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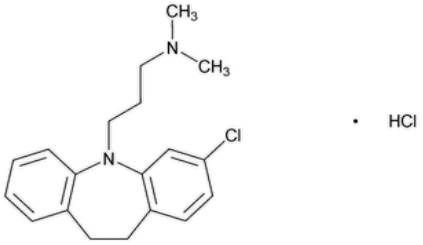
Clomipramine Hydrochloride



• HCl

$C_{19}H_{23}ClN_2 \cdot HCl$ 351.31

5*H*-Dibenz[*b*,*f*]azepine-5-propanamine, 3-chloro-10,11-dihydro-*N*,*N*-dimethyl-, monohydrochloride;

3-Chloro-5-[3-(dimethylamino)propyl]-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine monohydrochloride CAS RN®: 17321-77-6; UNII: 2LXW0L6GWJ.

DEFINITION

Clomipramine Hydrochloride contains NLT 98.0% and NMT 102.0% of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Change to read:

• **B.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Medium: 0.1 N hydrochloric acid

Solution: 100 µg/mL

Acceptance criteria: Absorptivities, calculated on the dried basis, do not differ by more than 1.0% at the wavelength of maximum absorbance.

ASSAY

• **Procedure**

Solution A: 55 g/L of sodium 1-heptanesulfonate prepared as follows. Transfer a suitable quantity of sodium 1-heptanesulfonate to an appropriate volumetric flask. Dissolve in 50% of the flask volume of water, and dilute with glacial acetic acid to volume.

Mobile phase: Transfer 20.0 mL of *Solution A* and 2.0 mL of triethylamine to a 500-mL volumetric flask, and dilute with water to volume. Transfer this solution to a 1-L volumetric flask, adjust with phosphoric acid to a pH of 3.2 ± 0.1, dilute with acetonitrile to volume, filter, and degas.

System suitability solution: 0.07 mg/mL of USP Desipramine Hydrochloride RS and 0.10 mg/mL of USP Imipramine Hydrochloride RS in methanol

Standard solution: 0.32 mg/mL of USP Clomipramine Hydrochloride RS in methanol

Sample solution: 0.32 mg/mL of Clomipramine Hydrochloride in methanol

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for desipramine and imipramine are 0.85 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 0.5 between desipramine and imipramine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clomipramine hydrochloride ($C_{19}H_{23}ClN_2 \cdot HCl$) in the portion of Clomipramine 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 Clomipramine Hydrochloride RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **ORGANIC IMPURITIES, PROCEDURE 1**

Solution A and **System suitability solution:** Proceed as directed in the *Assay*.

Mobile phase: Transfer 20.0 mL of *Solution A*, 2.0 mL of triethylamine, and 500 mL of water to a suitable container. Adjust with phosphoric acid to a pH of 3.2 ± 0.1, and dilute with water to 625 mL. Transfer to a 1-L volumetric flask, and dilute with acetonitrile to volume.

Sample solution: 2 mg/mL of Clomipramine Hydrochloride in methanol

Chromatographic system and **System suitability:** Proceed as directed in the *Assay*, except use an *Injection volume* of 5 µL.

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Clomipramine Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity

r_T = sum of all the peak responses

Acceptance criteria: See *Table 1*.

- **ORGANIC IMPURITIES, PROCEDURE 2**

Solution A, Mobile phase, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: 2 mg/mL of Clomipramine Hydrochloride in methanol

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Clomipramine Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity

r_T = sum of the responses of all the peaks

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any individual, unspecified impurity	—	0.5
Total impurities[a]	—	2.0

[a] Sum of all impurities from *Organic Impurities, Procedure 1* and *Organic Impurities, Procedure 2.*

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 100 mg/mL of Clomipramine Hydrochloride in water

Acceptance criteria: 3.5–5.0

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP Clomipramine Hydrochloride RS

USP Desipramine Hydrochloride RS

USP Imipramine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
CLOMIPRAMINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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