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Chlordiazepoxide and Amitriptyline Hydrochloride Tablets

DEFINITION

Change to read:

Chlordiazepoxide and Amitriptyline Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$) and an amount of amitriptyline hydrochloride equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of amitriptyline ($C_{20}H_{23}N$).

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

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.

Add the following:

▲• **B.** The UV spectra of the chlordiazepoxide and amitriptyline peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.▲ (USP 1-Dec-2022)

ASSAY

Change to read:

• **PROCEDURE**

▲**Solution A:** Transfer 7.0 mL of [ammonium hydroxide](#) to an appropriate 1-L flask containing about 500 mL of [water](#). Dilute with [water](#) to volume.

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	65	35
1.2	65	35
25.0	35	65
25.1	65	35
30.0	65	35

Diluent: [Acetonitrile](#) and [water](#) (50:50)

Standard solution: 50 µg/mL of [USP Chlordiazepoxide RS](#) and 141 µg/mL of [USP Amitriptyline Hydrochloride RS](#) (equivalent to 125 µg/mL of amitriptyline) in *Diluent*

Sample stock solution: Nominally 0.1 mg/mL of chlordiazepoxide and nominally 0.25 mg/mL of amitriptyline from Tablets (NLT 20) prepared as follows. Finely powder Tablets (NLT 20) and transfer a portion of the powder equivalent to 5 mg of chlordiazepoxide and 12.5 mg of amitriptyline to a 50-mL volumetric flask. Add 80% of the flask volume of [acetonitrile](#), sonicate for about 15 min, and then mechanically shake for about 1 h. Dilute with [acetonitrile](#) to volume. Centrifuge a portion of the resulting solution and use the supernatant. [NOTE—A centrifuge speed of 3250 rpm for 10 min may be suitable.]

Sample solution: Nominally 50 µg/mL of chlordiazepoxide and nominally 125 µg/mL of amitriptyline from *Sample stock solution* in [water](#)

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: 2.1-mm × 15-cm; 3.5-µm packing [L1](#)

Column temperature: 30°**Flow rate:** 0.4 mL/min**Injection volume:** 5 µL**System suitability****Sample:** *Standard solution*

[NOTE—The relative retention times for chlordiazepoxide and amitriptyline are 1.0 and 5.5, respectively.]

Suitability requirements**Resolution:** NLT 2.0 between chlordiazepoxide and amitriptyline**Tailing factor:** NMT 1.5 for chlordiazepoxide; NMT 2.0 for amitriptyline**Relative standard deviation:** NMT 1.0% each for chlordiazepoxide and amitriptyline ▲ (USP 1-Dec-2022)**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 of chlordiazepoxide from the *Sample solution* r_S = peak response of chlordiazepoxide from the *Standard solution* C_S = concentration of [USP Chlordiazepoxide RS](#) in the *Standard solution* ▲ (µg/mL) ▲ (USP 1-Dec-2022) C_U = nominal concentration of chlordiazepoxide in the *Sample solution* ▲ (µg/mL) ▲ (USP 1-Dec-2022)Calculate the percentage of the labeled amount of amitriptyline ($C_{20}H_{23}N$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

 r_U = peak response of amitriptyline from the *Sample solution* r_S = peak response of amitriptyline from the *Standard solution* C_S = concentration of [USP Amitriptyline Hydrochloride RS](#) in the *Standard solution* ▲ (µg/mL) ▲ (USP 1-Dec-2022) C_U = nominal concentration of amitriptyline in the *Sample solution* ▲ (µg/mL) ▲ (USP 1-Dec-2022) M_{r1} = molecular weight of amitriptyline, 277.40 M_{r2} = molecular weight of amitriptyline hydrochloride, 313.87**Acceptance criteria:** 90.0%–110.0% each of the labeled amounts of chlordiazepoxide ($C_{16}H_{14}ClN_3O$) and amitriptyline ($C_{20}H_{23}N$)**PERFORMANCE TESTS****Change to read:**• [DISSOLUTION \(711\)](#)**Medium:** [Simulated gastric fluid TS](#), prepared without [pepsin](#); 900 mL**Apparatus 1:** 100 rpm**Time:** 30 min**Standard solution A:** [USP Chlordiazepoxide RS](#) in *Medium***Standard solution B:** [USP Amitriptyline Hydrochloride 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 wavelengths:** 239 and 309 nm**Blank:** *Medium***Analysis****Samples:** *Standard solution A*, *Standard solution B*, *Sample solution*, and *Blank*Calculate the percentage of the labeled amount of chlordiazepoxide ($C_{16}H_{14}ClN_3O$) in the portion of Tablets ▲ dissolved: ▲ (USP 1-Dec-2022)

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

 A_U = absorbance from the *Sample solution*, 309 nm A_S = absorbance from *Standard solution A*, 309 nm