CLINDAMYCIN PHOSPHATE INJECTION
(CLINDAMYCINI PHOSPHATIS INJECTIO)

DRAFT MONOGRAPH FOR INCLUSION IN

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DRAFT FOR COMMENTS

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SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/16.679:
Clindamycin phosphate injection (Clindamycini phosphatis injectio)

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<td>Drafting of the monograph by a WHO Collaborating Centre</td>
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<td>Discussion at informal consultation on quality control laboratory tools and specifications for medicines</td>
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CLINDAMYCIN PHOSPHATE INJECTION
(CLINDAMYCINI PHOSPHATIS INJECTION)

Description. A clear, colourless or almost colourless solution.

Category. Antibacterial.

Storage. Clindamycin injection should be stored at a temperature not exceeding 30 °C. It should not be refrigerated and it should not be allowed to freeze.

Additional information. Strength in the current WHO Model List of Essential Medicines (EML): 150 mg (as phosphate) per mL. Strengths in the current EML for Children: 150 mg (as phosphate) per mL.

Labelling. The designation of the container should state that the active ingredient is the phosphate form and the quantity should be indicated in terms of equivalent amount of clindamycin.

Requirements

Complies with the monograph for Parenteral preparations.

Definition. Clindamycin phosphate injection is a sterile solution of Clindamycin phosphate in water for injections. It contains not less than 90.0% and not more than 110.0% of the amount of clindamycin \( \text{C}_{18}\text{H}_{33}\text{ClN}_{2}\text{O}_{5}\text{S} \) stated on the label.

Identity tests

- Either tests A and C or tests B and C may be applied.

A. 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 principle peak in the chromatogram obtained with solution (1) is similar to that in the chromatogram obtained with solution (2).

B. Carry out the test as described under 1.14.1 Thin-layer chromatography using silica gel R3 as the coating substance and a mixture of 20 volumes of glacial acetic acid R, 20 volumes of water R and 60 volumes of 1-butanol R as the mobile phase. Apply separately to the plate 5 \( \mu \)L of each of the following 3 solutions in methanol R. For solution (A) dilute a quantity of the injection to
obtain a solution containing the equivalent of 2.0 mg of Clindamycin per mL. For solution (B) use clindamycin phosphate RS to obtain a solution containing 2.0 mg of clindamycin phosphate per mL. For solution (C) dissolve 10 mg of lincomycin hydrochloride RS in 5 mL of solution (B). After removing the plate from the chromatographic chamber, allow it to dry at 105 °C for 30 minutes. Spray the plate with potassium permanganate (1 g/L) TS and examine the chromatogram in daylight.

The principal spot obtained with solution (A) corresponds in position, appearance and intensity to that obtained with solution (B). The test is not valid unless the chromatogram obtained with solution (C) shows two clearly separated spots.

C. Boil 1 mL of the injection under a reflux condenser with a mixture of 5 mL of sodium hydroxide (~400 g/L) TS and 5 mL of water for 90 minutes. Cool and add 5 mL of nitric acid (~1000 g/L) TS. Extract with three 15 mL quantities of dichloromethane R and discard the extracts. Filter the upper aqueous layer through a paper filter; the filtrate yields reaction B described under 2.1 General identification tests as characteristic of orthophosphates.

**pH value (1.13).** pH of the injection, 5.5–7.0.

**Related substances**

Carry out the test as described under 1.14.4 High-performance liquid chromatography using a stainless steel column (15 cm × 4.6 mm) packed with end-capped particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (5 µm).¹

Use the following conditions for gradient elution:

- mobile phase A: 21 volumes of acetonitrile for chromatography R and 79 volumes of phosphate buffer pH 6.0;
- mobile phase B: 60 volumes of acetonitrile for chromatography R and 40 volumes of phosphate buffer pH 6.0.

Prepare the phosphate buffer pH 6.0 by dissolving 13.6 g of potassium dihydrogen phosphate R in 750 mL of water R, adjust the pH to 6.0 with potassium hydroxide (~450g/L) TS and dilute to 1000 mL with water R.

¹ A Symmetry C18 column was found suitable.
operate with a flow rate of 1.1 mL per minute. As a detector use an ultraviolet
spectrophotometer set at a wavelength of 210 nm. Maintain the column temperature at
30 °C.

Prepare the following solutions in mobile phase A.

For solution (1) dilute 2.0 mL of the injection to 100.0 mL. For solution (2) dilute 1.0
mL of solution (1) to 100.0 mL. For solution (3) use a solution containing 0.12 mg
lincomycin hydrochloride RS per mL, 0.24 mg of clindamycin phosphate RS per mL
and 15 µg of benzyl alcohol R per mL.

Inject 20 µL of solution (3). The test is not valid unless in the chromatogram obtained
with solution (3), the resolution factor between the peaks due to lincomycin and
clindamycin phosphate is at least 7.7. The following peaks are eluted at the following
relative retentions with reference to clindamycin phosphate (retention time about 12
minutes): lincomycin: about x; benzyl alcohol: about 0.x. [to be added]

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

In the chromatogram obtained with solution (1):

- the area of any impurity peak is not greater than 3 times the area of the
principal peak in the chromatogram obtained with solution (3) (3.0%);
- the sum of the areas of all impurities is not greater than 8 times the area of the
principal peak in the chromatogram obtained with solution (2) (8.0%).

Disregard any peak due to benzyl alcohol, if present, and any peak with an
area less than 0.1 times the area of the principal peak in the chromatogram
obtained with solution (2) (0.1%).

**Assay**

Carry out the test as described under *1.14.4 High-performance liquid chromatography*
using a stainless steel column (15 cm × 4.6 mm) packed with end-capped 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 21 volumes of acetonitrile for chromatography R and 79 volumes of phosphate buffer pH 6.0. Prepare the phosphate buffer pH 6.0 by dissolving 13.6 g of potassium dihydrogen phosphate R in 750 mL of water R, adjust the pH to 6.0 with potassium hydroxide (~450 g/L) TS and dilute to 1000 mL with water R.

Prepare the following solutions in mobile phase. For solution (1) dilute 1.0 mL of the injection to 100.0 mL. For solution (2) dissolve 36 mg of clindamycin phosphate RS and dilute to 20.0 mL. For solution (3) use a solution containing 0.12mg lincomycin per mL, 0.24 mg of clindamycin phosphate RS per mL and 15 µg of benzyl alcohol R per mL.

Operate with a flow rate of 1.1 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 210 nm.

Inject 20 µL of solution (3). In the chromatogram the following peaks are eluted at the following relative retentions with reference to clindamycin phosphate (retention time about 8.0 minutes): benzyl alcohol about 0.6. The assay is not valid unless the resolution between the peaks due to clindamycin phosphate and benzyl alcohol is at least 3.0 and the resolution between the peaks due to clindamycin phosphate and lincomycin is at least 7.0.

Inject alternately 20 µL each of solutions (1) and (2). Measure the areas of the peaks corresponding to clindamycin phosphate obtained in the chromatograms from solutions (1) and (2) and calculate the percentage content of clindamycin (C₁₈H₃₄ClN₂O₈S) in the injection using the declared content of C₁₈H₃₄ClN₂O₈PS in clindamycin phosphate RS. Each mg of clindamycin phosphate (C₁₈H₃₄ClN₂O₈PS) is equivalent to 0.8416 mg of clindamycin (C₁₈H₃₃ClN₂O₅S).

**Bacterial endotoxins.** Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 0.10 IU of endotoxin RS per mg of clindamycin.

**Impurities**

The impurities limited by the requirements of this monograph include those listed in the monograph on Clindamycin phosphate.

² A Symmetry C18 column was found suitable.