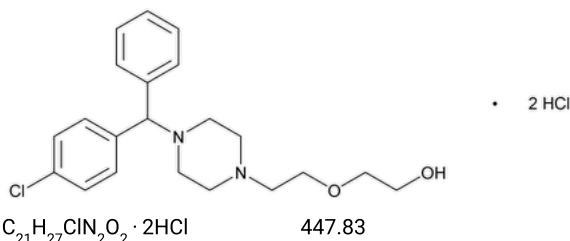


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Hydroxyzine Hydrochloride



Ethanol, 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]-, dihydrochloride, (±)-;
(±)-2-[2-[4-(p-Chloro-α-phenylbenzyl)-1-piperazinyl]ethoxy]ethanol dihydrochloride CAS RN®: 2192-20-3; UNII: 76755771U3.

DEFINITION
Hydroxyzine Hydrochloride contains NLT 98.0% and NMT 102.0% of hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$), calculated on the anhydrous basis.

IDENTIFICATION
• **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 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.

Change to read:

• **C.**
Sample solution: 2.5 mg/mL of Hydroxyzine Hydrochloride in [water](#)
Analysis: To 10 mL of the *Sample solution*, add 2 drops of [nitric acid](#) and 1 mL of [silver nitrate TS](#).
Acceptance criteria: A curdy, white precipitate, insoluble in [2 N nitric acid ▲TS](#) (USP 1-May-2022) but soluble in [6 N ammonium hydroxide](#), separates (presence of chloride).

ASSAY
• **PROCEDURE**
Solution A: [Trifluoroacetic acid](#) and [water](#) (0.1: 99.9)
Solution B: [Trifluoroacetic acid](#) and [acetonitrile](#) (0.05: 99.95)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
4	90	10
12	55	45
16	55	45
21	20	80
25	20	80
26	90	10
30	90	10

Diluent: [Acetonitrile](#) and [water](#) (30:70)

Standard solution: 0.05 mg/mL of [USP Hydroxyzine Hydrochloride RS](#) in *Diluent*

Sample solution: 0.05 mg/mL of Hydroxyzine Hydrochloride in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 230 nm

Column: 2.1-mm × 15-cm; 1.8-μm packing [L1](#)

Flow rate: 0.3 mL/min

Injection volume: 2 μL

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 hydroxyzine hydrochloride ($C_{21}H_{27}ClN_2O_2 \cdot 2HCl$) in the portion of Hydroxyzine Hydrochloride taken:

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

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

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

C_S = concentration of [USP Hydroxyzine Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.5%

Change to read:

- **ORGANIC IMPURITIES**

Solution A, Solution B, Mobile phase, and Diluent: Prepare as directed in the Assay.

Standard solution: 1.5 μg/mL each of [USP Hydroxyzine Hydrochloride RS](#), [USP Hydroxyzine Related Compound A RS](#), and [USP 4-Chlorobenzophenone RS](#) in *Diluent*

Sample solution: 500 μg/mL of Hydroxyzine Hydrochloride in *Diluent*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detectors

Decloxizine, hydroxyzine related compound A, and hydroxyzine: UV 230 nm

4-Chlorobenzophenone: UV 254 nm

Column: 2.1-mm × 15-cm; 1.8-μm packing [L1](#)

Flow rate: 0.3 mL/min

Injection volume: 2 μL

System suitability

Sample: *Standard solution*

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 5.0 between hydroxyzine related compound A and hydroxyzine

Relative standard deviation: NMT 3.0% for hydroxyzine related compound A, hydroxyzine, and 4-chlorobenzophenone

Analysis

Samples: *Standard solution* and *Sample solution*

For impurities detected at UV 230 nm

Calculate the percentage of hydroxyzine related compound A in the portion of Hydroxyzine Hydrochloride taken:

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

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

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