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Clonazepam Orally Disintegrating Tablets

DEFINITION

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

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**

Mobile phase: Acetonitrile, methanol, and water (25:25:50)

Standard solution: 0.01 mg/mL of USP Clonazepam RS in *Mobile phase*

Sample solution: Nominally 0.01 mg/mL of clonazepam in *Mobile phase* prepared as follows. Transfer an equivalent to about 2 mg of clonazepam, from finely powdered Tablets (NLT 20), to a 200-mL volumetric flask. Add 120 mL of *Mobile phase* and sonicate for about 15 min with intermittent shaking. Shake the flask on a mechanical shaker for about 30 min. Dilute with *Mobile phase* to volume. Pass a portion of this solution through a nylon membrane filter of 0.45-µm or finer pore size. Use the filtrate after discarding the first 4 mL. This solution is stable for 48 h at room temperature.

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 210–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 60 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

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

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

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)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩:** NMT 60 s

• **Dissolution ⟨711⟩**

Medium: Water; 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 60 min

Mobile phase, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* except for *Injection volume*.

Injection volume: 100 µL

Standard stock solution: 0.01 mg/mL of USP Clonazepam RS in *Mobile phase*

Standard solution: Dilute the *Standard stock solution* with *Medium* according to the Tablet strength. See *Table 1* for the concentration of the *Standard solution* corresponding to each Tablet strength.

Table 1

Tablet Strength (mg/Tablet)	Standard Solution (µg/mL of clonazepam)
0.125	0.125
0.25	0.25
0.5	0.50
1.0	1.0
2.0	2.0

Sample solution: Pass a portion of the solution under test through a nylon membrane filter of 0.45-µm pore size, discarding the first few milliliters.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clonazepam ($C_{15}H_{10}ClN_3O_3$) dissolved:

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

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)

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

• **Organic Impurities**

Mobile phase: Proceed as directed in the *Assay*.

System suitability solution: 0.2 µg/mL each of USP Clonazepam Related Compound A RS and USP Clonazepam Related Compound B RS in *Mobile phase*

Standard stock solution: Use the *Standard solution* from the *Assay*.

Standard solution: 0.2 µg/mL of USP Clonazepam RS from the *Standard stock solution* in *Mobile phase*

Sample solution: Nominally 0.1 mg/mL of clonazepam from Tablets prepared as follows. Transfer an equivalent to about 2 mg of clonazepam, from finely powdered Tablets (NLT 20), to a 50-mL volumetric flask. Pipet 20.0 mL of *Mobile phase* into the flask, and sonicate for about 2 min with intermittent shaking. Do not dilute to volume. Shake the flask for 30 min on a mechanical shaker. Pass a portion of this solution through a nylon membrane filter of 0.45-µm or finer pore size, and use the filtrate after discarding the first 4 mL of the filtrate.

Chromatographic system: Proceed as directed in the *Assay* except for *Injection volume*.

Injection volume: 100 µL

Run time: NLT 4 times the retention time of clonazepam

System suitability

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

Suitability requirements

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

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 6.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample 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 of each impurity 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)

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any peaks with a relative retention time less than 0.63.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Clonazepam	1.0	—	—
Clonazepam related compound A	1.71	0.67	0.4
Clonazepam related compound B	2.25	0.79	1.0
Any other unspecified degradation product	—	1.0	0.2
Total impurities	—	—	2.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store at controlled room temperature.
- **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

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

Chromatographic Database Information: Chromatographic Database

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