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Mercaptopurine Tablets

DEFINITION
Mercaptopurine Tablets contain NLT 93.0% and NMT 110.0% of the labeled amount of mercaptopurine ($C_5H_4N_4S \cdot H_2O$).

IDENTIFICATION

- **A.** The UV absorption spectrum exhibits a maximum at 325 ± 2 nm, and the ratio A_{255}/A_{325} does not exceed 0.09.

  Sample: 5 µg/mL of mercaptopurine in a mixture of methanol and water (1:1), from the *Sample solution* in the *Assay*
- **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

- **Procedure**

  Solution A: 0.77 g/L of ammonium acetate in water

  Solution B: Methanol and *Solution A* (5:95)

  Solution C: Methanol and *Solution A* (30:70)

  Mobile phase: *Solution B* and *Solution C* (80:20)

  Diluent: Methanol and water (1:1)

  Standard solution: 0.25 mg/mL of USP Mercaptopurine RS in a mixture of methanol and water (1:1). Transfer USP Mercaptopurine RS into a suitable volumetric flask, and add methanol equivalent to 50% of the final volume. Shake mechanically to dissolve, and dilute with water to volume.

  Sample stock solution: 0.5 mg/mL of mercaptopurine in *Diluent* from NLT 5 Tablets. Place the Tablets into a suitable volumetric flask, add methanol equivalent to 50% of the final volume, and shake mechanically for a minimum of 30 min. Dilute with water to volume. Pass through a PVDF filter of 0.45-µm pore size, and discard the first 3 mL of filtrate.

  Sample solution: 0.25 mg/mL of mercaptopurine in *Diluent* from the *Sample stock solution*

  Chromatographic system

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

  Mode: LC

  Detector: UV 260 nm

  Column: 4.6-mm × 10-cm; 3-µm packing L1

  Column temperature: 30°

  Flow rate: 1.0 mL/min

  Injection size: 10 µL

  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 mercaptopurine ($C_5H_4N_4S \cdot H_2O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

  r_U = peak response from the *Sample solution*

  r_S = peak response from the *Standard solution*

  C_S = concentration of USP Mercaptopurine RS in the *Standard solution* (mg/mL)

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

M_{r1} = molecular weight of mercaptopurine, 170.19

M_{r2} = molecular weight of anhydrous mercaptopurine, 152.18

Acceptance criteria: 93.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Mobile phase: 0.1% acetic acid in water

Standard solution: USP Mercaptopurine RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium* to a concentration that is similar to the *Standard solution*, if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 3.9-mm × 15-cm; packing L1

Flow rate: 2.5 mL/min

Injection size: 10 µL

System suitability

Sample: *Standard solution*

[Note—The retention time for mercaptopurine is NLT 4 min.]

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 80% (*Q*) of the labeled amount of $C_5H_4N_4S \cdot H_2O$ is dissolved.

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

Medium, Apparatus 2, Chromatographic system, and **Analysis:** Proceed as directed for *Test 1*.

Time: 120 min

Tolerances NLT 80% (*Q*) of the labeled amount of $C_5H_4N_4S \cdot H_2O$ is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meets the requirements

IMPURITIES

Organic Impurities

• **Procedure**

Solution A: 0.1% (v/v) formic acid in water

Solution B: Methanol and *Solution A* (2:98)

Solution C: Methanol and *Solution A* (1:1)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
8	100	0
20	0	100

Time (min)	Solution B (%)	Solution C (%)
25	0	100
27	100	0
30	100	0

Standard stock solution: 0.06 mg/mL of USP Mercaptopurine RS in *Solution A*. [NOTE—Use methanol equivalent to 2.5% of the final volume to help dissolve.]

Standard solution: 1.2 µg/mL of USP Mercaptopurine RS in *Solution B* from the *Standard stock solution*

Sensitivity solution: 0.06 µg/mL of USP Mercaptopurine RS in *Solution B* from the *Standard solution*

Sample stock solution: 0.5 mg/mL of mercaptopurine in a mixture of methanol and *Solution A* (1:9) from NLT 5 Tablets. Place the Tablets into a suitable volumetric flask, add methanol equivalent to 10% of the final volume, and shake mechanically for a minimum of 30 min. Dilute with *Solution A* to volume. Pass through a PVDF filter of 0.45-µm pore size, and discard the first 3 mL of filtrate.

Sample solution: 0.12 mg/mL of mercaptopurine in *Solution A*. Transfer 6.0 mL of the *Sample stock solution* into a 25-mL volumetric flask, and dilute with *Solution A* to volume. Pass through a PVDF filter of 0.45-µm pore size, and discard the first 5 mL of filtrate. [NOTE—Inject the *Sample solution* within 1 h of preparation.]

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 10-cm; 3-µm packing L1

Temperature

Column: 30°

Sample: 4°

Flow rate: 1.0 mL/min

Injection size: 50 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

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

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each impurity from the *Sample solution*

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

C_S = concentration of USP Mercaptopurine RS in the *Standard solution* (mg/mL)

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

F = relative response factor for each individual impurity (see *Table 2*)

Acceptance criteria

Individual impurities: See *Table 2*. [NOTE—Disregard any impurity peak less than 0.05%.]

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Didanosine related compound A[a]	0.54	6.3	0.3
Mercaptopurine	1.00	—	—
Mercaptopurine disulfide[b]	2.90	4.4	0.4
Any unspecified impurity	—	1.0	0.2
Total impurities	—	—	0.6

[a] Hypoxanthine.

[b] 1,2-Di(9*H*-purin-6-yl)disulfane.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩
  USP Mercaptopurine RS

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

Topic/Question	Contact	Expert Committee
MERCAPTOPURINE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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