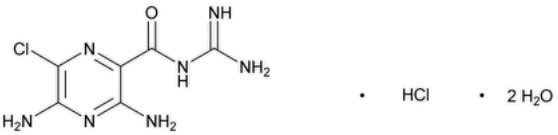
Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Aug-2022
Document Type: USP Monographs
DocId: GUID-D1CB8853-E10A-4EE9-B8FA-DF1C9D9543CC_5_en-US
DOI: https://doi.org/10.31003/USPNF_M2650_05_01
DOI Ref: nmt8h

Amiloride Hydrochloride

Change to read:



$C_6H_8ClN_7O \cdot HCl \cdot 2H_2O$ 302.12

Pyrazinecarboxamide, 3,5-diamino-*N*-(aminoiminomethyl)-6-chloro-, monohydrochloride dihydrate;
N-Amidino-3,5-diamino-6-chloropyrazinecarboxamide monohydrochloride dihydrate;
▲3,5-Diamino-*N*-carbamimidoyl-6-chloropyrazine-2-carboxamide hydrochloride dihydrate▲ (USP 1-Aug-2022) CAS RN®: 17440-83-4; UNII: FZJ37245UC.

▲Amiloride hydrochloride (anhydrous)

$C_6H_8ClN_7O \cdot HCl$ 266.09 CAS RN®: 2016-88-8; UNII: 7M458Q65S3.

Amiloride (free base)

$C_6H_8ClN_7O$ 229.63 CAS RN®: 2609-46-3; UNII: 7DZO8EB0Z3.▲ (USP 1-Aug-2022)

Change to read:

DEFINITION

Amiloride Hydrochloride contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-Aug-2022) of amiloride hydrochloride ($C_6H_8ClN_7O \cdot HCl$), calculated on the ▲anhydrous▲ (USP 1-Aug-2022) basis.

IDENTIFICATION

Change to read:

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M ▲or 197A▲ (USP 1-Aug-2022)

Change to read:

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

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements

ASSAY

Change to read:

• **Procedure**

▲**Mobile phase:** Dissolve 0.8 g of sodium 1-hexanesulfonate, monohydrate in 900 mL of water. Add 100 mL of acetonitrile. Adjust with phosphoric acid to a pH of 3.0.

Standard solution: 0.1 mg/mL of USP Amiloride Hydrochloride RS in *Mobile phase*

Sample solution: 0.1 mg/mL of Amiloride Hydrochloride in *Mobile Phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.0-mm × 12.5-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of amiloride

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amiloride hydrochloride ($C_6H_8ClN_7O \cdot HCl$) in the portion of Amiloride Hydrochloride 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 = concentration of Amiloride Hydrochloride in the *Sample solution* (mg/mL)▲ (USP 1-Aug-2022)

Acceptance criteria: 98.0%–▲102.0%▲ (USP 1-Aug-2022) on the ▲anhydrous▲ (USP 1-Aug-2022) basis

IMPURITIES

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

Change to read:

• **Organic Impurities**

▲**Mobile phase** and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 1 µg/mL each of USP Amiloride Hydrochloride RS and USP Amiloride Related Compound A RS in *Mobile phase*

Sensitivity solution: 0.5 µg/mL each of USP Amiloride Hydrochloride RS and USP Amiloride Related Compound A RS in *Mobile phase*, from *Standard solution*

Sample solution: 1 mg/mL of Amiloride Hydrochloride in *Mobile phase*

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 5.0% for amiloride and amiloride related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10 for amiloride and amiloride related compound A, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amiloride related compound A in the portion of Amiloride Hydrochloride taken:

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

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

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

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

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

Calculate the percentage of amiloride acid, 5-hydroxyamiloride, and any unspecified impurity in the portion of Amiloride Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of amiloride acid, 5-hydroxyamiloride, or any unspecified 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 = concentration of Amiloride Hydrochloride 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 (%)
Amiloride acid[a]	0.23	1.32	0.10
5-Hydroxyamiloride[b]	0.50	0.86	0.10
Amiloride related compound A	0.60	—	0.15
Amiloride	1.0	—	—
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0▲ (USP 1-Aug-2022)

[a] 3,5-Diamino-6-chloropyrazine-2-carboxylic acid.

[b] 3-Amino-*N*-carbamimidoyl-6-chloro-5-hydroxypyrazine-2-carboxamide.

SPECIFIC TESTS

• **Acidity**

Sample: 1.0 g

Analysis: Dissolve the *Sample* in 100 mL of a mixture of methanol and water (1:1). Titrate with 0.10 N sodium hydroxide to a potentiometric endpoint.

Acceptance criteria: NMT 0.30 mL is required (0.1% as hydrochloride).

Delete the following:

▲• **Loss on Drying**

(See *Thermal Analysis* ⟨891⟩.)

[Note—The quantity taken for the determination may be adjusted, if necessary, for instrument sensitivity.]

Sample: 10 mg

Analysis: Determine the percentage of volatile substances by thermogravimetric analysis on an appropriately calibrated instrument using the *Sample*. Heat the specimen at the rate of 10°/min between ambient temperature and 225° in an atmosphere of nitrogen at a flow rate of 40 mL/min. From the thermogram determine the accumulated loss in weight between ambient temperature and about 200° on the plateau.

Acceptance criteria: 11.0%–13.0%▲ (USP 1-Aug-2022)

Add the following:

▲• **Water Determination** ⟨921⟩, *Method I, Method Ia*

Sample: 0.2 g

Acceptance criteria: 11.0%–13.0%▲ (USP 1-Aug-2022)

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Amiloride Hydrochloride RS

▲ USP Amiloride Related Compound A RS

Methyl 3,5-diamino-6-chloropyrazine-2-carboxylate.

$C_6H_7ClN_4O_2$ 202.60▲ (USP 1-Aug-2022)

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

Topic/Question	Contact	Expert Committee
AMILORIDE HYDROCHLORIDE	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(6)

Current DocID: GUID-D1CB8853-E10A-4EE9-B8FA-DF1C9D9543CC_5_en-US
DOI: https://doi.org/10.31003/USPNF_M2650_05_01
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