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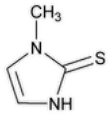
Methimazole



$C_4H_6N_2S$ 114.17

2*H*-Imidazole-2-thione, 1,3-dihydro-1-methyl-;

1-Methylimidazole-2-thiol CAS RN®: 60-56-0; UNII: 554Z48XN5E.

DEFINITION

Methimazole contains NLT 98.0% and NMT 101.0% of methimazole ($C_4H_6N_2S$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

ASSAY

• **Procedure**

Sample: 250 mg of Methimazole

Analysis: Dissolve the *Sample* in 75 mL of water. Add 15.0 mL of 0.1 N sodium hydroxide VS, mix, and add, with stirring, 30 mL of 0.1 N silver nitrate. Continue the titration with 0.1 N sodium hydroxide VS, determining the endpoint potentiometrically. Each milliliter of 0.1 N sodium hydroxide is equivalent to 11.42 mg of methimazole ($C_4H_6N_2S$).

Acceptance criteria: 98.0%–101.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Delete the following:

▲• **Selenium ⟨291⟩**

Sample: 200 mg of Methimazole

Acceptance criteria: NMT 30 ppm▲ (USP 1-May-2022)

Change to read:

• **Organic Impurities**

Standard solution: 0.01 mg/mL each of USP Methimazole RS, USP Methimazole Related Compound A RS, 1-methylimidazole, and USP Methimazole Related Compound C RS in chloroform

Sample solution: 10 mg/mL of Methimazole in chloroform

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 30-m × 0.25-mm; coated with a 0.5-µm film of phase G27

Temperatures

Injection port: 150°

Detector: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	—	100	2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	30	250	15

Carrier gas: Helium

Flow rate: 1.5 mL/min

Injection volume: 1 µL

Injection type: Split, split ratio 3:20

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between methimazole related compound A and 1-methylimidazole

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methimazole related compound A, 1-methylimidazole, and methimazole related compound C in the portion of Methimazole taken:

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

r_U = peak response of each related compound from the *Sample solution*

r_S = peak response of the corresponding related compound from the *Standard solution*

C_S = concentration of the corresponding related compound in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other individual impurity in the portion of Methimazole taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*. ▲The reporting threshold is▲ (USP 1-May-2022) 0.02%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Methimazole related compound A	0.3	0.1
1-Methylimidazole	0.4	0.1
Methimazole related compound C	0.7	0.1
Methimazole	1.0	—
Any other individual impurity	—	0.1
Total impurities	—	0.5

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers.
- **USP Reference Standards** ⟨11⟩

USP Methimazole RS

USP Methimazole Related Compound A RS

2,2-Dimethoxy-*N*-methylethanamine.

$C_5H_{13}NO_2$ 119.16

USP Methimazole Related Compound C RS

1-Methyl-2-(methylthio)-1*H*-imidazole.

$C_5H_8N_2S$ 128.20

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

Topic/Question	Contact	Expert Committee
METHIMAZOLE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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