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Alprazolam Tablets

DEFINITION

Alprazolam Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$).

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.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 0.77 g/L of ammonium acetate prepared as follows. Dissolve 0.77 g of ammonium acetate in each liter of water and adjust with acetic acid to a pH of 4.7.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
2.5	60	40
9.0	5	95
9.1	60	40
11.0	60	40

Diluent: Acetonitrile and water (40:60)

System suitability solution: 50 µg/mL of USP Alprazolam RS, 1 µg/mL of USP Alprazolam Related Compound A RS, and 1 µg/mL of USP Chlordiazepoxide Related Compound A RS in *Diluent*

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

Sample solution: Nominally 50 µg/mL of alprazolam from Tablets prepared as follows. Transfer a suitable portion of powder from NLT 10 Tablets to an appropriate volumetric flask. Add 80% of the total flask volume of *Diluent*. Sonicate for NLT 10 min. Dilute with *Diluent* to volume. Centrifuge a portion and use the clear supernatant. [Note—The use of a centrifuge speed of 3500 rpm for 10 min may be suitable.]

Chromatographic system

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

Mode: LC

Detector: UV 260 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 3-µm packing L7

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for chlordiazepoxide related compound A, alprazolam related compound A, and alprazolam are 0.7, 0.8, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between chlordiazepoxide related compound A and alprazolam related compound A, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$) 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 Alprazolam RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩, *Procedure, Apparatus 1 and Apparatus 2, Immediate-release dosage forms, Procedure for a pooled sample for immediate-release dosage forms*

Buffer stock solution: Dissolve 80 g of monobasic potassium phosphate and 20 g of dibasic potassium phosphate in 1 L of water. Add, with mixing, phosphoric acid or potassium hydroxide solution (45 in 100), as necessary to adjust the solution, such that the resulting solution has a pH of 6.0 ± 0.1.

Buffer: Prepare a 1-in-10 dilution of the *Buffer stock solution* to obtain a solution that has a pH of 6.0 ± 0.1.

Medium: *Buffer*; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Mobile phase: Acetonitrile, tetrahydrofuran, and *Buffer* (35:5:60)

Standard stock solution: 0.05 mg/mL of USP Alprazolam RS in methanol

Standard solution: Add 50 mL of *Buffer stock solution* and 250 mL of water to a 500-mL flask. Add to the flask 5.0 mL of *Standard stock solution* for every 0.25 mg of alprazolam contained in the Tablet being assayed. Dilute with water to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 10-cm; packing L7

Flow rate: 1 mL/min

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 500 theoretical plates

Relative standard deviation: NMT 3.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$) dissolved.

Tolerances: NLT 80% (*Q*) of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$) is dissolved.

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩**:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Mobile phase: Acetonitrile, chloroform, butyl alcohol, glacial acetic acid, and water (850: 80: 50: 0.5: 20)

Internal standard solution: 0.032 mg/mL of triazolam in acetonitrile

Standard solution: 0.025 mg/mL of USP Alprazolam RS in *Internal standard solution*

Sample solution: Transfer 1 Tablet to a container. Add 0.4 mL of water directly onto the Tablet, allow the Tablet to stand for 2 min, and then swirl the container to disperse the Tablet. For every 0.25 mg of alprazolam contained in the Tablet, add 10.0 mL of *Internal standard solution* to the container. Shake, and centrifuge if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 30-cm; packing L3

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between triazolam and alprazolam

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of alprazolam ($C_{17}H_{13}ClN_4$) in the Tablet taken:

$$\text{Result} = (R_U/R_S) \times C \times V \times (100/L)$$

R_U = peak area response ratio of alprazolam relative to the internal standard from the *Sample solution*

R_S = peak area response ratio of alprazolam relative to the internal standard from the *Standard solution*

C = concentration of USP Alprazolam RS in the *Standard solution* (mg/mL)

V = volume of the *Internal standard solution* used to prepare the *Sample solution* (mL)

L = label claim (mg/Tablet)

▲▲ (CN 1-Aug-2023)

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **USP Reference Standards** (11)

USP Alprazolam RS

USP Alprazolam Related Compound A RS

2-(2-Acetylhydrazino)-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine.

$C_{17}H_{15}ClN_4O$ 326.78

USP Chlordiazepoxide Related Compound A RS

7-Chloro-2-oxo-5-phenyl-2,3-dihydro-1*H*-benzo[e][1,4]diazepine 4-oxide;
Also known as 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

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

Topic/Question	Contact	Expert Committee
ALPRAZOLAM TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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