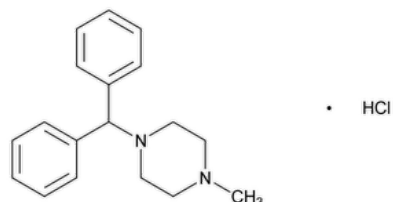


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## Cyclizine Hydrochloride



$C_{18}H_{22}N_2 \cdot HCl$  302.84

Piperazine, 1-(diphenylmethyl)-4-methyl-, monohydrochloride;

1-(Diphenylmethyl)-4-methylpiperazine monohydrochloride CAS RN<sup>®</sup>: 303-25-3; UNII: W001NHP4WE.

### DEFINITION

Cyclizine Hydrochloride contains NLT 98.0% and NMT 100.5% of cyclizine hydrochloride ( $C_{18}H_{22}N_2 \cdot HCl$ ), calculated on the dried basis.

### IDENTIFICATION

**Change to read:**

- A. [▲SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K▲](#) (CN 1-MAY-2020)
- B. [IDENTIFICATION TESTS—GENERAL, Chloride \(191\)](#): Meets the requirements

### ASSAY

#### PROCEDURE

[NOTE—In order to avoid overheating in the reaction medium, mix thoroughly throughout and stop the titration immediately after the endpoint has been reached.]

**Sample:** 120 mg

**Analysis:** Dissolve the *Sample* in 15 mL of anhydrous formic acid. Add 40 mL of acetic anhydride, and titrate with 0.1 N perchloric acid VS.

Perform a blank determination (see [Titrimetry \(541\)](#)), and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 15.14 mg of cyclizine hydrochloride ( $C_{18}H_{22}N_2 \cdot HCl$ ).

**Acceptance criteria:** 98.0%–100.5% on the dried basis

### IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%
- **ORGANIC IMPURITIES**

[NOTE—Prepare solutions immediately before use.]

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

**Impurity standard solution:** 0.25 mg/mL each of [USP Cyclizine Hydrochloride RS](#), [USP Cyclizine Related Compound A RS](#), and [USP Benzhydrol RS](#) in methanol

**Sample solution:** Prepare a solution containing 50 mg/mL of Cyclizine Hydrochloride by dissolving a suitable amount first in methanol, using 80% of the final volume, and then diluting with 1 N sodium hydroxide to volume.

#### Chromatographic system

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

**Mode:** GC

**Detector:** Flame ionization

**Column:** 0.33-mm × 25-m; coated with a 0.5-μm film of phase G27

#### Temperatures

**Injection port:** 250°

**Detector:** 290°

Column: See [Table 1](#).

**Table 1**

| Initial Temperature (°) | Temperature Ramp (°/min) | Final Temperature (°) | Hold Time at Final Temperature (min) |
|-------------------------|--------------------------|-----------------------|--------------------------------------|
| 100                     | 10                       | 240                   | 0                                    |
| 240                     | 15                       | 270                   | 14                                   |

**Carrier gas:** Helium

**Flow rate:** 1 mL/min

**Injection volume:** 1 µL

**Injection type:** Split ratio, 1:25

**System suitability**

**Sample:** *Impurity standard solution*

**Suitability requirements**

**Peak-to-valley ratio:** NLT 50 between cyclizine related compound A and methanol

**Analysis**

**Samples:** *Standard solution, Impurity standard solution, and Sample solution*

Calculate the percentage of cyclizine related compound A and benzhydrol in the portion of Cyclizine Hydrochloride taken:

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

$r_U$  = peak response of each related compound from the *Sample solution*

$r_S$  = peak response of the corresponding related compound from the *Impurity standard solution*

$C_S$  = concentration of the corresponding related compound in the *Impurity standard solution* (mg/mL)

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

Calculate the percentage of any other individual impurity in the portion of Cyclizine 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 cyclizine from the *Standard solution*

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

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

**Acceptance criteria:** See [Table 2](#). Disregard any peak below 0.05%.

**Table 2**

| Name                                              | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---------------------------------------------------|-------------------------|------------------------------|
| 1-Methylpiperazine (cyclizine related compound A) | 0.2                     | 0.5                          |
| Benzhydrol                                        | 0.7                     | 0.5                          |



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