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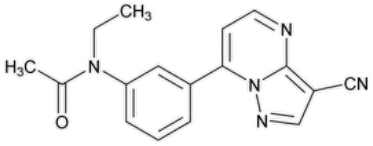
Zaleplon



$C_{17}H_{15}N_5O$ 305.33

Acetamide,*N*-[3-(3-cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)phenyl]-*N*-ethyl-;

3'-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)-*N*-ethylacetanilide CAS RN®: 151319-34-5; UNII: S62U433RMH.

DEFINITION

Zaleplon contains NLT 98.0% and NMT 102.0% of zaleplon ($C_{17}H_{15}N_5O$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

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

• **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: 0.3 g/L of ammonium formate in water. Adjust with formic acid to a pH of 4.0.

Mobile phase: Acetonitrile and *Buffer* (7:18)

Diluent: Acetonitrile and water (1:1)

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

Standard solution: 50 µg/mL of USP Zaleplon RS in *Diluent*

Sample solution: 50 µg/mL of Zaleplon in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 245 nm

Column: 4-mm × 10-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: 2 times the retention time of zaleplon

System suitability

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

[Note—The relative retention times for zaleplon and zaleplon related compound B are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2.0 between zaleplon and zaleplon related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of zaleplon ($C_{17}H_{15}N_5O$) in the portion of Zaleplon taken:

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

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

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

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

C_U = concentration of Zaleplon in the *Sample solution* (µg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Solution A: 1.4 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 3.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
15	60	40
25	45	55
26	80	20
35	80	20

Diluent: Acetonitrile and water (250:750)

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

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

Sample solution: 500 µg/mL of Zaleplon in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.2 between zaleplon related compound A and zaleplon related compound C; NLT 2.0 between zaleplon and zaleplon related compound B, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Zaleplon taken:

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

r_U = peak response of any individual impurity from the *Sample solution*

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

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

C_U = concentration of Zaleplon in the *Sample solution* (µg/mL)

F = relative response factor for the corresponding impurity peak (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cyanopyrazolamine[a]	0.15	0.50	0.15
Zaleplon related compound A	0.54	0.36	0.15
Zaleplon related compound C[b]	0.57	0.80	0.1
Desethylzaleplon[b,c]	0.70	1.1	0.1
Zaleplon	1.0	—	—
Zaleplon related compound B	1.11	0.65	0.15
Zaleplon oxopropenyl analog[b,d]	1.59	0.51	0.1
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] 3-Aminopyrazole-4-carbonitrile.

[b] Process impurity; may not be found in all manufacturing processes.

[c] *N*-[3-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)phenyl]acetamide.

[d] (*E*)-*N*-[3-(3-Cyano-6-{3-[3-(*N*-ethylacetamido)phenyl]-3-oxoprop-1-en-1-yl}pyrazolo[1,5-*a*]pyrimidin-7-yl)phenyl]-*N*-ethylacetamide.

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 2.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in light-resistant containers, and store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Zaleplon RS

USP Zaleplon Related Compound A RS

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

$C_{15}H_{20}N_2O_2$ 260.33

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

USP Zaleplon Related Compound C RS

7-[3-(*N*-Ethylacetamido)phenyl]pyrazolo[1,5-*a*]pyrimidine-3-carboxamide.

$C_{17}H_{17}N_5O_2$ 323.35

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

Topic/Question	Contact	Expert Committee
ZALEPLON	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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