Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-4F26D956-D00A-49E5-9F84-90002C5FA9B4_3_en-US
DOI: https://doi.org/10.31003/USPNF_M89996_03_01
DOI Ref: kia0b

Zonisamide Capsules

DEFINITION
Zonisamide Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of zonisamide ($C_8H_8N_2O_3S$).

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*.

Change to read:

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

Sample solution: Shake the contents of a sufficient quantity of Capsules, equivalent to about 100 mg of zonisamide, with 5 mL of methanol. Sonicate for 2 min and pass through a filter of 0.45-µm pore size or equivalent. Discard the initial 1-mL portion and evaporate the solution at 85°. Cool the residue. Use 1–2 mg of the residue.

Analysis: The IR spectrum of the *Sample solution* corresponds to the IR spectrum of similarly prepared USP Zonisamide RS.

ASSAY

• **Procedure**

Mobile phase: Acetonitrile, methanol, and 0.1% trifluoroacetic acid TS (20:16:64)

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

Standard solution: 0.1 mg/mL of zonisamide in *Mobile phase*, from the *Standard stock solution*

Sample stock solution: Nominally 1.0 mg/mL of zonisamide prepared as follows. Transfer a suitable amount of Capsule contents (NLT 10) to a suitable volumetric flask and add a suitable volume of methanol. Sonicate and shake for 15 min. Dilute with methanol to volume. Alternatively, the *Sample stock solution* can be prepared as follows. Transfer a suitable amount of Capsules (NLT 10) in a suitable volumetric flask, add 20% of the flask volume with water. Stir, and warm slightly for 30 min. Dilute with *Mobile phase* to volume.

Sample solution: 0.1 mg/mL of zonisamide in *Mobile phase*, from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 237 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: 1.5 times the retention time of the zonisamide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zonisamide ($C_8H_8N_2O_3S$) in the portion of Capsules taken:

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

r_U = peak response of zonisamide from the *Sample solution*

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

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

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

Acceptance criteria: 90.0%–110.0%

Change to read:

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: ▲75 rpm. Use suitable sinkers, if necessary.▲ (ERR 1-May-2018)

Time: 45 min

Determine the percentage of zonisamide dissolved using one of the following procedures.

Spectrophotometric procedure

Standard stock solution: 0.6 mg/mL of USP Zonisamide RS in methanol

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain solutions with final concentrations as given in *Table 1*.

Table 1

Capsule Strength (mg)	Final Concentration (µg/mL)
25	13
50	13
100	22

Sample solution: 10 mL of the solution under test. Dilute the filtrate with *Medium* as given in *Table 2*.

Table 2

Capsule Strength (mg)	Volume of Filtrate (mL)	Final Volume (mL)
25	5.0	10.0
50	5.0	25.0
100	5.0	25.0

Instrumental conditions

Mode: UV

Analytical wavelength: 241 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zonisamide ($C_8H_8N_2O_3S$) dissolved:

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

A_U = absorbance from the *Sample solution*

A_S = absorbance from the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Chromatographic procedure

Solution A: Dilute 52 mL of 40% tetrabutylammonium hydroxide solution with 948 mL of water. Adjust with phosphoric acid to a pH of 7.5.

Mobile phase: Acetonitrile, methanol, and *Solution A* (25:5:70)

Standard stock solution: 0.4 mg/mL of USP Zonisamide RS prepared as follows. Transfer a suitable amount of USP Zonisamide RS to a suitable volumetric flask, and dissolve in 20% of the flask volume of acetonitrile. Dilute with *Medium* to volume.

Standard solution: (L/1000) mg/mL of USP Zonisamide RS in *Medium*, where L is the label claim in mg/Capsule from *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 238 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 3.0%

Calculate the percentage of the labeled amount of zonisamide ($C_8H_8N_2O_3S$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 70% (Q) of the labeled amount of zonisamide ($C_8H_8N_2O_3S$) is dissolved.

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

IMPURITIES

- **Organic Impurities**

Solution A: Dilute 52 mL of 40% tetrabutylammonium hydroxide solution with 948 mL of water. Adjust with phosphoric acid to a pH of 7.5.

Mobile phase: Acetonitrile, methanol, and *Solution A* (25:5:70)

Standard stock solution: 0.32 mg/mL of USP Zonisamide RS. Transfer a suitable amount of USP Zonisamide RS in a suitable volumetric flask, dissolve in 20% of flask volume of acetonitrile and dilute with *Mobile phase* to volume.

Standard solution: 0.32 µg/mL of zonisamide in *Mobile phase*, from the *Standard stock solution*

System suitability stock solution: 0.4 mg/mL of zonisamide related compound C. Transfer a suitable amount of USP Zonisamide Related Compound C RS to a suitable volumetric flask, and dissolve in 20% flask volume of methanol. Dilute with *Mobile phase* to volume.

System suitability solution: Equal volumes of *Standard stock solution* and *System suitability stock solution*

Sample stock solution: Transfer a suitable number of Capsules (NLT 10) to a suitable volumetric flask, dissolve in 20% flask volume of water and dilute with *Mobile phase* to volume to obtain a solution of concentration as given in *Table 3*. [Note—Stir and warm slightly for 30 min to dissolve the Capsules.]

Table 3

Capsule Strength (mg)	Final Concentration (mg/mL)
25	2
50	2
100	4

Sample solution: 0.32 mg/mL of zonisamide in *Mobile phase*, from the *Sample stock solution*

Chromatographic system

Mode: LC

Detector: UV 238 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 20 µL

Run time: 6 times the retention time of the zonisamide peak

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between zonisamide and zonisamide related compound C, *System suitability solution*

Tailing factor: NMT 1.5 for the zonisamide peak, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each 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 degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 4*. Disregard any peak below 0.1%.

Table 4

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Zonisamide	1.0	—
Zonisamide related compound C[a]	1.3	—
Methyl zonisamide[b]	1.6	0.2
Zonisamide related compound A[c]	2.5	0.2
Any unspecified degradation product	—	0.2
Total degradation products	—	0.5

[a] Process impurity included in the table for identification and system suitability only. Process impurities are controlled in the drug substance and are not to be reported or included in the total degradation products for the drug product.

[b] 1-Benzisoxazol-3-yl-*N*-methylmethanesulfonamide.

[c] 1,2-Benzisoxazole-3-methane sulfonic acid.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers and protected from light. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Zonisamide RS

USP Zonisamide Related Compound C RS

N'-(Benzisoxazol-3-ylmethylsulfonyl)-*N*,*N*-dimethylformimidamide.

$C_{11}H_{13}N_3O_3S$ 267.30

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

Topic/Question	Contact	Expert Committee
ZONISAMIDE CAPSULES	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(4)

Current DocID: GUID-4F26D956-D00A-49E5-9F84-90002C5FA9B4_3_en-US

DOI: https://doi.org/10.31003/USPNF_M89996_03_01

DOI ref: kia0b