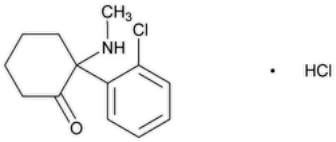
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Aug-2024
Document Type: USP Monographs
DocId: GUID-67E52145-1649-4C46-B824-8AEB1FD6DB9E_5_en-US
DOI: https://doi.org/10.31003/USPNF_M43960_05_01
DOI Ref: 9bwh7

Change to read:

Ketamine Hydrochloride

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-ketamine-hcl-20240726.

▲



▲ (RB 1-Aug-2024)

$C_{13}H_{16}ClNO \cdot HCl$ 274.19

Cyclohexanone, 2-(2-chlorophenyl)-2-(methylamino)-, hydrochloride;

(±)-2-(*o*-Chlorophenyl)-2-(methylamino)cyclohexanone hydrochloride CAS RN®: 1867-66-9; UNII: O18YUO0I83.

DEFINITION

Ketamine Hydrochloride contains NLT 98.0% and NMT 102.0% of ketamine hydrochloride ($C_{13}H_{16}ClNO \cdot HCl$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K. Do not dry specimens.

• **B.**

Acid solvent

Standard solution: 0.33 mg/mL of USP Ketamine Hydrochloride RS in 0.1 N hydrochloric acid

Sample solution: 0.33 mg/mL in 0.1 N hydrochloric acid

Acceptance criteria: Both solutions exhibit maxima and minima at the same wavelengths, and the respective absorptivities, at the wavelengths of maximum absorbance at 269 and 276 nm, do not differ by more than 3.0%.

Basic solvent

Standard solution: 0.8 mg/mL of USP Ketamine Hydrochloride RS in 0.01 N sodium hydroxide in a mixture of water and methanol (1 in 20)

Sample solution: 0.8 mg/mL in 0.01 N sodium hydroxide in a mixture of water and methanol (1 in 20)

Acceptance criteria: Both solutions exhibit maxima and minima at the same wavelengths, and the respective absorptivities, at the wavelengths of maximum absorbance at 302 nm, do not differ by more than 3.0%.

ASSAY

Change to read:

• **Procedure**

Buffer: Dissolve 5.75 g of monobasic ammonium phosphate in 1 L of water. Add 6 mL of triethylamine to each liter of this solution and adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Methanol and *Buffer* (35:65)

System suitability solution: 0.025 mg/mL each of USP Ketamine Hydrochloride RS and USP Ketamine Related Compound A RS in *Mobile phase*. Sonicate to dissolve, if necessary.

Standard solution: 0.2 mg/mL of USP Ketamine Hydrochloride RS in *Mobile phase*. Sonicate to dissolve, if necessary.

Sample solution: 0.2 mg/mL of Ketamine Hydrochloride in *Mobile phase*. Sonicate to dissolve, if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The order of elution is ketamine followed by ketamine related compound A]

Suitability requirements

Resolution: NLT 2.0 between ketamine and ketamine related compound A, *System suitability solution*

▲▲ (RB 1-Aug-2024)

Tailing factor: NMT 1.6 for ketamine, *System suitability solution*

Relative standard deviation: NMT 0.6%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ketamine hydrochloride ($C_{13}H_{16}ClNO \cdot HCl$) in the portion of Ketamine Hydrochloride taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A: Acetonitrile and water (25:75)

Mobile phase: Dissolve 0.95 g of sodium 1-hexanesulfonate in 1 L of *Solution A*. Add 4 mL of acetic acid to each liter of this solution.

Standard solution: 0.005 mg/mL each of USP Ketamine Hydrochloride RS and USP Ketamine Related Compound A RS in *Mobile phase*. Sonicate to dissolve, if necessary. Prepare immediately before use.

Sample solution: 1.0 mg/mL of Ketamine Hydrochloride in *Mobile phase*. Sonicate to dissolve, if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Columns

Guard: 4.0-mm × 4.0-mm

Analytical: 4.0-mm × 12.5-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The order of elution is ketamine followed by ketamine related compound A. The retention time of ketamine is between 3.0 and 4.5 min (if necessary, adjust the concentration of water and acetonitrile).]

Suitability requirements

Resolution: NLT 2.0 between ketamine and ketamine related compound A

Tailing factor: NMT 1.5

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any impurity in the portion of Ketamine 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 ketamine from the *Standard solution*

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Acceptance Criteria,

	NMT (%)
Ketamine related compound A	0.1
Any unknown impurity	0.3
Total impurities[a]	1.0

[a] Sum of all the unknown impurities.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 100 mg/mL of Ketamine Hydrochloride

Acceptance criteria: 3.5–4.1

• **Clarity and Color of Solution**

Sample solution: 200 mg/mL of Ketamine Hydrochloride in water

Acceptance criteria: The solution is clear and colorless.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed containers. ▲Store at controlled room temperature.▲ (RB 1-Aug-2024)

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Ketamine Hydrochloride RS

USP Ketamine Related Compound A RS

1-[(2-Chlorophenyl)(methylimino)methyl]cyclopentanol.

▲$C_{13}H_{16}ClNO$▲ (RB 1-Aug-2024) 237.73

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 29(6)

Current DocID: GUID-67E52145-1649-4C46-B824-8AEB1FD6DB9E_5_en-US

DOI: https://doi.org/10.31003/USPNF_M43960_05_01

DOI ref: 9bwh7