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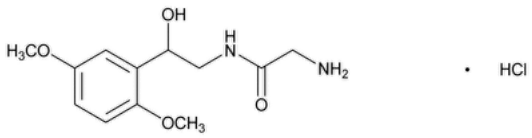
Midodrine Hydrochloride



$C_{12}H_{18}N_2O_4 \cdot HCl$ 290.74

Acetamide, 2-amino-*N*-[2-(2,5-dimethoxyphenyl)-2-hydroxyethyl]-, monohydrochloride, (±)-;

(±)-2-Amino-*N*-(β-hydroxy-2,5-dimethoxyphenethyl)acet amide monohydrochloride CAS RN®: 3092-17-9.

DEFINITION

Midodrine Hydrochloride contains NLT 98.0% and NMT 102.0% of midodrine hydrochloride ($C_{12}H_{18}N_2O_4 \cdot HCl$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. Identification Tests—General, *Chloride* ⟨191⟩:** A 10 mg/mL solution of Midodrine Hydrochloride in water meets the requirements.

ASSAY

- **Procedure**

Buffer: 13.6 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 4.00 ± 0.05.

Mobile phase: Acetonitrile and *Buffer* (3:22)

Standard solution: 0.05 mg/mL of USP Midodrine Hydrochloride RS in *Mobile phase*

Sample solution: 0.05 mg/mL of Midodrine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{12}H_{18}N_2O_4 \cdot HCl$ in the portion of Midodrine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.2%. A 1-g sample is used.

Organic Impurities

- **Procedure**

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

Standard solution: 1.0 µg/mL of USP Midodrine Hydrochloride RS and 2.0 µg/mL of USP Midodrine Related Compound A RS in *Mobile phase*

Sample solution: 1.0 mg/mL of Midodrine Hydrochloride in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay* except for the following:

Injection size: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between midodrine hydrochloride and midodrine hydrochloride related compound A

Tailing factor: NMT 2.0 for midodrine hydrochloride

Relative standard deviation: NMT 2.0% for both midodrine hydrochloride and midodrine related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of midodrine related compound A in the portion of Midodrine Hydrochloride taken:

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

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

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

C_S = concentration of USP Midodrine Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any individual impurity in the portion of Midodrine Hydrochloride 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 midodrine from the *Standard solution*

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

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

Acceptance criteria: See *Impurity Table 1*.

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Midodrine related compound A[a]	0.8	0.2%
Midodrine hydrochloride	1	—
Individual unspecified impurity	—	0.1%
Total impurities	—	0.5%

[a] 1-(2,5 Dimethoxyphenyl)-2-aminoethanol.

SPECIFIC TESTS

- **Water Determination, *Method I* ⟨921⟩:** NMT 0.5%
- **pH ⟨791⟩:** 4.0–5.0. Use 50 mg/mL of the midodrine hydrochloride sample.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers and store at room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Midodrine Hydrochloride RS

USP Midodrine Related Compound A RS

▲2-Amino-1-(2,5 Dimethoxyphenyl)ethanol.▲ (CN 1-Dec-2023)

$C_{10}H_{15}NO_3$ 197.23

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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