CLINDAMYCIN PALMITATE
POWDER FOR ORAL SOLUTION
(CLINDAMYCINI PALMITAS
PULVIS PRO SOLUTIONE PERORALI)
Draft proposal for The International Pharmacopoeia
(Febuary 2018)
DRAFT FOR COMMENT

Should you have any comments on this draft, please send these to Dr Herbert Schmidt, Medicines Quality Assurance Programme, Technologies Standards and Norms, Department of Essential Medicines and Health Products, World Health Organization, 1211 Geneva 27, Switzerland; fax: (+41 22) 791 4730 or email: schmidt@who.int by 13 April 2018.

In order to speed up the process for receiving draft monographs and for sending comments, please let us have your email address (to bonnyw@who.int) and we will add it to our electronic mailing list. Please specify if you wish to receive monographs.
SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/16.655:
CLINDAMYCIN PALMITATE POWDER FOR ORAL SOLUTION
(CLINDAMYCIN PALMITAS PULVIS PRO SOLUTIONE PERORALI)

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Drafting of the monograph by a WHO Collaborating Centre</td>
<td>October 2015–January 2016</td>
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<tr>
<td>Discussion at informal consultation on quality control laboratory tools and specifications for medicines</td>
<td>9–11 May 2016</td>
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<tr>
<td>Draft revision sent out for public consultation</td>
<td>July–September 2016</td>
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<tr>
<td>Presentation to WHO Expert Committee on Specifications for Pharmaceutical Preparations</td>
<td>October 2016</td>
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<td>Discussion at the informal consultation on quality control laboratory tools and specifications for medicines</td>
<td>2–4 May 2017</td>
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<td>Further laboratory investigations in response to comments received</td>
<td>June–September 2017</td>
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<tr>
<td>Presentation of revised version (Rev.1) to WHO Expert Committee on Specifications for Pharmaceutical Preparations</td>
<td>October 2017</td>
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<tr>
<td>Revision 1 sent out for public consultation</td>
<td>February–April 2018</td>
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<td>Further follow-up action as required</td>
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CLINDAMYCIN PALMITATE POWDER FOR ORAL SOLUTION

(CLINDAMYCINI PALMITAS PULVIS PRO SOLUTIONE PERORALI)

**Category.** Antibacterial.

**Storage.** Clindamycin palmitate powder for oral solution should be kept in a tightly closed container.

**Additional information.** Strength in the current WHO Model List of Essential Medicines (EML): 75 mg/5 mL (as palmitate). Strengths in the current WHO EML for Children: 75 mg/5 mL (as palmitate).

Clindamycin palmitate powder for oral solution may contain excipients that are suspended in the reconstituted solution. Shake until the solution is uniform.

**Labelling.** The designation on the container of clindamycin palmitate powder for oral solution should state that the active ingredient is clindamycin palmitate hydrochloride and the quantity should be indicated in terms of equivalent amount of clindamycin.

**Requirements**

Complies with the monograph for *Liquid preparations for oral use*; the powder complies with the section of the monograph entitled *Powders for oral solutions, oral suspensions and oral drops*.

**Definition.** Clindamycin palmitate powder for oral solution is a solution of clindamycin palmitate hydrochloride in a suitable vehicle, which may be flavoured. It is prepared from the powder as stated on the label before use. When freshly constituted the oral solution contains not less than 90.0% and not more than 110.0% of the labelled amount of clindamycin (C₁₈H₃₃ClN₂O₅S).

**Identity test**

Carry out the test as described under 1.14.4 *High-performance liquid chromatography* using the conditions given under “Assay”. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that of the principal peak in the chromatogram obtained with solution (2).

**pH value** *(1.13)*. pH of a solution constituted as directed in the labelling, 2.5–5.0.

**Loss on drying.** Dry the powder for oral solution to constant mass at 60 °C under reduced pressure; it loses not more than 20 mg/g.
Related substances

Use the oral solution immediately after preparation.

Carry out the test as described under 1.14.4 High-performance liquid chromatography using a column (25 cm × 4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octylsilyl groups (5 μm).\(^1\)

Use the following conditions for gradient elution:

- Mobile phase A: Ammonium acetate (~0.40 g/L) TS – acetonitrile R (50:50);
- Mobile phase B: Acetonitrile R.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Mobile phase A (%) v/v</th>
<th>Mobile phase B (%) v/v</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–30</td>
<td>100 to 0</td>
<td>0 to 100</td>
<td>Linear gradient</td>
</tr>
<tr>
<td>30–80</td>
<td>0</td>
<td>100</td>
<td>Isocratic</td>
</tr>
<tr>
<td>80–81</td>
<td>0 to 100</td>
<td>100 to 0</td>
<td>Return to initial composition</td>
</tr>
<tr>
<td>81–90</td>
<td>100</td>
<td>0</td>
<td>Re-equilibration</td>
</tr>
</tbody>
</table>

Prepare the following solutions in methanol R. For solution (1) transfer a quantity of the oral solution, equivalent of about 57 mg of clindamycin to a 10 mL volumetric flask and dilute to volume. For solution (2) dilute 2.0 mL of solution (1) to 100.0 mL. For solution (3) dissolve about 75 mg clindamycin palmitate hydrochloride RS (containing clindamycin palmitate hydrochloride and impurity A) and dilute to 10.0 mL.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 230 nm.

Inject alternately 20 μL each of solution (1), (2) and (3).

In the chromatogram obtained with solution (3) the retention time of clindamycin palmitate is about 37 minutes. The test is not valid unless the resolution between the peaks due to clindamycin palmitate and impurity A (relative retention about 0.9) is at least 3.0.

In the chromatogram obtained with solution (1) the following impurities, if present, are eluted at the following relative retention with reference to clindamycin palmitate: impurity B about 0.8 and impurity A about 0.9.

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\(^1\) Agilent® Zorbax Elipse XDB- C8 (4.6 x 250 mm, 5 μm) has been found suitable.
In the chromatogram obtained with solution (1):

- the area of any impurity peak is not more than the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);
- the sum of the areas of all impurity peaks is not more than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (8.0%).

Disregard any peak with an area less than 0.025 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

**Assay.** Use the oral solution immediately after preparation.

Carry out the test as described under 1.14.4 High-performance liquid chromatography using a stainless steel column (25 cm × 4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (5 μm).\(^2\)

As the mobile phase, use a mixture of 10 volumes of ammonium acetate (~0.40 g/L) TS and 90 volumes of acetonitrile R.

Prepare the following solutions in mobile phase. For solution (1) dissolve a quantity of the oral solution, equivalent to about 30 mg of clindamycin, accurately weighed, and dilute to 50.0 mL, filter and use the filtrate. For solution (2) dissolve about 50 mg clindamycin palmitate hydrochloride RS and dilute to 50.0 mL.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 230 nm.

Inject alternately 20 μL each of solutions (1) and (2) and record the chromatograms for about 40 minutes.

Measure the areas of the peak responses corresponding to clindamycin palmitate obtained in the chromatograms from solutions (1) and (2). Determine the weight per mL (1.3.1) of the oral solution and calculate the percentage content of clindamycin (C\(_{18}\)H\(_{33}\)ClN\(_2\)O\(_5\)S) in the oral solution, using the declared content of clindamycin palmitate hydrochloride (C\(_{34}\)H\(_{63}\)ClN\(_2\)O\(_6\)S.HCl) in clindamycin palmitate hydrochloride RS. Each mg of clindamycin palmitate hydrochloride (C\(_{34}\)H\(_{63}\)ClN\(_2\)O\(_6\)S.HCl) is equivalent to 0.607 mg clindamycin (C\(_{18}\)H\(_{33}\)ClN\(_2\)O\(_5\)S).

**Impurities**

The impurities limited by the requirements of this monograph include those listed in the monograph for Clindamycin palmitate hydrochloride.

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\(^2\) Waters Symmetry C8 has been found suitable.