Zaleplon

C₁₇H₁₅N₅O₃ 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 (C₁₇H₁₅N₅O₃), calculated on the anhydrous basis.

IDENTIFICATION
- A. INFRARED ABSORPTION (‘97K)
- 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 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: 4.6-mm x 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 (C₁₇H₁₅N₅O₃) in the portion of Zaleplon taken:

Result = \( \frac{r_f}{r_s} \times \frac{(C_f/C_s)}{\times (1/F) \times 100} \)

\( r_f \) = 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)
\( C_f \) = concentration of USP Zaleplon RS in the Sample solution (µg/mL)
\( F \) = relative response factor for the corresponding impurity peak (see Table 2)

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 x 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:

Result = \( \frac{r_f}{r_s} \times \frac{(C_f/C_s)}{\times (1/F) \times 100} \)

\( r_f \) = 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)
\( C_f \) = concentration of Zaleplon in the Sample solution (mg/mL)

Change to read:

- **ORGANIC IMPURITIES**
  - Diluent: Acetonitrile and water (1:1)
  - Solution A: Use the Buffer in the Assay.
  - Solution B: Acetonitrile

Table 1

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>11.0</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>17.0</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>30.0</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>31.0</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>35.0</td>
<td>80</td>
<td>20</td>
</tr>
</tbody>
</table>

©2011 The United States Pharmacopeial Convention  All Rights Reserved.
Acceptance criteria: See Table 2.

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanopyrazolamine*</td>
<td>0.18</td>
<td>1.0</td>
<td>0.15 (RB 1: Jan-2012)</td>
</tr>
<tr>
<td>Zaleplon related compound A&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.58</td>
<td>0.76</td>
<td>0.15 (RB 1: Jan-2012)</td>
</tr>
<tr>
<td>Zaleplon</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Zaleplon related compound B&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1.08</td>
<td>0.92</td>
<td>0.15 (RB 1: Jan-2012)</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.10</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>0.5</td>
</tr>
</tbody>
</table>

<sup>*</sup> 3-Aminopyrazole-4-carbonitrile.
<sup>1</sup> (E)-N-[3-(3-Dimethylamino)acryloyl]phenyl]-N-ethylacetamide.
<sup>2</sup> 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_{2}O_{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_{17}N_{5}O 305.33