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Carbamazepine Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-carbamazepine-tabs-20220930.

DEFINITION
Carbamazepine Tablets contain NLT 92.0% and NMT 108.0% of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M

Sample solution: Nominally 250 mg of carbamazepine from powdered Tablets in 15 mL of acetone

Analysis: Boil the *Sample solution* for 5 min in a suitable beaker. Filter while hot, using two 5-mL portions of hot acetone to effect transfer. Evaporate the filtrate with the aid of nitrogen to 5 mL, and cool in an ice bath until crystals are formed. Filter the crystals, wash with 3 mL of cold acetone, and dry under vacuum at 70° for 30 min. Use the crystals.

Acceptance criteria: Meet 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**

Mobile phase: Methanol, tetrahydrofuran, and water (12:3:85). Add 0.22 mL of formic acid and then 0.5 mL of triethylamine to each L.

Diluent: Methanol and water (50:50)

System suitability stock solution: 0.1 mg/mL of USP Carbamazepine RS and 0.5 mg/mL of USP Carbamazepine Related Compound A RS in methanol. Sonication may be used to aid in dissolution.

System suitability solution: 0.01 mg/mL of USP Carbamazepine RS and 0.05 mg/mL of USP Carbamazepine Related Compound A RS from *System suitability stock solution* in *Diluent*

Standard stock solution: 2 mg/mL of USP Carbamazepine RS in methanol. Sonication may be used to aid in dissolution.

Standard solution: 0.2 mg/mL of USP Carbamazepine RS from *Standard stock solution* in *Diluent*

Sample stock solution: Nominally 2 mg/mL of carbamazepine from NLT 20 Tablets prepared as follows. Finely powder the Tablets, and transfer a portion of the powder to a suitable volumetric flask. Add 80% of the final flask volume of methanol, sonicate for 15 min, and allow to cool to room temperature. Dilute with methanol to volume. Pass through a suitable filter and discard the first few mL of filtrate.

Sample solution: Nominally 0.2 mg/mL of carbamazepine from *Sample stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.0- or 4.6-mm × 25-cm; 7-µm packing L10

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.6 times the retention time of carbamazepine

System suitability

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

[Note—See *Table 3* for the relative retention times.]

Suitability requirements

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

Relative standard deviation: NMT 2.0%, *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 Tablets 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: 92.0%–108.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

For products labeled as 100-mg chewable Tablets

Test 1: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 1*.

Medium: Water containing 1% sodium lauryl sulfate; 900 mL

Apparatus 2: 75 rpm

Time: 60 min

Standard solution: USP Carbamazepine RS in *Medium*. [Note—A volume of methanol NMT 1% of the final total volume of the *Standard solution* may be used to dissolve the carbamazepine.]

Sample solution: Filtered portion of the solution under test, diluted with *Medium* if necessary

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum absorbance at about 288 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$) dissolved:

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

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)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$) is dissolved. Use *Dissolution* ⟨711⟩, *Acceptance Table 1* with the following exceptions: at S_2, no unit is less than Q − 5%; at S_3, no unit is less than Q − 10%; and NMT 2 of the 24 units are less than Q − 5%.

For products labeled as 200-mg Tablets

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium, Apparatus 2, Standard solution, Sample solution, and **Instrumental conditions:** Proceed as directed in *Test 1*.

Times: 15 and 60 min

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of carbamazepine ($C_{15}H_{12}N_2O$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S$$

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)

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

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V_2) + (C_1 \times V_S)] \times (1/L) \times 100$$

C_i = concentration of carbamazepine in the portion of sample withdrawn at the specified time point (i) (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_2 = volume of the *Medium* at time point 2 (mL)

V_S = volume of the *Sample solution* withdrawn at each time point (*i*) (mL)

Tolerances: See *Table 1*.

Table 1

Time Point (*i*)	Time (min)	Amount Dissolved (%)
1	15	45–75
2	60	NLT 75

Use *Dissolution ⟨711⟩*, *Acceptance Table 2* with the following exceptions. At 15 min: at L_2, no unit is more than 5% outside the stated range; at L_3, no unit is more than 10% outside the stated range; and NMT 2 of the 24 units are more than 5% outside the stated range. At 60 min: at L_2, no unit is less than Q − 5%; at L_3, no unit is less than Q − 10%; and NMT 2 of the 24 units are less than Q − 5%.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium, Apparatus 2, Standard solution, Sample solution, and **Instrumental conditions:** Proceed as indicated in *Test 1*.

Times: 15 and 60 min

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of carbamazepine ($C_{15}H_{12}N_2O$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result} = (A_U/A_S) \times C_S$$

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)

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

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V_2) + (C_1 \times V_S)] \times (1/L) \times 100$$

C_i = concentration of carbamazepine in the portion of sample withdrawn at the specified time point (*i*) (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_2 = volume of the *Medium* at time point 2 (mL)

V_S = volume of the *Sample solution* withdrawn at each time point (*i*) (mL)

Tolerances: See *Table 2*.

Table 2

Time Point (*i*)	Time (min)	Amount Dissolved (%)
1	15	60–85
2	60	NLT 75

Use *Dissolution ⟨711⟩*, *Acceptance Table 2* with the following exceptions. At 15 min: at L_2, no unit is more than 5% outside the stated range; at L_3, no unit is more than 10% outside the stated range; and NMT 2 of the 24 units are more than 5% outside the stated range. At 60 min: at L_2, no unit is less than Q − 5%; at L_3, no unit is less than Q − 10%; and NMT 2 of the 24 units are less than Q − 5%.

▲**Test 4:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: Water containing 1% sodium dodecyl sulfate; 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Standard stock solution: 0.9 mg/mL of USP Carbamazepine RS in methanol. Sonicate to dissolve as needed.

Standard solution: 9 µg/mL of USP Carbamazepine RS from *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first 3 mL of the filtrate. Dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 288 nm

Cell length: 1 cm

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:

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

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)

D = dilution factor

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of carbamazepine ($C_{15}H_{12}N_2O$) is dissolved.▲ (RB 22-Sep-2022)

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

IMPURITIES

• **Organic Impurities**

Mobile phase, Diluent, and **System suitability solution:** Proceed as directed in the *Assay*.

Standard stock solution: 0.02 mg/mL each of USP Carbamazepine RS, USP Carbamazepine Related Compound B RS, and USP 9-Methylacridine RS in methanol. Sonication may be used to aid in dissolution.

Standard solution: 0.001 mg/mL each of USP Carbamazepine RS, USP Carbamazepine Related Compound B RS, and USP 9-Methylacridine RS from *Standard stock solution* in *Diluent*

Sample solution: Nominally 1 mg/mL of carbamazepine from NLT 20 Tablets prepared as follows. Finely powder the Tablets, and transfer a portion of the powder to a suitable volumetric flask. Add about 50% of the final flask volume of *Diluent*, sonicate for 15 min, and allow to cool to room temperature. Dilute with *Diluent* to volume. Pass through a suitable filter and discard the first few mL of filtrate.

Chromatographic system: Proceed as directed in the *Assay* except use a *Run time* of NLT 3.5 times the retention time of carbamazepine.

System suitability

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

[Note—See *Table 3* for the relative retention times.]

Suitability requirements

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

Relative standard deviation: NMT 10.0% each for carbamazepine, carbamazepine related compound B, and 9-methylacridine, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of carbamazepine related compound B and 9-methylacridine in the portion of Tablets taken:

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

r_U = peak response of carbamazepine related compound B or 9-methylacridine from the *Sample solution*

r_S = peak response of carbamazepine related compound B or 9-methylacridine from the *Standard solution*

C_S = concentration of USP Carbamazepine Related Compound B RS or USP 9-Methylacridine RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of other degradation products in the portion of Tablets taken:

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

r_U = peak response of any individual 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 3*. Disregard peaks below 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
9-Methylacridine	0.54	0.2
Carbamazepine related compound A[a]	0.87	—
Carbamazepine	1.0	—
Carbamazepine related compound B	3.1	0.2
Any individual unspecified degradation product	—	0.2
Total degradation products	—	0.30

[a] This is a process impurity that is controlled in the drug substance. It is not to be reported or included in the total degradation products.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, preferably of glass. Protect from light and moisture. Store at controlled room temperature.
- **Labeling:** The labeling indicates the *Dissolution* test with which the product complies.
- **USP Reference Standards** ⟨11⟩

USP Carbamazepine RS

USP Carbamazepine Related Compound A RS

10,11-Dihydrocarbamazepine.

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

USP Carbamazepine Related Compound B RS

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

$C_{14}H_{11}N$ 193.25

USP 9-Methylacridine RS

9-Methylacridine.

$C_{14}H_{11}N$ 193.25

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

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

Chromatographic Database Information: Chromatographic Database

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