

Status: Currently Official on 15-Feb-2025
 Official Date: Official as of 01-Jan-2023
 Document Type: USP Monographs
 DocId: GUID-124B9B1B-A41F-44FF-B068-02DBA0C5812D_4_en-US
 DOI: https://doi.org/10.31003/USPNF_M53470_04_01
 DOI Ref: yla38

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Metolazone Tablets

DEFINITION

Metolazone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of metolazone ($C_{16}H_{16}ClN_3O_3S$).

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible Spectroscopy:** 197U

Sample solution: Dilute 3 mL of the *Sample solution* in the Assay with methanol to 25 mL.

Acceptance criteria: Meet the requirements

ASSAY

Change to read:

PROCEDURE

[NOTE—Use low-actinic glassware throughout the Assay.]

Buffer: 1.38 g of ▲[monobasic sodium phosphate](#)▲ (ERR 1-Jan-2023) in 900 mL of [water](#). Adjust with [phosphoric acid](#) to a pH of 3.0, and dilute with [water](#) to 1000 mL.

Mobile phase: [Methanol](#), [acetonitrile](#), and *Buffer* (28:7:65)

Standard stock solution: 0.25 mg/mL of [USP Metolazone RS](#) in methanol

Standard solution: 5 µg/mL of [USP Metolazone RS](#) in *Mobile phase* from *Standard stock solution*

Sample stock solution: Transfer 10 Tablets to a 200-mL volumetric flask. Add 3 mL of [water](#) and 100 mL of [methanol](#), and sonicate for 30 min. If disintegration is not complete, sonicate for an additional 30 min. Shake by mechanical means for 30 min. Dilute with [methanol](#) to volume.

Sample solution: Nominally equivalent to 5 µg/mL of metolazone in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 3.9-mm × 15-cm; packing L1

Flow rate: 1.1 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metolazone ($C_{16}H_{16}ClN_3O_3S$) 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 Metolazone RS](#) in the *Standard solution* (µg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

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

[NOTE—Protect all solutions from light.]

Test 1

Medium: 2% w/v [sodium lauryl sulfate](#) in 0.05 M [monobasic sodium phosphate](#). Heat the mixture to about 37° to dissolve the [sodium lauryl sulfate](#), and adjust with 10 N [sodium hydroxide](#) to a pH of 7.5; 900 mL, deaerated

Apparatus 2: 75 rpm

Time: 120 min

Buffer: 0.05 M [monobasic potassium phosphate](#). Adjust with [phosphoric acid](#) to a pH of 3.00.

Mobile phase: [Acetonitrile](#), [methanol](#), and *Buffer* (270:50:680)

Standard stock solution: 0.28 mg/mL of [USP Metolazone RS](#). Initially add [methanol](#) to 2% of the volume of the flask. Sonicate to dissolve, and dilute with *Medium* to volume.

Standard solution: ($L/900$) mg/mL in *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 of 0.45-μm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-μm packing L7

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 50 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Column efficiency: NLT 2000 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metolazone ($C_{16}H_{16}ClN_3O_3S$) dissolved:

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

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*, 900 mL

Tolerances: NLT 75% (Q) of the labeled amount of metolazone ($C_{16}H_{16}ClN_3O_3S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: Prepare a solution of 0.05 M [dibasic sodium phosphate](#) in a suitable flask, and adjust with [phosphoric acid](#) to a pH of 7.5.

Dissolve a suitable amount of [sodium lauryl sulfate](#) to obtain a 20-g/L solution; 900 mL

Apparatus 2: 75 rpm

Time: 120 min

Standard stock solution: 0.275 mg/mL of [USP Metolazone RS](#). Initially add methanol to 10% of the volume of the flask. Sonicate to dissolve, and dilute with *Medium* to volume.

Standard solution: ($L/900$) mg/mL in *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 of 0.45-μm pore size.

Detector: UV 238 nm

Path length: 1 cm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metolazone ($C_{16}H_{16}ClN_3O_3S$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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