononitrate 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 from USP Diluted Isosorbide Mononitrate RS

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.

Sample solution: Nominally 0.48 mg/mL of isosorbide mononitrate in absolute alcohol from the *Sample stock solution*

Chromatographic system

▲Adsorbent: 0.25-mm layer of chromatographic silica gel mixture▲ (USP 1-May-2024)

Application volume: 20 µL

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 about 10 min.

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

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

ASSAY

Change to read:

• **Procedure**

Mobile phase: Methanol and water (30:70)

System suitability solution: 0.5 µg/mL each of isosorbide mononitrate and isosorbide mononitrate related compound A ▲in water▲ (USP 1-May-2024) from USP Diluted Isosorbide Mononitrate RS and USP Diluted Isosorbide Mononitrate Related Compound A RS

Standard solution: 0.1 mg/mL of isosorbide mononitrate in water from USP Diluted Isosorbide Mononitrate RS. Pass a portion of the solution through a suitable filter of 0.45-µm or finer pore size, and use the filtrate.

Sample solution: Nominally 0.1 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 50% of the final volume of water, and sonicate for about 10 min. Dilute with water to volume. Pass a portion of the solution through a suitable filter of 0.45-µm or finer pore size, and use 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-May-2024) packing L1

Flow rate: ▲1 mL/min▲ (USP 1-May-2024)

Injection volume: 50 µL

▲Run time: NLT 6 times the retention time of isosorbide mononitrate▲ (USP 1-May-2024)

System suitability

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

▲[Note—The relative retention times for isosorbide mononitrate related compound A and isosorbide mononitrate are 0.9 and 1.0, respectively.]▲ (USP 1-May-2024)

Suitability requirements

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

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

Analysis

Samples: *Standard solution* 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 the *Standard solution*

C_S = concentration of isosorbide mononitrate in the *Standard solution* (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⟩

Medium: Water; 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 15 min

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.02 mg/mL of ▲isosorbide mononitrate from USP Diluted Isosorbide Mononitrate RS in *Medium*▲ (USP 1-May-2024)

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) dissolved:

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

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)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) is dissolved

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements▲▲ (USP 1-May-2024)

IMPURITIES

Add the following:

▲• **Limit of Nitrate**

[Note—Use water with a resistivity of NLT 18 megohm-cm to prepare the solutions.]

Mobile phase: 20 mM potassium hydroxide in water. [Note—*Mobile phase* can be generated electrolytically using an automatic eluant generator.]

Sensitivity solution: 0.5 µg/mL of USP Potassium Nitrate RS in water

Standard solution: 1.0 µg/mL of USP Potassium Nitrate RS in water

Sample solution: Nominally 200 µg/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 water to about 80% of the final flask volume. Sonicate for about 10 min with intermittent shaking, cool to ambient temperature, and dilute with water to volume. Centrifuge a portion of the solution and use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: Conductivity with suppression

Columns

Guard: 4.0-mm × 0.5-cm; 5.0-µm packing L91

Analytical: 4.0-mm × 15-cm; 5.0-µm packing L91

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 100 µL

Run time: NLT 2 times the retention time of nitrate

System suitability

Sample: *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nitrate as potassium nitrate in the portion of Tablets taken:

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

r_U = peak response of the nitrate ion from the *Sample solution*

r_S = peak response of the nitrate ion from the *Standard solution*

C_S = concentration of USP Potassium Nitrate RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: NMT 0.5%, calculated as potassium nitrate▲ (USP 1-May-2024)

Change to read:

• **Organic Impurities**

▲[Note—It is recommended to use GC-grade methanol to prepare the solutions.]

Sensitivity solution: 3 µg/mL of isosorbide mononitrate in methanol prepared as follows. Transfer a suitable amount of USP Diluted Isosorbide Mononitrate RS to a suitable volumetric flask. Add methanol to about 80% of the final flask volume and sonicate for 30 min with intermittent shaking. Dilute with methanol to volume. Centrifuge a portion of the solution and use the clear supernatant.

Standard solution: 6 µg/mL of isosorbide mononitrate, 30 µg/mL of isosorbide, and 15 µg/mL each of ▲isosorbide mononitrate related compound A▲ (ERR 1-May-2024) and isosorbide dinitrate in methanol prepared as follows. Transfer a suitable amount of USP Diluted Isosorbide Mononitrate RS, USP Diluted Isosorbide Mononitrate Related Compound A RS, and USP Diluted Isosorbide Dinitrate RS to a suitable volumetric flask. Add methanol to about 80% of the final flask volume and sonicate for 30 min with intermittent shaking. Add an appropriate amount of USP Isosorbide RS and dilute with methanol to volume. Centrifuge a portion of the solution and use the clear supernatant.

Sample solution: Nominally 3 mg/mL of isosorbide mononitrate in methanol prepared as follows. Finely powder NLT 20 Tablets and transfer a suitable portion of the powder to a suitable volumetric flask. Add methanol to about 80% of the final flask volume. Sonicate for 30 min with intermittent shaking, cool to ambient temperature, and dilute with methanol to volume. Centrifuge a portion of the solution and use the clear supernatant.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m fused-silica capillary; coated with a 1.5-µm film of phase G2

Temperatures

Injection port: 150°

Column: 125°, isothermal

Detector: 275°

Carrier gas: Hydrogen

Flow rate: 180 cm/s (linear velocity)

Injection volume: 1 µL

Injection type: Split, split ratio 1:6

Run time: NLT 3 times the retention time of isosorbide mononitrate

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Relative standard deviation: NMT 5% each for isosorbide mononitrate, isosorbide, ▲isosorbide mononitrate related compound A▲ (ERR 1-May-2024), and isosorbide dinitrate, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of isosorbide, ▲isosorbide mononitrate related compound A▲ (ERR 1-May-2024), and isosorbide dinitrate 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, ▲isosorbide mononitrate related compound A▲ (ERR 1-May-2024), or isosorbide dinitrate from the *Sample solution*

r_S = peak response of isosorbide, ▲isosorbide mononitrate related compound A▲ (ERR 1-May-2024), or isosorbide dinitrate from the *Standard solution*

C_S = concentration of isosorbide, ▲isosorbide mononitrate related compound A▲ (ERR 1-May-2024), or isosorbide dinitrate in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified degradation product 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 unspecified degradation product 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)

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.1%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Isosorbide	0.4	1.0
▲Isosorbide mononitrate related compound A▲ (ERR 1-May-2024)	0.6	0.5
Isosorbide mononitrate	1.0	—
Isosorbide dinitrate	1.6	0.5
Any unspecified degradation product	—	0.2
Total degradation products	—	1.0

▲ (USP 1-May-2024)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers and store at a temperature between 20° and 30°, ▲excursions permitted between 15° and 30°.▲ (USP 1-May-2024)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Isosorbide RS

[NOTE—USP Diluted Isosorbide Dinitrate RS, USP Diluted Isosorbide Mononitrate RS, and USP Diluted Isosorbide Mononitrate Related Compound A RS are dry mixtures of an active component and suitable excipients to permit safe handling. For quantitative applications, calculate the concentration of the active component based on the content stated on the label.]

USP Diluted Isosorbide Dinitrate RS
USP Diluted Isosorbide Mononitrate RS
USP Diluted Isosorbide Mononitrate Related Compound A RS

1,4:3,6-Dianhydro-D-glucitol 2-nitrate ▲in lactose.▲ (USP 1-May-2024)

$C_6H_9NO_6$ 191.14

▲ USP Potassium Nitrate RS▲ (USP 1-May-2024)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ISOSORBIDE MONONITRATE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(4)

Current DocID: GUID-2CBE0A8C-0B02-46A9-B279-61C2F5306845_4_en-US
DOI: https://doi.org/10.31003/USPNF_M43615_04_01
DOI ref: auqes