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Chlordiazepoxide Tablets

DEFINITION
Chlordiazepoxide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$).

IDENTIFICATION

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

• **B.**

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

Solution B: 5 mg/mL of ammonium sulfamate in water

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

Sample: Nominally 20 mg of chlordiazepoxide from a portion of finely powdered Tablets

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*, shake, add 1 mL of *Solution B*, shake for 2 min, and add 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 RS in *Mobile phase*

Sample solution: Nominally 0.2 mg/mL of chlordiazepoxide from NLT 20 Tablets prepared as follows. Finely powder NLT 20 Tablets, and transfer a portion of powder equivalent to 5 mg of chlordiazepoxide to a 25-mL volumetric flask. Add 20 mL of *Mobile phase*, sonicate for 5 min, dilute with *Mobile phase* to volume, and pass through a membrane filter of 5-µm pore size. Discard the first 5 mL of the filtrate.

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 the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$) in the portion of Tablets 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 RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of chlordiazepoxide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Simulated gastric fluid TS, prepared without pepsin; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: USP Chlordiazepoxide RS in *Medium*

Sample solution: Pass a portion of solution under test through a suitable filter. Dilute with *Medium,* if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: The wavelength of maximum absorbance at about 309 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$) dissolved.

Tolerances: NLT 85% (*Q*) of the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Standard solution A: 1 mg/mL of USP Chlordiazepoxide Related Compound A RS in acetone

Standard solution B: 100 µg/mL of USP 2-Amino-5-chlorobenzophenone RS in acetone

Sample solution: Transfer a portion of finely powdered Tablets equivalent to 25 mg of chlordiazepoxide 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: 20 µL

Standard solution B: 5 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*) in *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 4.0% of chlordiazepoxide related compound A, and NMT 0.1% of 2-amino-5-chlorobenzophenone.

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

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

USP Chlordiazepoxide 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 TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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