CLINDAMYCIN PALMITATE FOR ORAL SUSPENSION
(CLINDAMYCINI PALMITAS AD SUSPENSIONEM PERORALEM)

Draft proposal for The International Pharmacopoeia
(July 2016)
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 16 September 2016.

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.

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<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</td>
<td>9–11 May 2016</td>
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<td>tools and specifications for medicines</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>Further follow-up action as required</td>
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CLINDAMYCIN PALMITATE FOR ORAL SUSPENSION
(CLINDAMYCIN PALMITAS AD SUSPENSIONEM PERORALEM)

**Category.** Antibacterial.

**Storage.** Clindamycin palmitate hydrochloride for oral suspension 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).

**Labelling.** The designation on the container of clindamycin palmitate for oral suspension 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 for oral suspension is a suspension of Clindamycin palmitate hydrochloride in a suitable vehicle, which may be flavoured. It is prepared from the powder as stated on the label just before issue for use. When freshly constituted the oral suspension contains not less than 90.0% and not more than 110.0% of the labelled amount of clindamycin (C_{18}H_{33}ClN_{2}O_{5}S).

**Identity tests**

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

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

Use the oral suspension 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 octylsilyle groups (5 μm).

Use the following conditions for gradient elution:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Mobile phase A (%)</th>
<th>Mobile phase B (%)</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</td>
</tr>
<tr>
<td>81–90</td>
<td>100</td>
<td>0</td>
<td>composition</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Re-equilibration</td>
</tr>
</tbody>
</table>

Prepare the following solutions in methanol R. For solution (1) transfer a quantity of the oral suspension, 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 74 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 time about 0.9) is at least 3.0.

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%).

¹ Agilent® Zorbax Elipse XDB-C8 (4.6 × 250 mm, 5 μm) has been found suitable.
**Assay**  [The method is currently under validation. Some parameters need to be amended.]

Use the oral suspension 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 octylsilyl 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 the mobile phase. For solution (1) dissolve a quantity of the oral suspension, equivalent to about 225 mg of clindamycin, accurately weighed, and dilute to 50.0 mL, filter and use the filtrate. For solution (2) dissolve about 74 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 solutions (1) and (2). The retention time of clindamycin palmitate is about x minutes. The assay is not valid unless in the chromatogram obtained with solution (2) the resolution between the peaks due to clindamycin palmitate and impurity A (relative retention time is about x) is at least x.

Measure the areas of the peak responses obtained in the chromatograms from solutions (1) and (2). Determine the weight per mL (1.3.1) of the oral suspension and calculate the percentage content of clindamycin (C₁₈H₃₃ClN₂O₅S) in the oral suspension, using the declared content of clindamycin palmitate hydrochloride (C₃₄H₆₃ClN₂O₆S.HCl) in clindamycin palmitate hydrochloride RS. Each mg of clindamycin palmitate hydrochloride (C₃₄H₆₃ClN₂O₆S.HCl) is equivalent to 0.607 mg clindamycin (C₁₈H₃₃ClN₂O₅S).

**Impurities**

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

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² Agilent Zorbax Elipse XDB- C8 has been found suitable.