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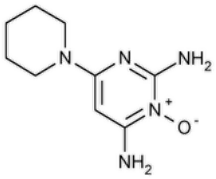
Minoxidil



$C_9H_{15}N_5O$ 209.25

2,4-Pyrimidinediamine, 6-(1-piperidinyl)-, 3-oxide;

2,4-Diamino-6-piperidinopyrimidine 3-oxide CAS RN®: 38304-91-5; UNII: 5965120SH1.

DEFINITION

Minoxidil contains NLT 97.0% and NMT 103.0% of minoxidil ($C_9H_{15}N_5O$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*▲ (CN 1-May-2020): ▲[Note—Methods described in 197A or 197M may be used.]▲ (USP 1-May-2020) Do not dry specimens.

Add the following:

▲• **B.** The retention time of the minoxidil peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2020)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Methanol, glacial acetic acid, and water (70:1:30). Add 3.0 g/L of docusate sodium. Adjust with perchloric acid to a pH of 3.0. ▲▲ (USP 1-May-2020)

Standard solution: 0.25 mg/mL of USP Minoxidil RS in ▲*Mobile phase*▲ (USP 1-May-2020)

Sample solution: 0.25 mg/mL of Minoxidil in ▲*Mobile phase*▲ (USP 1-May-2020)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 25-cm; ▲5-µm▲ (USP 1-May-2020) packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2 times the retention time of the minoxidil peak▲ (USP 1-May-2020)

System suitability

Sample: *Standard solution*▲▲ (USP 1-May-2020)

Suitability requirements

▲**Tailing factor:** NMT 2.0▲ (USP 1-May-2020)

Relative standard deviation: NMT ▲1.10%▲ (USP 1-May-2020)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of minoxidil ($C_9H_{15}N_5O$) in the portion of Minoxidil taken:

$$\text{Result} = {}^{\blacktriangle}(r_U/r_S)_{\blacktriangle\ (\text{USP 1-May-2020})} \times (C_S/C_U) \times 100$$

r_U (USP 1-May-2020) = peak response of minoxidil (USP 1-May-2020) from the *Sample solution*

r_S (USP 1-May-2020) = peak response of minoxidil (USP 1-May-2020) from the *Standard solution*

C_S = concentration of USP Minoxidil RS in (USP 1-May-2020) the *Standard solution* (mg/mL)

C_U = concentration of Minoxidil in (USP 1-May-2020) the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.5%

Change to read:

• **Organic Impurities**

Mobile phase: Dissolve 2.0 g of sodium lauryl sulfate in a mixture of 600 mL of methanol, 10 mL of glacial acetic acid, and 400 mL of water. Adjust with perchloric acid to a pH of 3.0 ± 0.1.

Diluent: Methanol and water (50:50)

Standard solution: 0.005 mg/mL of USP Minoxidil RS in *Diluent*

Sensitivity solution: 0.125 µg/mL of USP Minoxidil RS in *Diluent* from the *Standard solution*

Sample solution: 0.25 mg/mL of Minoxidil in *Diluent* prepared as follows. Transfer a suitable amount of Minoxidil in an appropriate volumetric flask. Initially add *Diluent* to about 60% of the flask volume, shake on a mechanical shaker for 20 min, and then dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 0.5 mL/min

Injection volume: 40 µL

Run time: NLT 3 times the retention time of the minoxidil peak

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of the Minoxidil 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 minoxidil from the *Standard solution*

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Pyrimidine oxide analog[a]	0.19	0.35	0.2
Pyrimidine analog[b]	0.37	0.49	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Minoxidil	1.00	1.0	—
Deoxyminoxidil[c]	1.45	1.32	0.2
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	1.0

[a] 4-Chloropyrimidine-2,6-diamine-1-oxide.

[b] 6-Chloropyrimidine-2,4-diamine.

[c] 6-(Piperidin-1-yl)pyrimidine-2,4-diamine.

▲ (USP 1-May-2020)

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 50° and at a pressure not exceeding 5 mm of mercury for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards ⟨11⟩**

USP Minoxidil RS

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

Topic/Question	Contact	Expert Committee
MINOXIDIL	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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