Potassium Chloride Extended-Release Capsules

Type of Posting: Revision Bulletin
Posting Date: 31–Aug–2018
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Expert Committee: Chemical Medicines Monographs 5
Reason for Revision: Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 5 Expert Committee has revised the Potassium Chloride Extended-Release Capsules monograph. The purpose for the revision is to add **Dissolution Test 2** to accommodate FDA-approved drug products with different tolerances than the existing dissolution test. **Labeling** information has been incorporated to support the inclusion of **Dissolution Test 2**.

Additionally, minor editorial changes have been made to update the monograph to current USP style.

The Potassium Chloride Extended-Release Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Ren-Hwa Yeh, Ph.D., Senior Scientific Liaison (301-998-6818 or rhy@usp.org).
Potassium Chloride Extended-Release Capsules

**DEFINITION**
Potassium Chloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of potassium chloride (KCl).

**IDENTIFICATION**
- **A. IDENTIFICATION TESTS—GENERAL** (191), Chemical Identification Tests, Potassium
  - Sample solution: A portion of the filtrate, obtained as directed for Sample stock solution in the Assay
  - Acceptance criteria: Meet the requirements
- **B. IDENTIFICATION TESTS—GENERAL** (191), Chemical Identification Tests, Chloride
  - Sample solution: A portion of the filtrate, obtained as directed for Sample stock solution in the Assay
  - Acceptance criteria: Meet the requirements

**ASSAY**
- **PROCEDURE**
  - **Standard stock solution**: 19.07 µg/mL of potassium chloride, previously dried at 105° for 2 h, in water. This solution contains 10 µg/mL of potassium.
  - **Standard solutions**: To separate 100-mL volumetric flasks transfer 10.0, 15.0, and 20.0 mL, respectively, of Standard stock solution. To each flask add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with water to volume. The Standard solutions contain, respectively, 1.0, 1.5, and 2.0 µg/mL of potassium.
  - **Sample stock solution**: Place NLT 20 Capsules in a suitable container with 400 mL of water, heat to boiling, and boil for 20 min. Allow to cool, transfer the solution to a 1000-mL volumetric flask, and dilute with water to volume. Filter, discarding the first 20 mL of the filtrate. Transfer a measured volume of the subsequent filtrate, equivalent to 60 mg of potassium chloride, to a 1000-mL volumetric flask, and dilute with water to volume.
  - **Note**: Retain a portion of the filtrate for use in the Identification tests.
  - **Sample solution**: Transfer 5.0 mL of Sample stock solution to a 100-mL volumetric flask. Add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

**Instrumental conditions**
(See Atomic Absorption Spectroscopy (852).)
- **Mode**: Atomic absorption spectrophotometry
- **Analytical wavelength**: Potassium emission line at 766.5 nm
- **Lamp**: Potassium hollow-cathode
- **Flame**: Air–acetylene
- **Blank**: Water

**Analysis**
- **Samples**: Standard solutions, Sample solution, and Blank
  - Plot the absorbance of the Standard solutions versus the concentration of potassium, in µg/mL, and draw the straight line best fitting the three plotted points. From the graph, determine the concentration of potassium in the Sample solution (µg/mL).
  - Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:
    \[
    \text{Result} = \left( \frac{C \times D}{V \times L} \right) \times (M/A) \times 100
    \]
  - **C** = concentration of potassium in the Sample solution as determined in this test (µg/mL)
  - **D** = dilution factor of the Sample solution
  - **V** = volume of Medium, 900 mL
  - **L** = labeled amount of potassium chloride (µg/Capsule)
  - **M** = molecular weight of potassium chloride, 74.55
  - **A** = atomic weight of potassium, 39.10

  **Acceptance criteria**: 90.0%–110.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution** (711)
  - **Test 1** (RB 1-Sep-2018)
    - **Medium**: Water; 900 mL
    - **Apparatus 1**: 100 rpm
    - **Time**: 2 h
  - **Standard stock solution**: 19.07 µg/mL of potassium chloride, previously dried at 105° for 2 h, in water. This solution contains 10 µg/mL of potassium.
  - **Standard solutions**: To separate 100-mL volumetric flasks transfer 10.0, 15.0, and 20.0 mL, respectively, of Standard stock solution. To each flask add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with water to volume. The Standard solutions contain, respectively, 1.0, 1.5, and 2.0 µg/mL of potassium.
  - **Sample solution**: Filter the solution under test, and dilute quantitatively with Medium to obtain a solution containing 60 µg/mL of potassium chloride.
  - **Sample solution**: Add 5.0 mL of the Sample stock solution to a 100-mL volumetric flask, add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

**Instrumental conditions**
(See Atomic Absorption Spectroscopy (852).)
- **Mode**: Atomic absorption spectrophotometry
- **Analytical wavelength**: Potassium emission line at 766.5 nm
- **Lamp**: Potassium hollow-cathode
- **Flame**: Air–acetylene
- **Blank**: Water

**Analysis**
- **Samples**: Standard solutions, Sample solution, and Blank
  - Plot the absorbance of the Standard solutions versus the concentration of potassium, in µg/mL, and draw the straight line best fitting the three plotted points. From the graph, determine the concentration of potassium in the Sample solution (µg/mL).
  - Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:
  
  **Tolerances**: NMT 35% (Q) of the labeled amount of potassium chloride (KCl) is dissolved in 2 h. The requirements are met if the quantities dissolved from the Capsules tested conform to Table 1 instead of to the table shown in Dissolution (711).
Table 1

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number Tested</th>
<th>Acceptance Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>S₁</td>
<td>6</td>
<td>Each unit is within the range $Q \pm 30%$.</td>
</tr>
<tr>
<td>S₂</td>
<td>6</td>
<td>Average of 12 units ($S_1 + S_2$) is within the range between $Q - 30%$ and $Q + 35%$, and no unit is outside the range $Q \pm 40%$.</td>
</tr>
<tr>
<td>S₃</td>
<td>12</td>
<td>Average of 24 units ($S_1 + S_2 + S_3$) is within the range between $Q - 30%$ and $Q + 35%$, and NMT 2 units are outside the range $Q \pm 40%$.</td>
</tr>
</tbody>
</table>

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

Standard stock solution and Standard solutions:
Prepare as directed in Test 1.

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Times: 1, 2, 4, and 6 h

Sample stock solution: Transfer 4.0 mL of the solution under test into a 50-mL volumetric flask, dilute with water to volume, and filter.

Sample solution: Transfer 4.0 mL of the Sample stock solution to a 100-mL volumetric flask. Add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

Blank solution: To a 100-mL volumetric flask, add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

Instrumental conditions: Proceed as directed in Test 1, except do not use the Blank.

System suitability
Samples: Standard solutions

Suitability requirements
Linearity: Correlation coefficient NLT 0.99
Relative standard deviation: NMT 5.0% from 5 replicate analyses of the 1.5-µg/mL Standard solution

Analysis
Samples: 1.5-µg/mL Standard solution, Sample solution, and Blank solution

Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:

\[
\text{Result, } \%	ext{ }= \left[ \frac{(A_U/A_S) \times C_S \times D \times (V/L)}{M_r/A_r} \right] \times 100
\]

\[A_U\] = absorbance of potassium in the Sample solution
\[A_S\] = absorbance of potassium in the Standard solution
\[C_S\] = concentration of potassium in the Standard solution (µg/mL)
\[D\] = dilution factor of the Sample solution
\[V\] = volume of Medium, 900 mL
\[L\] = labeled amount of potassium chloride (µg/Capsule)
\[M_r\] = molecular weight of potassium chloride, 74.55
\[A_r\] = atomic weight of potassium, 39.10

Tolerances: See Table 2

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25-45</td>
</tr>
<tr>
<td>2</td>
<td>45-65</td>
</tr>
<tr>
<td>3</td>
<td>70-90</td>
</tr>
<tr>
<td>4</td>
<td>NLT 85</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of potassium chloride (KCl), dissolved at the times specified, conform to Dissolution Table 2.

**Uniformity of Dosage Units (905):** Meet the requirements

**Additional Requirements**
- Packaging and Storage: Preserve in tight containers, and store at a temperature not exceeding 30°.

Add the following:

**Labeling:** When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used. ▲ (RB 1-Sep-2018)