Zolmitriptan Tablets

Type of Posting	Revision Bulletin
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Expert Committee	Chemical Medicines Monographs 4
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 4 Expert Committee has revised the Zolmitriptan Tablets monograph.

The purpose for the revision is to add *Dissolution Test* 2 to accommodate the FDA approved specifications for the sponsor product. *Dissolution Test* 2 was validated using a Inertsil ODS brand of L1 column. The typical retention time for zolmitriptan is about 4 min.

Additionally, minor editorial changes have been made to update the monograph to current USP style.

The Zolmitriptan Tablets Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in the *Second Supplement* to *USP 41–NF 35*.

Should you have any questions, please contact K. Kalyana Seela, Ph.D., Senior Scientific Liaison (kks@usp.org).

Zolmitriptan Tablets

DEFINITION

Zolmitriptan 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 in 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. Sonicate if necessary to aid dissolution.
Standard solution: 0.025 mg/mL of USP Zolmitriptan RS in *Mobile phase* from *Standard stock solution*
Sample stock solution: Nominally 0.25 mg/mL of zolmitriptan from Tablets in methanol prepared as follows. Transfer NLT 5 Tablets to a suitable volumetric flask. Add 70% of the flask volume of methanol. Sonicate for 30 min. Cool to room temperature, and dilute with methanol to volume.
Sample solution: Nominally 0.025 mg/mL of zolmitriptan in *Mobile phase* from *Sample stock solution* passed through a suitable membrane filter of 0.45-µm pore size
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 225 nm. For *Identification A,* a diode array detector can be used in the wavelength range of 200–300 nm.
Column: 4.6-mm × 15-cm; 5-µm packing L1
Column temperature: 30°
Flow rate: 1 mL/min
Injection volume: 20 µL
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

Change to read:

- **DISSOLUTION** ⟨711⟩

•Test 1• (RB 1-Nov-2017)
Medium: 0.1 N hydrochloric acid; 500 mL
Apparatus 2: 50 rpm
Time: 15 min
[NOTE—Analyze the sample under test using either the *Chromatographic procedure* or the *Instrumental procedure*.]
Chromatographic procedure
Buffer, Mobile phase, Standard stock solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Standard solution: (*L*/500) mg/mL of USP Zolmitriptan RS in *Medium* from *Standard stock solution*, where *L* is the Tablet label claim in mg
Sample solution: Pass a portion of the solution under test through a suitable membrane filter of 0.45-µm 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)
Instrumental procedure
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-µm 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: 30 min
Buffer: 5.8 g/L of ammonium dihydrogen phosphate in water. Adjust with triethylamine to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (15:85)
Standard solution: (*L*/500) mg/mL of USP Zolmitriptan RS in *Medium*, where *L* is the label claim in mg/Tablet
Sample solution: Pass a suitable portion of the solution under test through a suitable filter. Discard the first few mL of filtrate.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Column temperature: 40°
Flow rate: 1 mL/min
Injection volume: 20 µL
Run time: NLT 1.8 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 from the *Sample solution*
r_S = peak response 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 80% (*Q*) of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) is dissolved. ● (RB 1-Nov-2017)

- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES

- **ORGANIC IMPURITIES**

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
10	95	5
45	86	14
55	55	45
60	55	45
62	95	5
75	95	5

Diluent: Methanol and water (25:75)
System suitability 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 from *System suitability stock solution* 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 *System suitability stock solution* to the flask. Dilute with *Diluent* to volume.
Standard stock solution: 0.25 mg/mL of USP Zolmitriptan RS in methanol. Sonicate if necessary to aid dissolution.
Standard solution: 0.001 mg/mL of USP Zolmitriptan RS in *Diluent* from a suitable volume of *Standard stock solution*
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-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector
For zolmitriptan and zolmitriptan related compound E and any other unspecified degradation product: UV 223 nm
For zolmitriptan and zolmitriptan related compound G: UV 235 nm
Column: 4.6-mm × 15-cm; 5-µm packing L1
Column temperature: 30°
Flow rate: 1.5 mL/min
Injection volume: 20 µL
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 the zolmitriptan peak, *Standard solution*
Relative standard deviation: NMT 5.0%, *Standard solution*
Analysis
Sample: *Sample solution*
Calculate the percentage of zolmitriptan related compound G in the portion of the 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 the 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 the 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	0.50	1.2	0.2
Zolmitriptan	1.0	—	—
Zolmitriptan related compound E	1.28	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-Nov-2017)
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Zolmitriptan RS
  USP Zolmitriptan Related Compound E RS
  (*S*)-*N,N*-Dimethyl-2-{5-[(2-oxooxazolidin-4-yl)methyl]-1*H*-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