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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<sub>16</sub>H<sub>14</sub>ClN<sub>3</sub>O · 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**

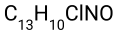
Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Chlordiazepoxide	1.0	—
Chlordiazepoxide related compound A	2.0	3.0

2 Total degradation products exclude chlordiazepoxide related compound A.		0.1
<b>ADDITIONAL REQUIREMENTS</b> Any unspecified degradation product	—	0.2
<b>Change to read:</b> • <b>Packaging and Storage:</b> Preserve in tight, light-resistant containers. ▲ Store at controlled room temperature. ▲ (USP 1-Dec-2022)c-2022)		

Change to read:

• **USP REFERENCE STANDARDS (11).**

[USP 2-Amino-5-chlorobenzophenone RS](#)

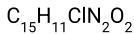


231.68

[USP Chlordiazepoxide Hydrochloride RS](#)

[USP Chlordiazepoxide Related Compound A RS](#)

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



▲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	<a href="#">Documentary Standards Support</a> Associate Scientific Liaison.	NBDS2020 Non-botanical Dietary Supplements

**Chromatographic Database Information:** [Chromatographic Database](#)

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