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Carbamazepine Oral Suspension

DEFINITION
Carbamazepine Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$).

IDENTIFICATION

Change to read:

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

Sample solution: Place 5 mL of Oral Suspension in a separator containing 20 mL of 0.1 N sodium hydroxide, and extract with 25 mL of chloroform. Pass the extract through anhydrous sodium sulfate supported on filter paper into a beaker. Wash the anhydrous sodium sulfate with 10 mL of chloroform, and add the washing to the extract. Evaporate the chloroform extract to dryness with the aid of a stream of nitrogen. Dissolve the residue in 10 mL of methylene chloride.

Acceptance criteria: Meets the requirements

• **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: 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 (%)
0.0	80	20
3.0	80	20
12.0	60	40
18.0	45	55
20.0	45	55
20.1	80	20
23.0	80	20

Diluent: Methanol

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

Standard solution: 0.1 mg/mL of USP Carbamazepine RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of carbamazepine from a volume of Oral Suspension prepared as follows. Weigh and transfer freshly mixed Oral Suspension equivalent to 20 mg of carbamazepine to a 200-mL volumetric flask. Add about 140 mL of *Diluent*, shake by mechanical means for about 30 min, sonicate for about 2 min, and dilute with *Diluent* 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 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$) in the portion of Oral Suspension 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 Carbamazepine RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements for oral suspension packaged in single-unit containers
- **Deliverable Volume ⟨698⟩:** Meets the requirements for oral suspension packaged in multiple-unit containers

IMPURITIES

- **Organic Impurities**

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

Standard solution: 0.002 mg/mL each of USP Carbamazepine RS, USP Carbamazepine Related Compound A RS, and USP Carbamazepine Related Compound B RS in *Diluent*

Sample solution: Nominally 1.0 mg/mL of carbamazepine from a volume of Oral Suspension prepared as follows. Weigh and transfer freshly mixed Oral Suspension equivalent to 50 mg of carbamazepine to a 50-mL volumetric flask. Add about 35 mL of *Diluent*, shake by mechanical means for about 30 min, sonicate for about 2 min, dilute with *Diluent* to volume, and shake for about 5 min. Pass through a suitable filter of 0.2-µm pore size.

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 1.7 between carbamazepine related compound A and carbamazepine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of carbamazepine related compound B in the portion of Oral Suspension taken:

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

r_U = peak response of carbamazepine related compound B from the *Sample solution*

r_S = peak response of carbamazepine related compound B from the *Standard solution*

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

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

Calculate the percentage of each individual unspecified impurity in the portion of Oral Suspension taken:

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

r_U = peak response of each 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 = nominal concentration of carbamazepine in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any impurity peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Carbamazepine related compound A[a,b]	0.96	—
Carbamazepine	1.00	—
Carbamazepine related compound B[c]	1.45	0.2
Individual unspecified impurity	—	0.2
Total impurities	—	0.5

[a] 10,11-Dihydrocarbamazepine.

[b] Process impurity included in the table for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total impurities for the drug product.

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

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total bacterial count does not exceed 1×10^2 cfu/g, and the tests for *Salmonella* species and *Escherichia coli* are negative.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, protected from freezing and from excessive heat.

• **USP Reference Standards ⟨11⟩**

USP Carbamazepine RS

USP Carbamazepine Related Compound A RS

10,11-Dihydrocarbamazepine.

$C_{15}H_{14}N_2O$ 238.28

USP Carbamazepine Related Compound B RS

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

$C_{14}H_{11}N$ 193.24

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

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

Chromatographic Database Information: Chromatographic Database

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