Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2024
Document Type: USP Monographs
DocId: GUID-0E82967E-B926-4871-9C08-93DB964D1A33_2_en-US
DOI: https://doi.org/10.31003/USPNF_M12540_02_01
DOI Ref: zz5rx

Add the following:

▲Carbamazepine Extended-Release Capsules

DEFINITION
Carbamazepine Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$).

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**

Solution A: Water, triethylamine, and phosphoric acid (100: 0.1: 0.1)

Solution B: Methanol

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
2	90	10
25	10	90
30	10	90
31	90	10
35	90	10

Standard solution: 0.08 mg/mL of USP Carbamazepine RS in methanol

Sample solution: 0.08 mg/mL of carbamazepine in methanol. Pass a portion of the solution through a suitable filter, discarding the first 3 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of carbamazepine 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: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: 0.05 M phosphate buffer, pH 6.8 (dissolve 6.8 g of potassium phosphate monobasic and 0.8 g of sodium hydroxide in 1000 mL of water, adjust with 1 N sodium hydroxide or with phosphoric acid to a pH of 6.8); deaerated. See *Table 2*.

Table 2

Strength (mg)	Medium Volume (mL)
100	500
200	750
300	1000

Apparatus 2: 75 rpm, with apex vessels

Times: 1, 4, and 8 h

Standard stock solution: 1 mg/mL of USP Carbamazepine RS in methanol

Standard solution: Prepare a solution of USP Carbamazepine RS in *Medium* as directed in *Table 3*.

Table 3

Strength (mg)	Concentration (mg/mL)
100	0.20
200	0.27
300	0.30

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 285 nm, with a background correction at 490 nm

Cell: 0.05-cm flow cell

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$) dissolved at each time point *(i)*:

$$\text{Result}_i = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Carbamazepine RS in the *Standard solution* (mg/mL) (see *Table 3*)

V = volume of *Medium* (see *Table 2*)

L = label claim for carbamazepine (mg/Capsule)

Tolerances: See *Table 4*.

Table 4

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	30–60
2	4	70–95
3	8	NLT 80

The percentages of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$) dissolved at the times specified conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Solution A: Methanol, tetrahydrofuran, and water (17:3:80). To each liter of this solution add 5 mL of triethylamine and 2 mL of formic acid.

Solution B: Methanol, tetrahydrofuran, and water (77:3:20). To each liter of this solution add 2.5 mL of triethylamine and 1 mL of formic acid.

Mobile phase: See *Table 5*.

Table 5

Time (min)	Solution A (%)	Solution B (%)
0	80	20
45	0	100
50	0	100
50.1	80	20
60	80	20

System suitability solution: 4 mg/mL of USP Carbamazepine RS and 0.004 mg/mL of USP Carbamazepine Related Compound A RS in methanol

Sensitivity solution: 0.002 mg/mL of USP Carbamazepine RS in methanol

Standard solution: 0.004 mg/mL of USP Carbamazepine RS and 0.008 mg/mL of USP Carbamazepine Related Compound B RS in methanol

Sample solution: Nominally 4 mg/mL of carbamazepine from Capsules prepared as follows. Transfer a portion of the contents from Capsules (NLT 20) to a suitable volumetric flask and add 80% of the flask volume of methanol. Sonicate with occasional shaking for NLT 20 min and dilute with methanol to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 45°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times in *Table 6* are provided as information that could aid in peak assignment.]

Table 6

Name	Relative Retention Time
9-Methylacridine	0.68

[a] 10,11-Dihydro-5*H*-dibenzo[*b*,*f*]azepine.	
Carbamazepine	1.0
Suitability requirements	
Resolution: NLT 2.0 between carbamazepine and carbamazepine related compound A, *System suitability solution*	
Carbamazepine related compound A	1.1
Relative standard deviation: NMT 5.0% for carbamazepine and carbamazepine related compound B, *Standard solution*	
Signal-to-noise ratio: NLT 10, *Sensitivity solution*	
Carbamazepine related compound B	2.3
Analysis	
Samples: *Standard solution* and *Sample solution*	
Iminostilbene	2.9

Calculate the percentage of carbamazepine related compound B in the portion of Capsules 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 any unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each unspecified degradation product 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 7*. The reporting threshold is 0.05%.

Table 7

Name	Acceptance Criteria, NMT (%)
Carbamazepine related compound B	0.2
Any unspecified degradation product	0.1
Total degradation products	0.5

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, protected from light and moisture, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Carbamazepine RS

USP Carbamazepine Related Compound A RS

10,11-Dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carboxamide.

$C_{15}H_{14}N_2O$ 238.29

USP Carbamazepine Related Compound B RS

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

$C_{14}H_{11}N$ 193.25▲ (USP 1-Dec-2024)

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

Topic/Question	Contact	Expert Committee
CARBAMAZEPINE EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 49(4)
Current DocID: GUID-0E82967E-B926-4871-9C08-93DB964D1A33_2_en-US
DOI: https://doi.org/10.31003/USPNF_M12540_02_01
DOI ref: zz5rx