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Zolmitriptan Orally Disintegrating Tablets

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DEFINITION

Zolmitriptan Orally Disintegrating Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$).

IDENTIFICATION

- **A.** The UV spectrum of the zolmitriptan peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **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

Buffer: Dissolve 2 mL of [triethylamine](#) in 1 L of [water](#). Adjust with [phosphoric acid](#) to a pH of 3.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (15:85)

Standard stock solution: 0.25 mg/mL of [USP Zolmitriptan RS](#) in [methanol](#)

Standard solution: 0.025 mg/mL of [USP Zolmitriptan RS](#) in *Mobile phase* from a suitable volume of *Standard stock solution*

Sample stock solution: 0.25 mg/mL of zolmitriptan in [methanol](#), prepared as follows. Transfer NLT 20 Tablets to a suitable volumetric flask.

Add 75% of the flask volume of [methanol](#). Sonicate for 30 min. Allow to cool to room temperature and dilute with [methanol](#) to volume.

Sample solution: Nominally 0.025 mg/mL of zolmitriptan in *Mobile phase* from a suitable volume of *Sample stock solution*. Pass a portion of the solution under test through a suitable membrane filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 225 nm. For *Identification test A*, use a diode-array detector in the wavelength range of 200–300 nm.

Column: 4.6-mm \times 15-cm; 5- μ m packing [L1](#)

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 20 μ L

Run time: NLT 2.5 times the retention time of zolmitriptan

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 zolmitriptan ($C_{16}H_{21}N_3O_2$) in the portion of Tablets taken:

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

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

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

C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISINTEGRATION (701):** NMT 30 s

Change to read:

- **DISSOLUTION (711):**

▲Test 1▲ (RB 1-May-2020)

Medium: 0.1 N [hydrochloric acid](#); 500 mL

Apparatus 2: 50 rpm

Time: 15 min

Analyze the sample under test using either the *Chromatographic procedure* or the ▲*Spectroscopic procedure*.▲ (RB 1-May-2020)

Chromatographic procedure

Buffer, Mobile phase, Standard stock solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Standard solution: 0.005 mg/mL of [USP Zolmitriptan RS](#) from *Standard stock solution* in *Medium*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) dissolved:

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

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

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

C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim of zolmitriptan (mg/Tablet)

▲Spectroscopic procedure▲ (RB 1-May-2020)

Standard solution: 0.01 mg/mL of [USP Zolmitriptan RS](#) from *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable membrane filter of 0.2- μ m pore size.

Instrumental conditions

Mode: UV

Analytical wavelength: About 283 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) 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 Zolmitriptan RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim of zolmitriptan (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) is dissolved.

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

Medium: 0.1 N [hydrochloric acid](#); 500 mL

Apparatus 2: 50 rpm

Time: 15 min

Buffer: Add 7.8 g of [monobasic sodium phosphate](#) to 1000 mL of [water](#). Adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (15:85)

Standard stock solution: 0.33 mg/mL of [USP Zolmitriptan RS](#) prepared as follows. Transfer a suitable quantity of [USP Zolmitriptan RS](#) to an appropriate volumetric flask and add 70% of the flask volume of *Medium*. Sonicate to aid dissolution. Dilute with *Medium* to volume.

Standard solution: (L/500) mg/mL of zolmitriptan from *Standard stock solution* in *Medium*, where L is the label claim of zolmitriptan in mg/Tablet

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

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 15-cm; 3-μm packing [L1](#)

Temperatures:

Autosampler: 5°

Column: 30°

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 2 times the retention time of zolmitriptan

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 zolmitriptan ($C_{16}H_{21}N_3O_2$) dissolved:

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

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

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

C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim of zolmitriptan (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) is dissolved.▲ (RB 1-May-2020)

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Diluent: [Methanol](#) and [water](#) (25:75)

Solution A: 2.7 g/L of [monobasic potassium phosphate](#) in [water](#)

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5

Time (min)	Solution A (%)	Solution B (%)
15	92	8
45	86	14
55	55	45
60	55	45
62	95	5
75	95	5

Impurities stock solution: 0.2 mg/mL each of [USP Zolmitriptan Related Compound E RS](#) and [USP Zolmitriptan Related Compound G RS](#) in [methanol](#)

System suitability solution: 0.25 mg/mL of [USP Zolmitriptan RS](#) and 0.002 mg/mL each of [USP Zolmitriptan Related Compound E RS](#) and [USP Zolmitriptan Related Compound G RS](#) in *Diluent* prepared as follows. Dissolve a suitable quantity of [USP Zolmitriptan RS](#) in a suitable volumetric flask containing 50% of the flask volume of *Diluent*. Sonicate to dissolve. Transfer a suitable volume of *Impurities stock solution* to the flask. Dilute with *Diluent* to volume.

Standard stock solution: 0.25 mg/mL of [USP Zolmitriptan RS](#) in [methanol](#)

Standard solution: 0.001 mg/mL of [USP Zolmitriptan RS](#) from *Standard stock solution* in *Diluent*

Sample solution: Nominally 0.25 mg/mL of zolmitriptan from NLT 5 Tablets prepared as follows. Transfer the required number of Tablets to a suitable volumetric flask. Add 25% of the flask volume of [methanol](#). Sonicate for 30 min with intermittent shaking. Cool to room temperature. Dilute with [water](#) to volume. Pass through a suitable filter of 0.45- μ m pore size.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector

For zolmitriptan and zolmitriptan related compound E and any other unspecified degradation products: UV 223 nm

For zolmitriptan and zolmitriptan related compound G: UV 235 nm

Column: 4.6-mm \times 25-cm; 5- μ m packing [L1](#)

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 20 μ L

System suitability

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

[NOTE—See [Table 2](#) for relative retention times.]

Suitability requirements: Use 223 nm for system suitability evaluation.

Resolution: NLT 5.0 between zolmitriptan and zolmitriptan related compound E, *System suitability solution*

Tailing factor: NMT 2.0 for zolmitriptan, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of zolmitriptan related compound G in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of zolmitriptan related compound G at 235 nm from the *Sample solution*

r_S = peak response of zolmitriptan at 235 nm from the *Standard solution*

C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL)

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

F = relative response factor for zolmitriptan related compound G (see [Table 2](#))

Calculate the percentage of zolmitriptan related compound E and any other unspecified degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of zolmitriptan related compound E or any other unspecified degradation product at 223 nm from the *Sample solution*

r_S = peak response of zolmitriptan at 223 nm from the *Standard solution*

C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL)

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

F = relative response factor (see [Table 2](#))

Acceptance criteria: See [Table 2](#). Disregard any impurity less than 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Zolmitriptan related compound G	0.66	1.2	0.2
Zolmitriptan	1.0	—	—
Zolmitriptan related compound E	1.30	1.0	0.6
Any individual unspecified degradation product	—	1.0	0.2
Total degradation products	—	—	1.5

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.

Add the following:

▲ **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used. ▲ (RB 1-May-2020)

• [USP REFERENCE STANDARDS \(11\).](#)

[USP Zolmitriptan RS](#)

[USP Zolmitriptan Related Compound E RS](#)

(S)-N,N-Dimethyl-2-[[2-oxooxazolidin-4-yl)methyl]-1H-indol-3-yl]ethanamine oxide.

$C_{16}H_{21}N_3O_3$ 303.36

[USP Zolmitriptan Related Compound G RS](#)

(S)-4-(4-Aminobenzyl)oxazolidin-2-one.

$C_{10}H_{12}N_2O_2$ 192.21

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
ZOLMITRIPTAN ORALLY DISINTEGRATING TABLETS	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](#)

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