Clindamycin Phosphate

Type of Posting  Revision Bulletin
Posting Date  28–Apr–2017
Official Date  01–May–2017
Expert Committee  Chemical Medicines Monographs 1
Reason for Revision  Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 1 Expert Committee has revised the Clindamycin Phosphate monograph.

The purpose of the revision is to replace the USP Clindamycin Phosphate RS with USP Clindamycin Phosphate System Suitability RS for System suitability evaluation. The Assay and test for Organic Impurities are revised to include USP Clindamycin Phosphate System Suitability RS and a revised System suitability solution to be used for the evaluation of resolution between clindamycin phosphate and 7-epiclindamycin phosphate.

The Clindamycin Phosphate Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in USP 41–NF 36.

Should you have any questions, please contact Morgan Puderbaugh, Senior Scientific Liaison (301-998-6833 or mxp@usp.org.)
Chromatographic system

Sample solution: 2.2 mg/mL of Clindamycin Phosphate in Diluent. Shake, and sonicate to dissolve.

Clindamycin Phosphate has a potency equivalent to NLT 758 µg/mg of clindamycin (C₁₈H₃₃ClN₂O₅S), calculated on the anhydrous basis.

**Identification**

- **A. infrared absorption (197K)**
  - **Standard:** Add 0.2 mL of water to 50 mg of Clindamycin Phosphate RS, and heat to dissolve. Evaporate to dryness under vacuum, and dry the residue at 100°–105° for 2 h.
  - **Sample:** Add 0.2 mL of water to 50 mg of Clindamycin Phosphate, and heat to dissolve. Evaporate to dryness under vacuum, and dry the residue at 100°–105° for 2 h.
  - **Acceptance criteria:** Meets the requirements

- **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**

**Change to read:**

- **Procedure**
  - **Solution A:** Add 14 mL of phosphoric acid to 4000 mL of water. Add 10 mL of ammonium hydroxide, and adjust with ammonium hydroxide to a pH of 5.6 ± 0.1.
  - **Solution B:** Acetonitrile and methanol (90:100)
  - **Solution C:** Solution B and Solution A (80:20)
  - **Solution D:** Solution B and Solution A (480:520)
  - **Diluent:** Solution B and Solution A (20:80)
  - **Mobile phase:** See Table 1.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution C (%)</th>
<th>Solution D (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>40</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>46</td>
<td>95</td>
<td>5</td>
</tr>
</tbody>
</table>

**System suitability solution:** 2.2 mg/mL of USP Clindamycin Phosphate System Suitability RS in Diluent. Shake, and sonicate to dissolve.

**Impurities**

**Change to read:**

- **Organic impurities**
  - **Standard solution:** 14 µg/mL of USP Clindamycin Phosphate RS in Diluent. Shake, and sonicate to dissolve.

**System suitability**

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

**Suitability requirements**

- **Resolution:** NLT 3.0 between 7-epiclindamycin phosphate and clindamycin phosphate, System suitability solution

**Tailing factor:** NMT 2.0 for clindamycin phosphate, System suitability solution

**Relative standard deviation:** NMT 5.0% for clindamycin phosphate, Standard solution
Analysis

**Samples:**  Standard solution and Sample solution

Calculate the percentage of each impurity in the portion of Clindamycin Phosphate taken:

\[
\text{Result} = \frac{r_i}{r_R} \times \frac{C_i}{C_R} \times P \times \left(\frac{F_1}{F_2}\right) \times 100
\]

- \( r_i \) = peak response of each impurity from the Sample solution
- \( r_R \) = peak response of clindamycin phosphate from the Standard solution
- \( C_i \) = concentration of USP Clindamycin Phosphate in the Standard solution (mg/mL)
- \( C_R \) = concentration of Clindamycin Phosphate, corrected for water content, in the Sample solution (mg/mL)
- \( P \) = potency of clindamycin in USP Clindamycin Phosphate RS (µg/mg)
- \( F_1 \) = conversion factor, 0.001 mg/µg
- \( F_2 \) = relative response factor (see [Table 2](#)), <br/>Acceptance criteria: See Table 2. The reporting level is 0.05%.

<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>Lincomycin phosphate</td>
<td>0.36</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>0.50</td>
<td>2.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Clindamycin B phosphate</td>
<td>0.77</td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>7-Epiclindamycin phosphate</td>
<td>0.89</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Clindamycin 3-phosphate</td>
<td>0.93</td>
<td>1.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Clindamycin phosphate</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>1.4</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Any individual, unspecified</td>
<td>—</td>
<td>—</td>
<td>4.0</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>4.0</td>
</tr>
</tbody>
</table>

- Methyl 6,8-dideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside-2-phosphate.
- Methyl 6,8-dideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside.
- Methyl 7-chloro-6,7,8-trideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside-2-phosphate.
- Methyl 7-chloro-6,7,8-trideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside-2-phosphate.
- Methyl 7-chloro-6,7,8-trideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside-3-phosphate.
- Methyl 7-chloro-6,7,8-trideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside-2-phosphate.

**SPECIFIC TESTS**

- **CRYSTALLINITY** (695): Meets the requirements
- **pH** (791)
  - Sample solution: 10 mg/mL
  - Acceptance criteria: 3.5-4.5
- **WATER DETERMINATION** (921), Method h: NMT 6.0%
- **STERILITY TESTS** (71)
  - Sample solution: 6 g of specimen aseptically dissolved in 200 mL of Fluid A
  - Analysis: Test as directed in the Test for Sterility of the Product to Be Examined, Membrane Filtration.
  - Acceptance criteria: It meets the requirements where the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store below 30°.
- **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

**Change to read:**

- **USP REFERENCE STANDARDS (11)**
  - USP Clindamycin Phosphate RS
  - USP Clindamycin Phosphate System Suitability RS
  - Contains clindamycin phosphate and the following impurity:
    - 7-Epiclindamycin phosphate;
  - Methyl 7-chloro-6,7,8-trideoxy-6'-(2S,5R)-1-methyl-4-propylpyrrolidine-2-carboxamide-1-thio-4-erythro-o-α-galacto-octopyranoside 2-phosphate.
  - Clindamycin Phosphate RS (µg/mg): 504.96 (81 1-May-2017) USP Endotoxin RS