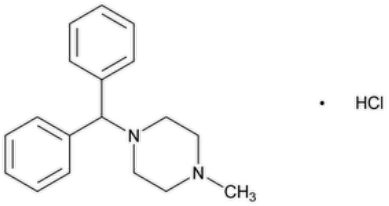
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-40F91509-FA70-4794-B6D1-076004511F5B_2_en-US
DOI: https://doi.org/10.31003/USPNF_M20950_02_01
DOI Ref: n6hs0

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®: 303-25-3; UNII: W0O1NHP4WE.

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

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cyclizine	1.0	—
Any other individual impurity	—	0.10
Total impurities	—	1.0

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 20 mg/mL in a mixture of alcohol and water (2:3)

Acceptance criteria: 4.5–5.5

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample at 120° for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Cyclizine Hydrochloride RS

USP Cyclizine Related Compound A RS

1-Methylpiperazine.

$C_5H_{12}N_2$ 100.16

USP Benzhydrol RS

Diphenylmethanol.

$C_{13}H_{12}O$ 184.23

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 38(2)

Current DocID: GUID-40F91509-FA70-4794-B6D1-076004511F5B_2_en-US

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