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. he Revision Bulletin will be incorporated in *USP 41–NF 36*.
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Should you have any questions, please contact Morgan Puderbaugh, Senior Scientific Liaison (301-998-6833 or mxp@usp.org.)

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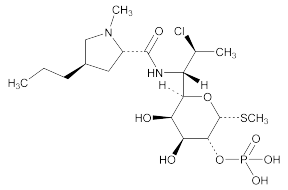
Clindamycin Phosphate



$C_{18}H_{34}ClN_2O_8PS$ 504.96

L-*threo*-α-D-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-;
Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-(dihydrogen phosphate) [24729-96-2].

DEFINITION

Clindamycin Phosphate has a potency equivalent to NLT 758 µg/mg of clindamycin ($C_{18}H_{33}ClN_2O_5S$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨197K⟩
  Standard: Add 0.2 mL of water to 50 mg of USP 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 (900:100)
  Solution C: *Solution B* and *Solution A* (80:920)
  Solution D: *Solution B* and *Solution A* (480:520)
  Diluent: *Solution B* and *Solution A* (20:80)
  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution C (%)	Solution D (%)
0	95	5
40	5	95
41	95	5
46	95	5

  System suitability solution: 2.2 mg/mL of USP Clindamycin Phosphate System Suitability RS in *Diluent*. Shake, and sonicate to dissolve. (RB 1-May-2017)
  Standard solution: 2.2 mg/mL of USP Clindamycin Phosphate RS in *Diluent*. Shake, and sonicate to dissolve.
  Sample solution: 2.2 mg/mL of Clindamycin Phosphate in *Diluent*. Shake, and sonicate to dissolve.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 214 nm
  Column: 4.6-mm × 25-cm; 5-µm packing L7
  Column temperature: 40°
  Flow rate: 1.2 mL/min
  Injection volume: 20 µL
  System suitability
  Samples: *System suitability solution* and *Standard solution* (RB 1-May-2017)
  Suitability requirements
  Resolution: NLT 3.0 between clindamycin phosphate and 7-epiclindamycin phosphate, *System suitability solution* (RB 1-May-2017)
  Tailing factor: NMT 2.0 for clindamycin phosphate, *Standard solution* (RB 1-May-2017)
  Relative standard deviation: NMT 0.73%, *Standard solution* (RB 1-May-2017)
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the quantity of clindamycin ($C_{18}H_{33}ClN_2O_5S$), in µg/mg, in the portion of Clindamycin Phosphate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P$$

  r_U = peak response from the *Sample solution*
  r_S = peak response from the *Standard solution*
  C_S = concentration of USP Clindamycin Phosphate RS in the *Standard solution* (mg/mL)
  C_U = concentration of Clindamycin Phosphate in the *Sample solution* (mg/mL)
  P = potency of clindamycin in USP Clindamycin Phosphate RS (µg/mg)
  Acceptance criteria: NLT 758 µg/mg on the anhydrous basis

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**
  Solution A, Solution B, Solution C, Solution D, Diluent, Mobile phase, System suitability solution, (RB 1-May-2017) **Sample solution,** and **Chromatographic system:** Proceed as directed in the *Assay*. (RB 1-May-2017)
  Standard solution: 14 µg/mL of USP Clindamycin Phosphate RS (RB 1-May-2017) in *Diluent*. Shake, and sonicate to dissolve. (RB 1-May-2017)
  System suitability
  Samples: *System suitability solution* and *Standard solution* (RB 1-May-2017)
  Suitability requirements
  Resolution: NLT 3.0 between 7-epiclindamycin phosphate and clindamycin phosphate, *System suitability solution*
  Tailing factor: NMT 2.0 for clindamycin phosphate, *Standard 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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times (F_1/F_2) \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of clindamycin phosphate from the *Standard solution*
C_S = concentration of USP Clindamycin Phosphate RS in the *Standard solution* (mg/mL)
C_U = 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*)

Acceptance criteria: See *Table 2*. The reporting level is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lincomycin phosphate[a]	0.36	1.0	1.0
Lincomycin[b]	0.50	2.0	0.5
Clindamycin B phosphate[c]	0.77	1.0	1.5
7-Epiclindamycin phosphate[d]	0.89	1.0	0.8
Clindamycin 3-phosphate[e]	0.93	1.0	0.3
Clindamycin phosphate	1.0	—	—
Clindamycin[f]	1.4	1.0	0.5
Any individual, unspecified impurity	—	1.0	1.0
Total impurities	—	—	4.0

[a] Methyl 6,8-dideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside 2-phosphate.
[b] Methyl 6,8-dideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside.
[c] Methyl 7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-ethylpyrrolidine-2-carboxamido]-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-phosphate.
[d] Methyl 7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside 2-phosphate.
[e] Methyl 7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-ethylpyrrolidine-2-carboxamido]-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 3-phosphate.
[f] Methyl 7-chloro-6,7,8-trideoxy-6-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-D-*threo*-α-D-*galacto*-octopyranoside.

SPECIFIC TESTS

- **CRYSTALLINITY ⟨695⟩:** Meets the requirements
- **pH ⟨791⟩**
  Sample solution: 10 mg/mL
  Acceptance criteria: 3.5–4.5
- **WATER DETERMINATION ⟨921⟩, *Method I*:** 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.
- **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** It contains NMT 0.58 USP Endotoxin Units/mg of clindamycin, where the label states that Clindamycin Phosphate 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-[(2*S*,4*R*)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside 2-phosphate.
  $C_{18}H_{34}ClN_2O_8PS$ 504.96● (RB 1-May-2017)
  USP Endotoxin RS