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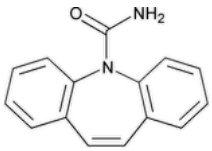
Carbamazepine

Change to read:



$C_{15}H_{12}N_2O$ 236.27

▲▲ (USP 1-Dec-2023)

5*H*-Dibenz[*b*,*f*]azepine-5-carboxamide CAS RN®: 298-46-4; UNII: 33CM23913M.

DEFINITION

Carbamazepine contains NLT 98.0% and NMT 102.0% of carbamazepine ($C_{15}H_{12}N_2O$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M ▲or 197A▲ (USP 1-Dec-2023)

• **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**

Solution A: Add 0.5 mL of triethylamine and 0.5 mL of formic acid to 1000 mL of water.

Solution B: Add 0.25 mL of formic acid to 1000 mL of methanol.

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
3	80	20
12	60	40
18	45	55
20	45	55
20.1	80	20
23	80	20

Diluent: Methanol and water (50:50)

System suitability stock solution: 0.02 mg/mL each of USP Carbamazepine RS and USP Carbamazepine Related Compound A RS prepared as follows. ▲Transfer suitable amounts of USP Carbamazepine RS and USP Carbamazepine Related Compound A RS to a suitable volumetric flask. Add 50% of the flask volume of methanol to dissolve.▲ (USP 1-Dec-2023) Dilute with water to volume.

System suitability solution: 0.002 mg/mL each of USP Carbamazepine RS and USP Carbamazepine Related Compound A RS from the *System suitability stock solution* in *Diluent*

Standard solution: 0.1 mg/mL of USP Carbamazepine RS prepared as follows. ▲Transfer a suitable amount of USP Carbamazepine RS to a suitable volumetric flask. Add 50% of the flask volume of methanol to dissolve.▲ (USP 1-Dec-2023) Dilute with water to volume.

Sample solution: 0.1 mg/mL of Carbamazepine prepared as follows. ▲Transfer a suitable amount of sample to a suitable volumetric flask. Add 50% of the flask volume of methanol to dissolve.▲ (USP 1-Dec-2023) Dilute with water to volume. Pass through a suitable filter of 0.2-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 2.1-mm × 10-cm; 1.8-µm packing L10

Column temperature: 40°

Flow rate: 0.3 mL/min

Injection volume: 2 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.7 between carbamazepine related compound A and carbamazepine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of carbamazepine ($C_{15}H_{12}N_2O$) in the portion of Carbamazepine taken:

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

r_U = peak response ▲of carbamazepine▲ (USP 1-Dec-2023) from the *Sample solution*

r_S = peak response ▲of carbamazepine▲ (USP 1-Dec-2023) from the *Standard solution*

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

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

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

IMPURITIES

• **Chloride and Sulfate ⟨221⟩, *Chloride***

Sample solution: Boil 1.0 g of Carbamazepine in 20.0 mL of water for 10 min, cool, adjust the volume to 20 mL, and filter. Use a 10.0-mL portion of the filtrate.

Acceptance criteria: 0.014%; the *Sample solution* contains no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid.

• **Residue on Ignition ⟨281⟩**

Sample: 2.0 g of Carbamazepine

Acceptance criteria: NMT 0.1%

Change to read:

• **Organic Impurities**

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

▲**Sensitivity stock solution:** 0.03 mg/mL each of USP Carbamazepine RS, USP Carbamazepine Related Compound A RS, and USP Carbamazepine Related Compound B RS, prepared as follows. Transfer suitable amounts of USP Carbamazepine RS, USP Carbamazepine Related Compound A RS, and USP Carbamazepine Related Compound B RS to a suitable volumetric flask. Add 50% of the flask volume of methanol to dissolve. Dilute with water to volume.

Sensitivity solution: 0.0003 mg/mL each of USP Carbamazepine RS, USP Carbamazepine Related Compound A RS, and USP Carbamazepine Related Compound B RS from the *Sensitivity stock solution* in *Diluent*▲ (USP 1-Dec-2023)

Standard stock solution: ▲0.03 mg/mL of USP Carbamazepine RS, and 0.05 mg/mL each of USP Carbamazepine Related Compound A RS and USP Carbamazepine Related Compound B RS, prepared as follows. Transfer a suitable amount of USP Carbamazepine RS, USP Carbamazepine Related Compound A RS, and USP Carbamazepine Related Compound B RS to a suitable volumetric flask. Add 50% of the flask volume of methanol to dissolve.▲ (USP 1-Dec-2023) Dilute with water to volume.

Standard solution: ▲0.0006▲ (USP 1-Dec-2023) mg/mL ▲▲ (USP 1-Dec-2023) of USP Carbamazepine RS, ▲and 0.001 mg/mL each of▲ (USP 1-Dec-2023) USP Carbamazepine Related Compound A RS and USP Carbamazepine Related Compound B RS from the *Standard stock solution* in *Diluent*

Sample solution: 1.0 mg/mL of Carbamazepine prepared as follows. ▲Transfer a suitable amount of sample to a suitable volumetric flask. Add 50% of the flask volume of methanol to dissolve.▲ (USP 1-Dec-2023) Dilute with water to volume. Pass through a suitable filter of 0.2-µm pore size.

System suitability

Samples: ▲*Sensitivity solution* and▲ (USP 1-Dec-2023) *Standard solution*

Suitability requirements

Resolution: NLT 1.7 between carbamazepine related compound A and carbamazepine▲, *Standard solution*▲ (USP 1-Dec-2023)

Relative standard deviation: NMT ▲5.0% for carbamazepine, carbamazepine related compound A, and carbamazepine related compound B, *Standard solution*

Signal-to-noise ratio: NLT 10 for carbamazepine, carbamazepine related compound A, and carbamazepine related compound B, *Sensitivity solution*▲ (USP 1-Dec-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲carbamazepine related compound A and carbamazepine related compound B▲ (USP 1-Dec-2023) in the portion of Carbamazepine taken:

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

r_U = peak response of ▲carbamazepine related compound A or carbamazepine related compound B▲ (USP 1-Dec-2023) from the *Sample solution*

r_S = peak response of the corresponding USP Reference Standard from the *Standard solution*

C_S = concentration of the corresponding USP Reference Standard in the *Standard solution* (mg/mL)

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

Calculate the percentage of ▲any▲ (USP 1-Dec-2023) unspecified impurity in the portion of Carbamazepine taken:

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

r_U = peak response of ▲any▲ (USP 1-Dec-2023) unspecified impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.03%.▲ (USP 1-Dec-2023)

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Carbamazepine related compound A▲▲ (USP 1-Dec-2023)	0.96	▲0.1▲ (USP 1-Dec-2023)
Carbamazepine	1.00	—
Carbamazepine related compound B▲▲ (USP 1-Dec-2023)	1.45	▲0.10▲ (USP 1-Dec-2023)
▲Any▲ (USP 1-Dec-2023) unspecified impurity	—	▲0.06▲ (USP 1-Dec-2023)
Total impurities	—	0.5

SPECIFIC TESTS

• **Acidity**

Sample solution: 50 mg/mL of Carbamazepine in water prepared as follows. Mix 2.0 g of Carbamazepine in 40.0 mL of water for 15 min, and filter through paper.

Analysis: To a 10.0-mL aliquot of *Sample solution* add 1 drop of phenolphthalein TS, and titrate with 0.01 N sodium hydroxide VS. Perform a blank determination, and make any necessary correction.

Acceptance criteria: NMT 1.0 mL of 0.01 N sodium hydroxide VS is required for each 1.0 g of Carbamazepine.

- **Alkalinity**

Sample solution: 50 mg/mL of Carbamazepine in water prepared as follows. Mix 2.0 g of Carbamazepine in 40.0 mL of water for 15 min, and filter through paper.

Analysis: To a 10.0-mL aliquot of *Sample solution* add 1 drop of methyl red TS, and titrate with 0.01 N hydrochloric acid VS. Perform a blank determination, and make any necessary correction.

Acceptance criteria: NMT 1.0 mL of 0.01 N hydrochloric acid VS is required for each 1.0 g of Carbamazepine.

- **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 0.5%

- **X-Ray Diffraction** ⟨941⟩**:** The X-ray diffraction pattern conforms to that of USP Carbamazepine RS, similarly determined.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.

Change to read:

- **USP Reference Standards** ⟨11⟩

USP Carbamazepine RS

USP Carbamazepine Related Compound A RS

▲10,11-Dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carboxamide.▲ (USP 1-Dec-2023)

$C_{15}H_{14}N_2O$ ▲238.29▲ (USP 1-Dec-2023)

USP Carbamazepine Related Compound B RS

5*H*-Dibenz[*b*,*f*]azepine.

$C_{14}H_{11}N$ ▲193.25▲ (USP 1-Dec-2023)

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

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

Chromatographic Database Information: Chromatographic Database

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