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Zaleplon Capsules

DEFINITION
Zaleplon Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of zaleplon ($C_{17}H_{15}N_5O$).

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

ASSAY
- **Procedure**

Solution A: 0.3 g/L of ammonium formate in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
30	50	50
31	95	5

Diluent: Acetonitrile and water (20:80)

Standard solution: 0.1 mg/mL of USP Zaleplon RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of zaleplon from NLT 5 Capsules in *Diluent*. Pass through a filter of 0.45-µm pore size. [Note—Use the entire Capsule with its contents. Shake for 10 min.]

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

Mode: LC

Detector: UV 240 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

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

Column temperature: 30°

Flow rate: 1.4 mL/min

Injection volume: 15 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zaleplon ($C_{17}H_{15}N_5O$) in the portion of Capsules 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 Zaleplon RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution**

Test 1

Medium: Water; 900 mL

Apparatus 2: 75 rpm, with sinkers if necessary

Time: 20 min

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

Spectrophotometric procedure

Standard stock solution: 0.044 mg/mL of USP Zaleplon RS prepared as follows. Transfer a suitable quantity of USP Zaleplon RS to an appropriate volumetric flask. Add 10.0% of the total flask volume of methanol to dissolve. Dilute with *Medium* to volume. [Note—This solution is stable for 7 days.]

Standard solution: (*L*/1000) mg/mL of USP Zaleplon RS from *Standard stock solution* in *Medium*, where *L* is the label claim in mg/Capsule. [Note—This solution is stable for 7 days.]

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

Instrumental conditions

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

Mode: UV

Analytical wavelength: About 333 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zaleplon ($C_{17}H_{15}N_5O$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Chromatographic procedure

Buffer: 0.77 g/L of ammonium acetate in water

Mobile phase: Methanol and *Buffer* (33:67)

Standard stock solution: 0.22 mg/mL of USP Zaleplon RS prepared as follows. Dissolve first in methanol using 5% of total flask volume and dilute with *Medium* to volume.

Standard solution: (*L*/900) mg/mL of USP Zaleplon RS from *Standard stock solution* in *Medium*, where *L* is the label claim in mg/Capsule

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 230 nm

Column: 4.6-mm × 5-cm; 3-µm packing L1

Column temperature: 35°

Flow rate: 2.0 mL/min

Injection volume: 50 µL

Run time: 2 times the retention time of zaleplon

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zaleplon ($C_{17}H_{15}N_5O$) 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 Zaleplon RS in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 85% (Q) of the labeled amount of zaleplon ($C_{17}H_{15}N_5O$) is dissolved.

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

Medium: Water; 900 mL

Apparatus 2: 75 rpm, with sinkers

Time: 20 min

Buffer: 1.36 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (30:70)

Standard stock solution: 1.1 mg/mL of USP Zaleplon RS in *Mobile phase*

Standard solution: (L/900) mg/mL of USP Zaleplon RS from *Standard stock solution* in *Medium*, where L is the label claim in mg/Capsule

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 225 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 28°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: 2 times the retention time of zaleplon

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

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 zaleplon ($C_{17}H_{15}N_5O$) 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 Zaleplon RS in the *Standard solution* (mg/mL)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of zaleplon ($C_{17}H_{15}N_5O$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Mobile phase, Diluent, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard stock solution: 0.5 mg/mL of USP Zaleplon RS in *Diluent*

System suitability solution: 0.5 µg/mL of USP Zaleplon Related Compound B RS and 0.5 mg/mL of USP Zaleplon RS in *Diluent*

Sensitivity solution: 0.05 µg/mL of USP Zaleplon RS in *Diluent*, from the *Standard stock solution*

Standard solution: 0.1 mg/mL of USP Zaleplon RS in *Diluent*, from the *Standard stock solution*

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

Resolution: NLT 1.5 between zaleplon and zaleplon related compound B, *System suitability solution*

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

Relative standard deviation: NMT 2.0% for the zaleplon peak, *System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of any individual 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 any individual degradation product from the *Sample solution*

r_S = peak response of USP Zaleplon RS from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cyanopyrazolamine[a,b]	0.16	—
Zaleplon related compound A[b,c]	0.76	—
Zaleplon	1.0	—
Zaleplon related compound B[b]	1.05	—
Any individual unspecified degradation product	—	0.2
Total degradation products	—	1.0

[a] 3-Aminopyrazole-4-carbonitrile.

[b] This is a process impurity that is included in the table for identification purposes only. It is controlled in the drug substance and is not to be reported or included in the total degradation products for the drug product.

[c] (*E*)-*N*-{3-[3-(Dimethylamino)acryloyl]phenyl}-*N*-ethylacetamide.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in light-resistant containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Zaleplon RS

USP Zaleplon Related Compound B RS

N-[3-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-5-yl)phenyl]-*N*-ethylacetamide.
$C_{17}H_{15}N_5O$ 305.33

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

Topic/Question	Contact	Expert Committee
ZALEPLON CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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