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Clonazepam Tablets

DEFINITION

Clonazepam Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clonazepam ($C_{15}H_{10}ClN_3O_3$).

IDENTIFICATION

Change to read:

• **A.** ▲The UV spectrum of the major peak of the *Identification sample solution* corresponds to that of the *Identification standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

Buffer: 6.6 g/L of ▲▲ (USP 1-May-2021) dibasic ammonium phosphate prepared as follows. Transfer a suitable amount of ▲▲ (USP 1-May-2021) dibasic ammonium phosphate to an appropriate volumetric flask. Add 95% of the flask volume of water and adjust with 1 N phosphoric acid ▲TS▲ (USP 1-May-2021) or 1 N sodium hydroxide ▲VS▲ (USP 1-May-2021) to a pH of 8.0. Dilute with water to volume.

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (52:13:60)

Diluent: Methanol, tetrahydrofuran, and water (52:13:60)

System suitability solution: ▲40 (µg/mL)▲ (USP 1-May-2021) each of USP Clonazepam Related Compound A RS, USP Clonazepam Related Compound B RS, and USP Clonazepam RS in *Diluent*

Standard solution: ▲100 (µg/mL)▲ (USP 1-May-2021) of USP Clonazepam RS in *Diluent*

▲**Identification standard solution:** 40 µg/mL of USP Clonazepam RS from the *Standard solution* in *Diluent*. [Note—This solution is used for *Identification A*.]▲ (USP 1-May-2021)

Sample solution: Nominally ▲100 (µg/mL)▲ (USP 1-May-2021) of clonazepam from Tablets prepared as follows. Finely powder NLT 10 Tablets. Transfer a portion of powder equivalent to 10 mg of clonazepam to a 100-mL volumetric flask, and dissolve, with sonication, in 75 mL of *Diluent*. Cool to room temperature, dilute with *Diluent* to volume, mix, and filter, discarding the first few milliliters of the filtrate.

▲**Identification sample solution:** Nominally 40 µg/mL of clonazepam from the *Sample solution* in *Diluent*. [Note—This solution is used for *Identification A*.]▲ (USP 1-May-2021)

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. ▲For *Identification A*, use a diode array detector in the range of 220–400 nm.▲ (USP 1-May-2021)

Column: 4.6-mm × 15-cm; ▲5-µm▲ (USP 1-May-2021) packing L7

Flow rate: 1 mL/min

Injection volume: 50 µL

▲**Run time:** NLT 3 times the retention time of clonazepam▲ (USP 1-May-2021)

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between clonazepam related compound A and clonazepam related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: ▲NMT 1.0%,▲ (USP 1-May-2021) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clonazepam ($C_{15}H_{10}ClN_3O_3$) in the portion of Tablets taken:

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

r_U = peak response for clonazepam from the *Sample solution*

r_S = peak response for clonazepam from the *Standard solution*

C_S = concentration of USP Clonazepam RS in the *Standard solution* ▲(µg/mL)▲ (USP 1-May-2021)

C_U = nominal concentration of clonazepam in the *Sample solution* ▲(µg/mL)▲ (USP 1-May-2021)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL, degassed

Apparatus 2: 75 rpm

Time: 45 min

Mobile phase: Methanol, acetonitrile, and water (30:30:40)

▲**Standard stock solution:** 0.05 mg/mL of USP Clonazepam RS in methanol▲ (USP 1-May-2021)

Standard solution: ▲(*L*/900) mg/mL of USP Clonazepam RS from *Standard stock solution* in *Medium* where *L* is the label claim in mg/Tablet▲ (USP 1-May-2021)

Sample solution: Use a portion of the solution under test.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm; ▲10-µm▲ (USP 1-May-2021) packing L1

Flow rate: 1 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of the labeled amount of clonazepam ($C_{15}H_{10}ClN_3O_3$) dissolved in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

r_U = peak response of clonazepam from the *Sample solution*

r_S = peak response of clonazepam from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)▲ (USP 1-May-2021)

Tolerances: NLT 75% (*Q*) of the labeled amount of clonazepam ($C_{15}H_{10}ClN_3O_3$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

• **Procedure**

Buffer, Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** ▲▲ (USP 1-May-2021) Proceed as directed in the *Assay*.

▲**Sensitivity solution:** 0.1 µg/mL of USP Clonazepam RS in *Diluent*

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between clonazepam related compound A and clonazepam related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-May-2021)

Analysis

Samples: *Sample solution*▲and *Standard solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Clonazepam RS in the *Standard solution* (µg/mL)

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

F = relative response factor (see *Table 1*)▲ (USP 1-May-2021)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is 0.1%.▲ (USP 1-May-2021)

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Unknown impurity▲[a]▲ (USP 1-May-2021)	0.7	▲0.41▲ (USP 1-May-2021)	0.8
Clonazepam	1.0	—	—
Clonazepam related compound A	2.2	▲0.54▲ (USP 1-May-2021)	0.4
Clonazepam related compound B	2.5	▲1.1▲ (USP 1-May-2021)	1.0
Any other impurity	—	▲1.0▲ (USP 1-May-2021)	0.2
Total impurities[b]	—	—	0.5

May not be present in all formulations.

[b] Clonazepam related compound A, clonazepam related compound B, and the unknown impurity with a relative retention time of 0.7 are not included in the total impurities.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. ▲Store at controlled room temperature.▲ (USP 1-May-2021)

• **USP Reference Standards** ⟨11⟩

USP Clonazepam RS

USP Clonazepam Related Compound A RS

3-Amino-4-(2-chlorophenyl)-6-nitrocarbostyril.

$C_{15}H_{10}ClN_3O_3$ 315.72

USP Clonazepam Related Compound B RS

2-Amino-2'-chloro-5-nitrobenzophenone.

$C_{13}H_9ClN_2O_3$ 276.68

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

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

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