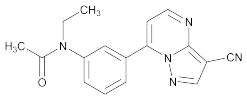
Zaleplon



$C_{17}H_{15}N_5O$ 305.33
Acetamide, *N*-[3-(3-cyanopyrazolo[1,5-α]pyrimidin-7-yl)phenyl]-*N*-ethyl-;
3′-(3-Cyanopyrazolo[1,5-α]pyrimidin-7-yl)-*N*-ethylacetanilide [151319-34-5].

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

IDENTIFICATION
- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **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: Two times the retention time of zaleplon
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
[NOTE—The relative retention times for zaleplon and zaleplon related compound B are 1.0 and 1.2, respectively.]
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
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm
- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.2%

Change to read:

- **ORGANIC IMPURITIES**

Diluent: Acetonitrile and water (1:1)
Solution A: Use the *Buffer* in the *Assay*.
Solution B: Acetonitrile
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
11.0	68	32
17.0	60	40
30.0	60	40
31.0	80	20
35.0	80	20

System suitability solution: Prepare as directed in the *Assay*.
Standard solution: 0.5 µg/mL of USP Zaleplon RS in *Diluent*
Sample solution: 0.5 mg/mL of Zaleplon in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 245 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 14.0 between zaleplon related compound A and zaleplon, and 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* (mg/mL)
C_U = concentration of Zaleplon in the *Sample solution* (mg/mL)
F = relative response factor for the corresponding impurity peak (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cyanopyrazolamine[a]	0.18	1.0	•0.15• (RB 1-Jan-2012)
Zaleplon related compound A[b]	0.58	0.76	•0.15• (RB 1-Jan-2012)
Zaleplon	1.0	—	—
Zaleplon related compound B[c]	1.08	0.92	•0.15• (RB 1-Jan-2012)
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] 3-Aminopyrazole-4-carbonitrile.
[b] (*E*)-*N*-{3-[3-(Dimethylamino)acryloyl]phenyl}-*N*-ethylacetamide.
[c] *N*-[3-(3-Cyanopyrazolo[1,5-α]pyrimidin-5-yl)phenyl]-*N*-ethylacetamide.

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** 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-α]pyrimidin-5-yl)phenyl]-*N*-ethylacetamide.
  $C_{17}H_{15}N_5O$ 305.33