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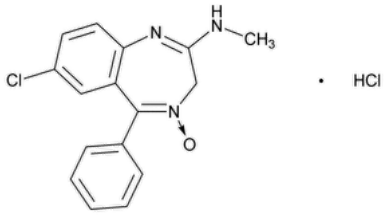
Chlordiazepoxide Hydrochloride



$C_{16}H_{14}ClN_3O \cdot HCl$ 336.22

3*H*-1,4-Benzodiazepin-2-amine, 7-chloro-*N*-methyl-5- phenyl-, 4-oxide, monohydrochloride;

7-Chloro-2-(methylamino)-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide monohydrochloride CAS RN®: 438-41-5; UNII: MFM6K1XWDK.

DEFINITION

Chlordiazepoxide Hydrochloride contains NLT 98.0% and NMT 102.0% of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

• **C.**

Solution A: 1 mg/mL of sodium nitrite in water

Solution B: 5 mg/mL ammonium sulfamate in water

Solution C: 1 mg/mL of *N*-(1-naphthyl)ethylenediamine dihydrochloride in water

Sample: 20 mg of Chlordiazepoxide Hydrochloride

Analysis: Add 5 mL of hydrochloric acid and 10 mL of water to the *Sample,* and heat to boiling to effect hydrolysis. Allow the solution to cool. Add 2 mL of *Solution A*, 1 mL of *Solution B*, and 1 mL of *Solution C*.

Acceptance criteria: A reddish-violet color is produced.

ASSAY

• **Procedure**

Use low-actinic glassware.

Mobile phase: Methanol and water (60:40)

Standard solution: 0.2 mg/mL of USP Chlordiazepoxide Hydrochloride RS in *Mobile phase*

Sample stock solution: 2 mg/mL of Chlordiazepoxide Hydrochloride in *Mobile phase* prepared as follows. Transfer a suitable portion of Chlordiazepoxide Hydrochloride to an appropriate volumetric flask, and dissolve in *Mobile phase*. Sonicate for 5 min, and dilute with *Mobile phase* to volume. Pass through a membrane filter of 0.5-µm or finer pore size.

Sample solution: 0.2 mg/mL of Chlordiazepoxide Hydrochloride from *Sample stock solution* in *Mobile phase*

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: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3600 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) in the portion of Chlordiazepoxide 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 Chlordiazepoxide Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Chlordiazepoxide 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**

Standard solution A: 100 µg/mL of USP Chlordiazepoxide Related Compound A RS in acetone

Standard solution B: 10 µg/mL of USP 2-Amino-5-chlorobenzophenone RS in acetone

Sample solution: Transfer 50.0 mg of Chlordiazepoxide Hydrochloride to a 10-mL conical flask, add 2.5 mL of acetone, and shake. Allow any undissolved particles to settle, and use the supernatant.

Chromatographic system

(See Chromatography ⟨621⟩.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel

Application volumes

Standard solution A and **Standard solution B:** 10 µL

Sample solution: 50 µL

Developing solvent system: Ethyl acetate

Spray reagent A: 2 N sulfuric acid

Spray reagent B: 1 mg/mL of sodium nitrite in water

Spray reagent C: 5 mg/mL of ammonium sulfamate in water

Spray reagent D: 1 mg/mL of *N*-(1-naphthyl)ethylenediamine dihydrochloride in water

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Develop the chromatogram in a chromatographic chamber (not previously saturated with the *Developing solvent system*) using the *Developing solvent system* until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by lightly spraying with *Spray reagent A*, drying at 105° for 15 min, and then spraying in succession with *Spray reagent B*, *Spray reagent C*, and *Spray reagent D*.

Acceptance criteria: Any spots from the *Sample solution* are not greater in size or intensity than the spots at the respective R_F values produced by the *Standard solutions*, corresponding to NMT 0.1% of chlordiazepoxide related compound A, and NMT 0.01% of 2-amino-5-chlorobenzophenone.

SPECIFIC TESTS

• **Melting Range or Temperature, *Class I* ⟨741⟩:** 212°–218°, with decomposition

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum over phosphorus pentoxide at 60° for 4 h.

Acceptance criteria: NMT 0.5%

• **Sterility Tests ⟨71⟩:** Where the label states that Chlordiazepoxide Hydrochloride is sterile, it meets the requirements

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Chlordiazepoxide Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 3.57 USP Endotoxin Units/mg of Chlordiazepoxide Hydrochloride.

• **Other Requirements:** Where the label states that Chlordiazepoxide Hydrochloride is sterile, it meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

• **USP Reference Standards ⟨11⟩**

USP 2-Amino-5-chlorobenzophenone RS	$C_{13}H_{10}ClNO$	231.68

USP Chlordiazepoxide Hydrochloride RS

USP Chlordiazepoxide Related Compound A RS

7-Chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one 4-oxide.

$C_{15}H_{11}ClN_2O_2$ 286.72

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

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

Chromatographic Database Information: Chromatographic Database

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