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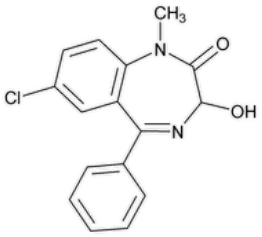
Temazepam



$C_{16}H_{13}ClN_2O_2$ 300.74

2*H*-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-3- hydroxy-1-methyl-5-phenyl-;

7-Chloro-1,3-dihydro-3-hydroxy-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one CAS RN®: 846-50-4; UNII: CHB1QD2QSS.

DEFINITION

Temazepam contains NLT 98.0% and NMT 102.0% of temazepam ($C_{16}H_{13}ClN_2O_2$), calculated on the dried basis. [**Caution—**Temazepam is a potent sedative; its powder should not be inhaled.]

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

• **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: 3.9 g/L of ammonium acetate in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*. [Note—Gradient based on a dwell volume of 1.0 mL.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
13	70	30
25	30	70
28	30	70
33	70	30
35	70	30

Diluent: Acetonitrile and *Solution A* (30:70)

System suitability solution: 0.1 mg/mL each of USP Temazepam RS, USP Temazepam Related Compound A RS, USP Temazepam Related Compound F RS, and USP Temazepam Related Compound G RS prepared as follows. Transfer suitable quantities of each USP Reference

Standard to a suitable volumetric flask. Dissolve in 30% of the flask volume of acetonitrile. Dilute with *Solution A* to volume.

Standard stock solution: 0.5 mg/mL of USP Temazepam RS prepared as follows. Transfer a suitable quantity of USP Temazepam RS to a suitable volumetric flask. Dissolve in 30% of the flask volume of acetonitrile. Dilute with *Solution A* to volume.

Standard solution: 0.1 mg/mL from *Standard stock solution* in *Diluent*

Sample stock solution: 0.5 mg/mL of Temazepam prepared as follows. Transfer a suitable quantity of Temazepam to a suitable volumetric flask. Dissolve in 30% of the flask volume of acetonitrile. Dilute with *Solution A* to volume.

Sample solution: 0.1 mg/mL from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 7.5-cm; 3.5-µm or 2.6-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between temazepam related compound F and temazepam; NLT 1.5 between temazepam and temazepam related compound G, *System suitability solution*

Relative standard deviation: NMT 0.73% for temazepam, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of temazepam ($C_{16}H_{13}ClN_2O_2$) in the portion of Temazepam 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 Temazepam RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, System suitability solution, and **Standard stock solution:** Proceed as directed in the *Assay*.

Standard solution: 0.005 mg/mL from *Standard stock solution* in *Diluent*

Sensitivity solution: 0.2 µg/mL of USP Temazepam RS in *Diluent* from *Standard stock solution*

Sample solution: 1 mg/mL of Temazepam prepared as follows. Dissolve in acetonitrile using 30% of the final volume, and dilute with *Solution A* to volume.

Chromatographic system: Prepare as directed in the *Assay*.

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between temazepam related compound F and temazepam; NLT 1.5 between temazepam and temazepam related compound G, *System suitability solution*

Relative standard deviation: NMT 5.0% for temazepam, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of Temazepam taken:

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

r_U = peak response of each individual impurity from the *Sample solution*

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

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

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

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

Acceptance criteria: See *Table 2*. The reporting limit is 0.02% for temazepam related compound A and 0.05% for all other impurities.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Oxazepam[a]	0.54	1.0	0.2
Methylnordazepam *N*-oxide[b]	0.63	1.5	0.2
Temazepam related compound F	0.83	0.65	0.2
Temazepam	1.0	—	—
Temazepam related compound G	1.3	0.68	0.2
O-Methyl temazepam[c]	1.6	1.0	0.2
Diazepam[d]	1.9	1.0	0.15
O-Acetyl temazepam[e]	2.0	1.0	0.2
Temazepam related compound A	2.6	1.2	0.05
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] 7-Chloro-1,3-dihydro-3-hydroxy-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

[b] 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one 4-oxide.

[c] 7-Chloro-1,3-dihydro-3-methoxy-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

[d] 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

[e] 7-Chloro-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-3-yl acetate.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.

• **USP Reference Standards ⟨11⟩**

USP Temazepam RS

USP Temazepam Related Compound A RS

5-Chloro-2-methylaminobenzophenone.

$C_{14}H_{12}ClNO$ 245.70

USP Temazepam Related Compound F RS

7-Chloro-1-methyl-5-phenyl-4,5-dihydro-1*H*-1,4-benzodiazepine-2,3-dione.

$C_{16}H_{13}ClN_2O_2$ 300.74

USP Temazepam Related Compound G RS

7-Chloro-1,4-dimethyl-5-phenyl-4,5-dihydro-1*H*-1,4-benzodiazepine-2,3-dione.

$C_{17}H_{15}ClN_2O_2$ 314.77

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

Topic/Question	Contact	Expert Committee
TEMAZEPAM	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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