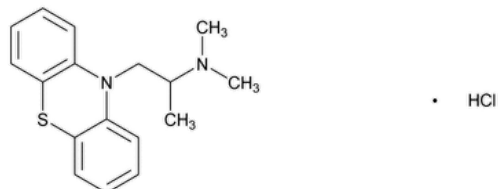


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Promethazine Hydrochloride



$C_{17}H_{20}N_2S \cdot HCl$ 320.88

10*H*-Phenothiazine-10-ethanamine, *N,N*, α -trimethyl-, monohydrochloride, ($\pm$);

($\pm$)-10-[2-(Dimethylamino)propyl]phenothiazine monohydrochloride CAS RN[®]: 58-33-3; UNII: R61ZE711I.

DEFINITION

Promethazine Hydrochloride contains NLT 97.0% and NMT 101.5% of promethazine hydrochloride ($C_{17}H_{20}N_2S \cdot HCl$), calculated on the dried basis.

[NOTE—Throughout the following procedures, protect the samples, the Reference Standards, and the solutions containing them, by conducting the procedures without delay under subdued light or using low-actinic glassware.]

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A or 197K
- **B. IDENTIFICATION TESTS—GENERAL (191), Chloride**
- **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Diluent: Dissolve 8.2 mL of [hydrochloric acid](#) in 1000 mL of water.

Mobile phase: Acetonitrile, water, and [triethylamine](#) (850:270:1)

System suitability stock solution: 1.2 mg/mL of [USP Promethazine Related Compound B RS](#) in *Diluent*. Sonicate to dissolve.

Standard solution: 0.1 mg/mL of [USP Promethazine Hydrochloride RS](#) in *Diluent*. Sonicate to dissolve.

System suitability solution: 0.09 mg/mL of [USP Promethazine Hydrochloride RS](#) and 0.12 mg/mL of [USP Promethazine Related Compound B RS](#) in *Diluent* from the *Standard solution* and *System suitability stock solution*, respectively

Sample solution: 0.1 mg/mL of Promethazine Hydrochloride in *Diluent*. Sonicate to dissolve.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm $\times$ 30-cm; 10- μ m packing L1

Flow rate: 2.5 mL/min

Injection volume: 20 μ L

Run time: NLT 2.5 times the retention time of promethazine

System suitability

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

[NOTE—The relative retention times for promethazine related compound B and promethazine are 0.82 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between promethazine and promethazine related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis**Samples:** *Standard solution* and *Sample solution*Calculate the percentage of promethazine hydrochloride ($C_{17}H_{20}N_2S \cdot HCl$) in the portion of Promethazine Hydrochloride taken:

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

 r_U = peak response from the *Sample solution* r_S = peak response from the *Standard solution* C_S = concentration of [USP Promethazine Hydrochloride RS](#) in the *Standard solution* (mg/mL) C_U = concentration of Promethazine Hydrochloride in the *Sample solution* (mg/mL)**Acceptance criteria:** 97.0%–101.5% on the dried basis**IMPURITIES**

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Change to read:

- **ORGANIC IMPURITIES**

Diluent: Methanol and [triethylamine](#) (999:1)**Buffer:** 3.7 g/L of [ammonium acetate](#) in water**Solution A:** Acetonitrile and *Buffer* (300:700)**Solution B:** Acetonitrile**Mobile phase:** See [Table 1](#).**Table 1**

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	60	40
18	60	40
18.1	100	0
25	100	0

System suitability stock solution: 0.5 mg/mL of [USP Promethazine Related Compound B RS](#) in *Diluent***Standard stock solution:** 0.5 mg/mL of [USP Promethazine Hydrochloride RS](#) in *Diluent***System suitability solution:** 5 µg/mL each of [USP Promethazine Hydrochloride RS](#) and [USP Promethazine Related Compound B RS](#) from the *Standard stock solution* and *System suitability stock solution*, respectively▲, in *Diluent*▲ (ERR 1-Sep-2022)**Standard solution:** 5 µg/mL of [USP Promethazine Hydrochloride RS](#) from the *Standard stock solution*▲ in *Diluent*▲ (ERR 1-Sep-2022)**Sensitivity solution:** 0.25 µg/mL of [USP Promethazine Hydrochloride RS](#) from the *Standard solution*▲ in *Diluent*▲ (ERR 1-Sep-2022)**Sample solution:** 0.5 mg/mL of Promethazine Hydrochloride in *Diluent***Chromatographic system**(See [Chromatography \(621\)](#), *System Suitability*.)**Mode:** LC**Detector:** UV 234 and 249 nm**Column:** 4.6-mm × 15-cm; 5-µm packing L1**Column temperature:** 30°**Flow rate:** 1.4 mL/min**Injection volume:** 15 µL**System suitability**