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Azathioprine Sodium for Injection

DEFINITION

Azathioprine Sodium for Injection is a sterile solid prepared by the freeze-drying of an aqueous solution of Azathioprine and Sodium Hydroxide. It contains NLT 93.0% and NMT 107.0% of the labeled amount of azathioprine ($C_9H_7N_7O_2S$).

IDENTIFICATION

• **A.** The principal spot from the *Sample solution* shows the same R_F value as that obtained from *Standard solution A* in the test for *Limit of Mercaptopurine*.

• **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: 1.6 g/L of sodium 1-heptanesulfonate in water

Mobile phase: Methanol and *Solution A* (30:70). Adjust with 1 N hydrochloric acid to a pH of 3.5 ± 0.1.

Standard stock solution: 0.5 mg/mL of USP Azathioprine RS prepared as follows. Transfer USP Azathioprine RS to a suitable volumetric flask. Add 25% of the flask volume of methanol and 1% of ammonium hydroxide to the flask, swirl, and sonicate for 2 min or until dissolved. Dilute with methanol to volume.

Standard solution: 0.1 mg/mL of USP Azathioprine RS in water from the *Standard stock solution*

Sample solution: Nominally equivalent to 0.1 mg/mL of azathioprine in water from Azathioprine Sodium for Injection

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of azathioprine ($C_9H_7N_7O_2S$) in the portion of Azathioprine Sodium for Injection taken:

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

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

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

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

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

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

IMPURITIES

• **Limit of Mercaptopurine**

Standard solution A: 10 mg/mL of USP Azathioprine RS in dimethylformamide

Standard solution B: 100 µg/mL of USP Mercaptopurine RS in dimethylformamide

Sample solution: 10 mg/mL of Azathioprine Sodium for Injection in dimethylformamide

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of microcrystalline cellulose

Application volume: 5 µL for *Standard solution A* and the *Sample solution*, and 15 µL for *Standard solution B*

Developing solvent system: Butyl alcohol saturated with 5 N ammonium hydroxide

Analysis

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

Proceed as directed in the chapter. Apply the *Samples* at points 2 cm from the bottom edge of a TLC plate. Allow the spots to dry, and develop the chromatogram in a suitable chamber until the solvent front has moved 15 cm from the point of application. Remove the plate, air-dry, and locate the spots by viewing under short- and long-wavelength UV light.

Acceptance criteria: 3.0%; any spot from the *Sample solution*, other than the principal spot, is not more intense than the spot from *Standard solution B*.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: The contents of one container dissolved in 10 mL of water

Acceptance criteria: 9.8–11.0

• **Bacterial Endotoxins Test** ⟨85⟩**:** It contains NMT 1.0 USP Endotoxin Unit/mg of azathioprine.

• **Water Determination** ⟨921⟩, *Method I***:** NMT 7.0%, when the *Test Preparation* is prepared as directed for a hygroscopic specimen

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products* ⟨1⟩.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements* ⟨659⟩, *Injection Packaging, Packaging for constitution*, at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Azathioprine RS

USP Mercaptopurine RS

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

Topic/Question	Contact	Expert Committee
AZATHIOPRINE SODIUM FOR INJECTION	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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