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Chlordiazepoxide Hydrochloride Capsules

DEFINITION

Change to read:

Chlordiazepoxide Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$).

▲Protect all solutions containing chlordiazepoxide from light.▲ (USP 1-Dec-2022)

IDENTIFICATION

Change to read:

• **A.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2022)

Change to read:

• **B.** ▲The UV spectrum of the chlordiazepoxide peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2022)

ASSAY

Change to read:

• **Procedure**

▲**Solution A:** 0.63 g/L of ammonium formate prepared as follows. Dissolve 2.52 g of ammonium formate in 4 L of water. Adjust with 98% formic acid to a pH of 3.0.

Solution B: Acetonitrile

Solution C: 0.1 N hydrochloric acid solution prepared as follows. To a 1-L volumetric flask containing about 400 mL of water, add 8.3 mL of hydrochloric acid and dilute with water to volume.

Solution D: Acetonitrile and *Solution C* (50:50)

Solution E: Transfer 12.0 mL of 10 N sodium hydroxide TS to a 100-mL volumetric flask containing about 40 mL of water. Dilute with water to volume.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
2.0	65	35
7.0	30	70
9.0	30	70
9.1	65	35
12.0	65	35

Diluent: *Solution D* and *Solution E* (96:4)

Standard solution: 50 µg/mL of USP Chlordiazepoxide Hydrochloride RS in *Diluent*

Sample solution: Nominally 50 µg/mL of chlordiazepoxide hydrochloride from Capsules (NLT 20) prepared as follows. Combine the contents of Capsules (NLT 20) in a suitable container and transfer a portion of the contents, equivalent to 5 mg of chlordiazepoxide hydrochloride, to a 100-mL volumetric flask. Dissolve in 80 mL of *Solution D* and sonicate for about 15 min. Add 4.0 mL of *Solution E* and dilute with *Solution*

D to volume. Centrifuge a portion of the resulting solution and use the supernatant within 10 h. [NOTE—Centrifuge speeds of 3750 rpm or 10,000 rpm for 10 min may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%▲ (USP 1-Dec-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) in the portion of Capsules 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* ▲(µg/mL)▲ (USP 1-Dec-2022)

C_U = nominal concentration of chlordiazepoxide hydrochloride in the *Sample solution*▲(µg/mL)▲ (USP 1-Dec-2022)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION ⟨711⟩**

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: ▲(*L*/900) mg/mL of▲ (USP 1-Dec-2022) USP Chlordiazepoxide Hydrochloride RS in *Medium*, ▲where *L* is the label claim, in mg/Capsule. Dilute with *Medium,* if necessary.▲ (USP 1-Dec-2022)

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

Instrumental conditions

Mode: UV

Analytical wavelength: ▲▲ (USP 1-Dec-2022) 245 nm

Cell: 1 cm

Blank: Remove the contents of 12 Capsules as completely as possible with the aid of a current of air. Dissolve the empty Capsule shells in 900 mL of *Medium.* Pass a portion of the resulting solution through a suitable filter. Dilute with *Medium,* if necessary, for consistency with the treatment of the *Sample solution.*

Analysis

Samples: *Standard solution* and *Sample solution*▲▲ (USP 1-Dec-2022)

▲Calculate▲ (USP 1-Dec-2022) the percentage of the labeled amount of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) dissolved:

$$\text{▲Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Chlordiazepoxide Hydrochloride RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

D = dilution factor of the *Sample solution*, if needed

L = label claim (mg/Capsule) ▲(USP 1-Dec-2022)

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

Change to read:

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

▲▲(USP 1-Dec-2022)

IMPURITIES

Change to read:

• **Organic Impurities**

▲**Solution A, Solution B, Solution C, Solution D, Solution E, Mobile phase,** and **Diluent:** Prepare as directed in the *Assay*.

Sensitivity solution: 0.025 µg/mL each of USP Chlordiazepoxide Hydrochloride RS and USP 2-Amino-5-chlorobenzophenone RS in *Diluent*

Standard solution: 1.5 µg/mL of USP Chlordiazepoxide Related Compound A RS and 0.05 µg/mL each of USP Chlordiazepoxide Hydrochloride RS and USP 2-Amino-5-chlorobenzophenone RS in *Diluent*

Sample solution: Nominally 50 µg/mL of chlordiazepoxide hydrochloride from Capsules (NLT 20) prepared as follows. Combine the contents of Capsules (NLT 20) in a suitable container, and transfer a portion of the contents, equivalent to 5 mg of chlordiazepoxide hydrochloride, to a 100-mL volumetric flask. Dissolve in 80 mL of *Solution D* and sonicate for about 15 min. Add 4.0 mL of *Solution E* and dilute with *Solution D* to volume. Centrifuge a portion of the resulting solution and use the supernatant within 4 h. [Note—Centrifuge speeds of 3750 rpm or 10,000 rpm for 10 min may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 5 between chlordiazepoxide and chlordiazepoxide related compound A, *Standard solution*

Relative standard deviation: NMT 5.0% each for chlordiazepoxide, 2-amino-5-chlorobenzophenone, and chlordiazepoxide related compound A, *Standard solution*

Signal-to-noise ratio: NLT 10 each for chlordiazepoxide and 2-amino-5-chlorobenzophenone, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of chlordiazepoxide related compound A, 2-amino-5-chlorobenzophenone, and each individual unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of chlordiazepoxide related compound A, 2-amino-5-chlorobenzophenone, or each individual unspecified degradation product from the *Sample solution*

r_S = peak response of chlordiazepoxide related compound A, 2-amino-5-chlorobenzophenone, or chlordiazepoxide from the *Standard solution*

C_S = concentration of USP Chlordiazepoxide Related Compound A RS, USP 2-Amino-5-chlorobenzophenone RS, or USP Chlordiazepoxide Hydrochloride RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.10%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Chlordiazepoxide	1.0	—
Chlordiazepoxide related compound A	2.0	3.0

[a] 2Total degradation products exclude chlordiazepoxide related compound A.		0.1
Any unspecified degradation product	—	0.2
Total degradation products[a]		1.0

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-Dec-2022)

Change to read:

• **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.

$C_{15}H_{11}ClN_2O_2$ ▲286.71▲ (USP 1-Dec-2022)

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

Topic/Question	Contact	Expert Committee
CHLORDIAZEPOXIDE HYDROCHLORIDE CAPSULES	Documentary Standards Support Associate Scientific Liaison.	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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