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Amiloride Hydrochloride Tablets

DEFINITION
Amiloride Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of amiloride hydrochloride ($C_6H_8ClN_7O \cdot HCl$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Change to read:

• **B.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2022)

ASSAY

Change to read:

• **Procedure**

Buffer: Dissolve 136 g of monobasic potassium phosphate in 800 mL of water. Adjust with phosphoric acid to a pH of 3.0. Dilute with water to 1000 mL.

Mobile phase: Methanol, water, and *Buffer* (25:71:4)

Standard stock solution: 1.0 mg/mL of USP Amiloride Hydrochloride RS in methanol

Standard solution: 0.1 mg/mL of USP Amiloride Hydrochloride RS from the *Standard stock solution*, prepared as follows. Transfer 5.0 mL of the *Standard stock solution* to a 50-mL volumetric flask. Add 10.0 mL of methanol and 2.0 mL of 0.1 N hydrochloric acid. Dilute with water to volume.

Sample solution: ▲Nominally 0.1 mg/mL of amiloride hydrochloride prepared as follows.▲ (USP 1-Dec-2022) Transfer an amount equivalent to 5 mg of amiloride hydrochloride, from finely powdered Tablets (NLT 20), to a 50-mL volumetric flask containing 15.0 mL of methanol and 2.0 mL of 0.1 N hydrochloric acid. Sonicate for 10 min, dilute with water to volume, sonicate for an additional 10 min, and filter.

Chromatographic system

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

Mode: LC

Detector: UV 286 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Dec-2022)

Column: 3.9-mm × 30-cm; ▲10-µm▲ (USP 1-Dec-2022) packing L1

Flow rate: 1 mL/min

Injection volume: 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 the labeled amount of amiloride hydrochloride ($C_6H_8ClN_7O \cdot HCl$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Instrumental conditions

Mode: UV

Analytical wavelength: 363 nm

Standard solution: A known concentration of USP Amiloride Hydrochloride RS in *Medium*. [Note—An amount of methanol not to exceed 2% of the total volume of the *Standard solution* may be used to dissolve the amiloride hydrochloride.]

Sample solution: Sample per *Dissolution ⟨711⟩*. Dilute with *Medium* as necessary.

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of the labeled amount of amiloride hydrochloride ($C_6H_8ClN_7O \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

D = dilution factor, if needed

L = label claim of amiloride hydrochloride (mg/Tablet)▲ (USP 1-Dec-2022)

Tolerances: NLT 80% (Q) of the labeled amount of amiloride hydrochloride ($C_6H_8ClN_7O \cdot HCl$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (USP 1-Dec-2022)

IMPURITIES

Change to read:

• **Organic Impurities**

Diluent: Methanol, 1 N hydrochloric acid, and water (40:4:56)

Buffer: 0.9 g/L of sodium 1-hexanesulfonate in water. Initially add water to about 90% of the volume of the flask, adjust with diluted phosphoric acid to a pH of 3.0 ± 0.1, and dilute with water to volume.

Mobile phase: Acetonitrile and *Buffer* (10:90)

Standard solution: 0.01 mg/mL of USP Amiloride Hydrochloride RS in *Diluent*

▲**Sensitivity solution:** 0.001 mg/mL of USP Amiloride Hydrochloride RS in *Diluent*, from the *Standard solution*▲ (USP 1-Dec-2022)

Sample solution: Nominally 2 mg/mL of amiloride hydrochloride in *Diluent* from powdered Tablets (NLT 20). Initially add methanol to fill about 40% of the volume of the flask and 1 N hydrochloric acid to about 4% of the volume of the flask. Sonicate for 10 min, dilute with water to volume, and sonicate for another 10 min. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 350 nm

Column: 4.6-mm × 15-cm; 4-µm packing L1

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution* ▲and *Sensitivity solution*▲ (USP 1-Dec-2022)

Suitability requirements

Relative standard deviation: NMT 3.0%, *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual 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 amiloride from the *Standard solution*

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

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

F = relative response factor (see *Table 1*) (USP 1-Dec-2022)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%. (USP 1-Dec-2022)

Table 1

Name	Relative Retention Time	Relative Response Factor (USP 1-Dec-2022)	Acceptance Criteria, NMT (%)
Amiloride acid (USP 1-Dec-2022) [a]	0.15	1.25	1.0 (USP 1-Dec-2022)
Amiloride related compound A (USP 1-Dec-2022) [b]	0.48	1.15	1.0 (USP 1-Dec-2022)
5-Hydroxyamiloride hydrochloride (USP 1-Dec-2022) [c]	0.56	1.15	1.0 (USP 1-Dec-2022)
Amiloride	1.00	— (USP 1-Dec-2022)	—
Any other unknown impurity	—	1.0 (USP 1-Dec-2022)	0.5
Total impurities[d]	—	— (USP 1-Dec-2022)	2.0

a 3,5-Diamino-6-chloropyrazine-2-carboxylic acid. (USP 1-Dec-2022)

b Methyl 3,5-diamino-6-chloropyrazine-2-carboxylate. (USP 1-Dec-2022)

c 3-Amino-*N*-carbamimidoyl-6-chloro-5-hydroxypyrazine-2-carboxamide hydrochloride. (USP 1-Dec-2022)

d Total impurities is the sum of all the impurities including process-related ones. (USP 1-Dec-2022)

ADDITIONAL REQUIREMENTS

Change to read:

- **Packaging and Storage:** Preserve in well-closed containers at controlled room temperature. (USP 1-Dec-2022)
- **USP Reference Standards** ⟨11⟩
  USP Amiloride Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
AMILORIDE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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