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Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules

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<https://www.uspnf.com/rb-chlordiazepoxide-hcl-clidinium-br-caps-20211104>.

DEFINITION

Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules contain NLT 90.0% and NMT 110.0% of the labeled amounts of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) and clidinium bromide ($C_{22}H_{26}BrNO_3$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

[NOTE—Use low-actinic glassware.]

Buffer: Dissolve 1.92 g of [sodium 1-pentanesulfonate](#) in 900 mL of [water](#) in a 1-L volumetric flask. Adjust with 1 N [sulfuric acid](#) to a pH of 3.8 $\pm$ 0.1. Dilute with [water](#) to volume.

Mobile phase: [Methanol](#), [tetrahydrofuran](#), and *Buffer* (6:24:70)

Diluent: [Methanol](#) and [water](#) (1:1)

Standard solution: 0.1 mg/mL of [USP Chlordiazepoxide Hydrochloride RS](#) and 0.05 mg/mL of [USP Clidinium Bromide RS](#) in *Diluent*

Sample solution: Weigh the contents of NLT 20 Capsules, and calculate the average weight per Capsule. Mix the combined contents of the Capsules, and transfer an amount equivalent to about 5 mg of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) to a 50-mL volumetric flask. Add about 25 mL of *Diluent*, sonicate for 5 min, and shake by mechanical means for 10 min. Dilute with *Diluent* to volume, and filter, discarding the first 20 mL of the filtrate.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 212 nm

Column: 8-mm $\times$ 10-cm; packing [L1](#)

Flow rate: 3 mL/min

Injection size: 20 μ L

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for clidinium bromide and chlordiazepoxide hydrochloride are about 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 5.0 between the clidinium bromide and chlordiazepoxide hydrochloride peaks

Relative standard deviation: NMT 2.0%

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 of chlordiazepoxide hydrochloride from the *Sample solution*

r_S = peak response of chlordiazepoxide hydrochloride from the *Standard solution*

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

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

Calculate the percentage of the labeled amount of clidinium bromide ($C_{22}H_{26}BrNO_3$) in the portion of Capsules taken:

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

r_U = peak response of clidinium bromide from the *Sample solution*

r_S = peak response of clidinium bromide from the *Standard solution*

C_S = concentration of [USP Clidinium Bromide RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION](#)  (RB-5-Nov-2021) [\(711\)](#).

▲ **Test 1:** Use [Dissolution \(711\), Procedure, Apparatus 1 and Apparatus 2, Immediate-release dosage forms, Procedure for a pooled sample for immediate-release dosage forms](#). ▲ (RB 5-Nov-2021)

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Buffer: Dissolve 1.92 g of [sodium 1-pentanesulfonate](#) in 900 mL of [water](#) in a 1-L volumetric flask. Adjust with [dilute sulfuric acid](#) to a pH of 3.8 ± 0.1 . Dilute with [water](#) to volume.

Mobile phase: [Methanol](#), [tetrahydrofuran](#), and *Buffer* (6:18:75)

Standard solution: Prepare a solution having known concentrations of [USP Chlordiazepoxide Hydrochloride RS](#) and [USP Clidinium Bromide RS](#) in *Medium*.

Sample solution: Pass a portion of the solution under test through a suitable filter. Combine equal volumes of the filtered solutions and use the pooled sample for the analysis. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*, if necessary.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 212 nm

Column: 4-mm × 25-cm; packing [L1](#)

Flow rate: 2 mL/min

Injection size: 100 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for clidinium bromide and chlordiazepoxide hydrochloride are about 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 5.0 between the clidinium bromide and chlordiazepoxide hydrochloride peaks

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the average percentage of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) or clidinium bromide ($C_{22}H_{26}BrNO_3$) dissolved:

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

r_U = peak response of chlordiazepoxide hydrochloride or clidinium bromide from the *Sample solution*

r_S = peak response of chlordiazepoxide hydrochloride or clidinium bromide from the *Standard solution*

C_S = concentration of [USP Chlordiazepoxide Hydrochloride RS](#) or [USP Clidinium Bromide RS](#) in the *Standard solution* (mg/mL)

L = chlordiazepoxide hydrochloride or clidinium bromide label claim (mg)

V = volume of *Medium* (mL), 900

Tolerances: NLT 75% (Q) each of the labeled amounts of chlordiazepoxide hydrochloride ($C_{16}H_{14}ClN_3O \cdot HCl$) and clidinium bromide ($C_{22}H_{26}BrNO_3$) are dissolved.

▲ **Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Protect the *Standard stock solution*, *Standard solution*, and *Sample solution* from light.

Medium: 0.1 N [hydrochloric acid](#); 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Buffer: Transfer 1.36 g of [monobasic potassium phosphate](#) to 1000 mL of [water](#). Add 1.0 mL of [triethylamine](#) and adjust with 25% phosphoric acid to a pH of 3.6.