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Eszopiclone Tablets

DEFINITION

Eszopiclone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of eszopiclone ($C_{17}H_{17}ClN_6O_3$).

IDENTIFICATION

Change to read:

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

Standard: USP Eszopiclone RS

Sample: Nominally 37.5 mg of eszopiclone from Tablets prepared as follows. Powder a number of Tablets, and mix the resulting powder. Transfer a portion of powder, equivalent to 37.5 mg of eszopiclone, to a suitable container, add 30 mL of *acetone*, and shake. Dilute with *acetone* to 50 mL and pass the resulting solution through a suitable filter. Evaporate the filtrate to dryness on a water bath and dry the residue in an oven at 60° for 2 h.

Acceptance criteria: Meets 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**

Solution A: 1.4 g/L of anhydrous dibasic sodium phosphate in water

Mobile phase: *Acetonitrile* and *Solution A* (25:75) adjusted with dilute phosphoric acid to a pH of 6.5 ± 0.05

Standard stock solution: 0.5 mg/mL of USP Eszopiclone RS prepared as follows. Transfer a suitable quantity of USP Eszopiclone RS to an appropriate volumetric flask and add 50% of the final flask volume of acetonitrile. Sonication may be used to promote dissolution. Dilute with acetonitrile to volume.

Standard solution: 0.03 mg/mL of USP Eszopiclone RS from *Standard stock solution* in *Mobile phase* passed through a suitable filter of 0.45-µm pore size. Use the filtrate.

Sample stock solution: Nominally 0.2 mg/mL of eszopiclone from Tablets prepared as follows. Transfer NLT 5 intact Tablets to a suitable volumetric flask. Add 5% of the final flask volume of *Solution A* and sonicate in cool water for 5 min with constant shaking. Add 30% of the final flask volume of acetonitrile and sonicate for 15 min. Dilute with acetonitrile to volume. Centrifuge the resulting solution and use the supernatant.

Sample solution: Nominally 0.03 mg/mL of eszopiclone from *Sample stock solution* in *Mobile phase* passed through a suitable filter of 0.45-µm pore size. Use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 303 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 1.9 times the retention time of eszopiclone

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 eszopiclone ($C_{17}H_{17}ClN_6O_3$) 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 Eszopiclone RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Solution A: 1.4 g/L of anhydrous dibasic sodium phosphate in water

Mobile phase: Acetonitrile and *Solution A* (30:70) adjusted with dilute phosphoric acid (1 in 10) to a pH of 6.5 ± 0.05

Standard stock solution: 0.1 mg/mL of USP Eszopiclone RS in acetonitrile. Sonication may be used to promote dissolution.

Standard solution: (*L*/500) mg/mL of USP Eszopiclone RS from *Standard stock solution* in *Medium*, where *L* is the Tablet label claim in mg. Pass the resulting solution through a suitable filter of 0.45-µm pore size and use the filtrate.

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

Chromatographic system

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

Mode: LC

Detector: UV 303 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 100 µL

Run time: NLT 1.5 times the retention time of eszopiclone

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 eszopiclone ($C_{17}H_{17}ClN_6O_3$) 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 Eszopiclone RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Acceptance criteria: NLT 80% (*Q*) of the labeled amount of eszopiclone ($C_{17}H_{17}ClN_6O_3$) is dissolved.

Test 2

Medium: *0.1 N hydrochloric acid VS*; 500 mL

Apparatus 2: 50 rpm

Time: 20 min

Buffer: To each liter of water add 1.0 mL of *phosphoric acid* and adjust with *2 N sodium hydroxide TS* to a pH of 4.0.

Mobile phase: Acetonitrile and *Buffer* (20:80)

Standard stock solution: 0.1 mg/mL of USP Eszopiclone RS in *Medium*. Sonication may be used to promote dissolution.

Standard solution: (*L*/500) mg/mL of USP Eszopiclone RS from *Standard stock solution* in *Medium*, where *L* is the label claim in mg/Tablet. Pass the resulting solution through a suitable filter of 0.45-µm pore size and use the filtrate.

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

Chromatographic system

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

Mode: LC

Detector: UV 303 nm

Column: 4.6-mm × 15.0-cm; 5-µm packing L1

Column temperature: 45°

Flow rate: 1 mL/min

Injection volume: 80 µL

Run time: NLT 1.5 times the retention time of eszopiclone

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 eszopiclone ($C_{17}H_{17}ClN_6O_3$) 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 Eszopiclone RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of eszopiclone ($C_{17}H_{17}ClN_6O_3$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Protect all solutions from light.

Solution A: 8.1 g/L of sodium dodecyl sulfate and 6.9 g/L of monobasic sodium phosphate in water. Sonicate for NLT 15 min and do not let the temperature of the water bath exceed 25°. Pass the resulting solution through a suitable filter of 0.45-µm pore size. Foam may form during filtration.

Mobile phase: Acetonitrile and *Solution A* (37:63) adjusted with dilute phosphoric acid (1 in 100) to a pH of 4.8 ± 0.05

Diluent: Acetonitrile and *Solution A* (37:63) adjusted with dilute phosphoric acid (1 in 100) to a pH of 2.5 ± 0.05

System suitability solution: 0.008 mg/mL each of USP Eszopiclone Related Compound A RS and USP Eszopiclone RS in *Diluent*. Sonication may be used to promote dissolution.

Standard solution: 0.008 mg/mL of USP Eszopiclone RS in *Diluent* passed through a suitable membrane filter of 0.45-µm pore size. Use the filtrate. Sonication may be used to promote dissolution.

Sample solution: Nominally 0.8 mg/mL of eszopiclone in *Diluent* prepared as follows. Crush NLT 20 Tablets to a fine powder and transfer a suitable portion to an appropriate volumetric flask. Add 60% of the final flask volume of *Diluent*, sonicate for 15 min in cold water with periodic shaking, and dilute with *Diluent* to volume. Pass the resulting solution through a suitable membrane filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 303 nm

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

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 2 times the retention time of eszopiclone

System suitability

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

Suitability requirements

Resolution: NLT 10 between eszopiclone related compound A and eszopiclone, *System suitability solution*

Tailing factor: NMT 2.0 for eszopiclone, *Standard 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 Tablets taken:

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

r_U = peak response of each degradation product from the *Sample solution*

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

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard peaks less than 0.04%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Zopiclone alcohol[a]	0.11	1.7	1.0
2-Amino-5-chloropyridine	0.21	0.76	1.0
Eszopiclone related compound A	0.44	0.86	1.0
Eszopiclone	1.0	—	—
Any individual unspecified degradation product	—	1.0	0.50
Total degradation products	—	—	2.0

[a] 6-(5-Chloropyridin-2-yl)-7-hydroxy-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-one.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

- **USP Reference Standards** ⟨11⟩

USP Eszopiclone RS

USP Eszopiclone Related Compound A RS

[Note—This material may be available in the free base or salt form.]

6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-yl 4-methylpiperazine-1-carboxylate 4-oxide.

$C_{17}H_{17}ClN_6O_4$ 404.81

6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-yl 4-methylpiperazine-1-carboxylate 4-oxide, 3-▲chlorobenzoate▲ (ERR 1-Jun-2018) salt (1:1).

$C_{17}H_{17}ClN_6O_4 \cdot$ ▲$C_7H_5ClO_2$▲ (ERR 1-Jun-2018) 561.38

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

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

Chromatographic Database Information: Chromatographic Database

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