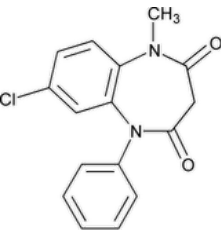


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Add the following:

**^Clobazam**



$C_{16}H_{13}ClN_2O_2$       300.74  
 1*H*-1,5-Benzodiazepine-2,4(3*H*,5*H*)-dione, 7-chloro-1-methyl-5-phenyl-;  
 7-Chloro-1-methyl-5-phenyl-1*H*-1,5-benzodiazepine-2,4-(3*H*,5*H*)-dione;  
 7-Chloro-1-methyl-5-phenyl-1,5-dihydro-2*H*-benzo[*b*][1,4]diazepine-2,4(3*H*)-dione    CAS RN<sup>®</sup>: 22316-47-8; UNII: 2MRO291B4U.

**DEFINITION**  
 Clobazam contains NLT 97.0% and NMT 103.0% of clobazam ( $C_{16}H_{13}ClN_2O_2$ ), calculated on the dried basis.

**IDENTIFICATION**  
 • **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197K or 197A  
 • **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**  
 • **PROCEDURE**  
**Solution A:** Transfer 1.0 mL of [phosphoric acid](#) to a 1-L volumetric flask containing about 950 mL of [water](#). Dilute with [water](#) to volume.  
**Solution B:** [Acetonitrile](#) and *Solution A* (30:70)  
**Solution C:** [Acetonitrile](#) and *Solution A* (80:20)  
**Mobile phase:** See [Table 1](#).

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
25	0	100
25.1	100	0
32	100	0

**Diluent:** [Acetonitrile](#) and [water](#) (60:40)  
**Standard stock solution:** 0.5 mg/mL of [USP Clobazam RS](#) prepared as follows. Transfer a suitable amount of [USP Clobazam RS](#) to an appropriate volumetric flask and dissolve in 60% of the flask volume of [acetonitrile](#). Dilute with [water](#) to volume.  
**Standard solution:** 0.125 mg/mL of [USP Clobazam RS](#) from the *Standard stock solution* in *Diluent*  
**Sample stock solution:** 0.5 mg/mL of Clobazam prepared as follows. Transfer a suitable amount of Clobazam to an appropriate volumetric flask and dissolve in 60% of the flask volume of [acetonitrile](#). Dilute with [water](#) to volume.  
**Sample solution:** 0.125 mg/mL of Clobazam from the *Sample stock solution* in *Diluent*

# Chromatographic system

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

**Mode:** LC

**Detector:** UV 230 nm

**Column:** 4.6-mm × 25-cm; 5-μm packing [L1](#)

**Autosampler temperature:** 20°

**Flow rate:** 1 mL/min

**Injection volume:** 5 μL

## System suitability

**Sample:** *Standard solution*

### Suitability requirements

**Tailing factor:** 0.8–1.5

**Relative standard deviation:** NMT 1.10%

## Analysis

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

Calculate the percentage of clobazam (C<sub>16</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>2</sub>) in the portion of Clobazam taken:

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

$r_U$  = peak response of clobazam from the *Sample solution*

$r_S$  = peak response of clobazam from the *Standard solution*

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

$C_U$  = concentration of Clobazam in the *Sample solution* (mg/mL)

**Acceptance criteria:** 97.0%–103.0% on the dried basis

## IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

• **ORGANIC IMPURITIES**

**Solution A, Solution B, Solution C, Diluent, and Chromatographic system:** Proceed as directed in the Assay.

**Mobile phase:** See [Table 2](#).

**Table 2**

Time (min)	Solution B (%)	Solution C (%)
0	100	0
25	0	100
35	0	100
35.1	100	0
42	100	0

**Sensitivity solution:** 0.25 μg/mL of [USP Clobazam RS](#) in *Diluent*

**Standard stock solution:** 50 μg/mL each of [USP Clobazam RS](#), [USP Clobazam Related Compound A RS](#), [USP Clobazam Related Compound E RS](#), and [USP Clobazam Related Compound G RS](#) in [acetonitrile](#)

**Standard solution:** 0.5 μg/mL each of [USP Clobazam RS](#), [USP Clobazam Related Compound A RS](#), [USP Clobazam Related Compound E RS](#), and [USP Clobazam Related Compound G RS](#) from the *Standard stock solution* in *Diluent*

**Sample solution:** 500 μg/mL of Clobazam prepared as follows. Transfer a suitable amount of Clobazam to an appropriate volumetric flask and dissolve in 60% of the flask volume of [acetonitrile](#). Dilute with [water](#) to volume.

## System suitability

**Samples:** *Sensitivity solution* and *Standard solution*

[NOTE—See [Table 3](#) for the relative retention times.]

**Suitability requirements**

**Resolution:** NLT 4.0 between clobazam related compound A and clobazam, *Standard solution*

**Tailing factor:** NMT 2.0 each for clobazam, clobazam related compound A, clobazam related compound E, and clobazam related compound G, *Standard solution*

**Relative standard deviation:** NMT 5.0% each for clobazam, clobazam related compound A, clobazam related compound E, and clobazam related compound G, *Standard solution*

**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*

**Analysis**

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

Calculate the percentage of clobazam related compound A, clobazam related compound E, and clobazam related compound G in the portion of Clobazam taken:

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

$r_U$  = peak response of clobazam related compound A, clobazam related compound E, or clobazam related compound G from the *Sample solution*

$r_S$  = peak response of clobazam related compound A, clobazam related compound E, or clobazam related compound G from the *Standard solution*

$C_S$  = concentration of [USP Clobazam Related Compound A RS](#), [USP Clobazam Related Compound E RS](#), or [USP Clobazam Related Compound G RS](#) in the *Standard solution* (µg/mL)

$C_U$  = concentration of Clobazam in the *Sample solution* (µg/mL)

Calculate the percentage of any other specified and unspecified impurity in the portion of Clobazam taken:

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

$r_U$  = peak response of any other specified or unspecified impurity from the *Sample solution*

$r_S$  = peak response of clobazam from the *Standard solution*

$C_S$  = concentration of [USP Clobazam RS](#) in the *Standard solution* (µg/mL)

$C_U$  = concentration of Clobazam in the *Sample solution* (µg/mL)

$F$  = relative response factor (see [Table 3](#))

**Acceptance criteria:** See [Table 3](#). The reporting threshold is 0.05%.

**Table 3**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Clobazam related compound G	0.38	—	0.15
Deschloroclobazam <sup>a</sup>	0.74	1.0	0.2
Clobazam related compound A	0.79	—	0.2
Clobazam	1.00	—	—
3-Methylclobazam <sup>b</sup>	1.19	1.0	0.2
3,3-Dimethylclobazam <sup>c</sup>	1.39	0.80	0.2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Clobazam related compound E	1.45	—	0.2
Malonate analog <sup>d</sup>	1.49	0.29	0.2
Any unspecified impurity	—	1.0	0.10
Total impurities <sup>e</sup>	—	—	1.0

- <sup>a</sup> 1-Methyl-5-phenyl-1,5-dihydro-2*H*-benzo[*b*][1,4]diazepine-2,4(3*H*)-dione.  
<sup>b</sup> 7-Chloro-1,3-dimethyl-5-phenyl-1,5-dihydro-2*H*-benzo[*b*][1,4]diazepine-2,4(3*H*)-dione.  
<sup>c</sup> 7-Chloro-1,3,3-trimethyl-5-phenyl-1,5-dihydro-2*H*-benzo[*b*][1,4]diazepine-2,4(3*H*)-dione.  
<sup>d</sup> Methyl 3-[(4-chloro-2-(phenylamino)phenyl](methylamino)-3-oxopropanoate.  
<sup>e</sup> Not including clobazam related compound A.

SPECIFIC TESTS

- [Loss on Drying \(731\)](#)

**Analysis:** Dry at 105° for 1 h.

**Acceptance criteria:** NMT 0.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Store at controlled room temperature.

- [USP REFERENCE STANDARDS \(11\)](#)

[USP Clobazam RS](#)

[USP Clobazam Related Compound A RS](#)

8-Chloro-1-phenyl-1,5-dihydro-2*H*-benzo[*b*][1,4]diazepine-2,4(3*H*)-dione.



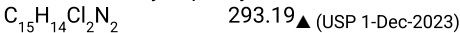
[USP Clobazam Related Compound E RS](#)

*N*-[4-chloro-2-(phenylamino)phenyl]-*N*-methylacetamide.



[USP Clobazam Related Compound G RS](#)

6-Chloro-2,3-dimethyl-1-phenyl-1*H*-benzimidazol-3-ium chloride.



**Auxiliary Information** - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
CLOBAZAM	<a href="#">Documentary Standards Support</a>	SM42020 Small Molecules 4

**Chromatographic Database Information:** [Chromatographic Database](#)

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