

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

65-049

APPROVED DRAFT LABELING

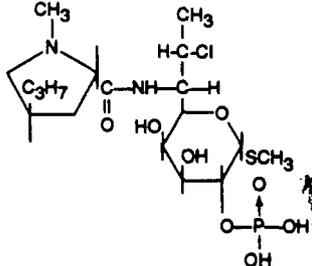
Clindamycin Phosphate Topical Solution USP, 1% For External Use Only

DESCRIPTION

Clindamycin Phosphate Topical Solution contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per milliliter. Each Clindamycin Phosphate Topical Solution pleglet applicator contains approximately 1 mL of topical solution.

Clindamycin phosphate is a water soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent antibiotic lincomycin.

The solution contains isopropyl alcohol 50% v/v, propylene glycol, sodium hydroxide (to adjust the pH to between 4.0 - 7.0) and purified water. The structural formula is represented below:



The chemical name for clindamycin phosphate is 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). It has a molecular weight of 504.96, and the molecular formula is $C_{18}H_{34}ClN_2O_8PS$. Flash Point 75° F.

CLINICAL PHARMACOLOGY

Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

Cross resistance has been demonstrated between clindamycin and lincomycin.

Antagonism has been demonstrated between clindamycin and erythromycin.

Following multiple topical applications of clindamycin phosphate at a concentration equivalent to 10 mg clindamycin per mL in an isopropyl alcohol and water solution, very low levels of clindamycin are present in the serum (0-3 ng/mL) and less than 0.2% of the dose is recovered in urine as clindamycin.

Clindamycin activity has been demonstrated in comedones from acne patients. The mean concentration of antibiotic activity in extracted comedones after application of Clindamycin Phosphate Topical Solution for 4 weeks was 597 mcg/g of comedonal material (range 0-1490). Clindamycin *in vitro* inhibits all *Propionibacterium acnes* cultures tested (MICs 0.4 mcg/mL). Free fatty acids on the skin surface have been decreased from approximately 14% to 2% following application of clindamycin.

INDICATIONS AND USAGE

Clindamycin Phosphate Topical Solution is indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate. (See CONTRAINDICATIONS, WARNINGS and ADVERSE REACTIONS.)

CONTRAINDICATIONS

Clindamycin Phosphate Topical Solution is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.

WARNINGS

Orally and parenterally administered clindamycin has been associated with severe colitis which may result in patient death. Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skin surface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin.

Studies indicate a toxin(s) produced by clostridia is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Endoscopic examination may reveal pseudomembranous colitis. Stool culture for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.

When significant diarrhea occurs, the drug should be discontinued. Large bowel endoscopy should be considered to establish a definitive diagnosis in cases of severe diarrhea.

Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen the condition. Vancomycin has been found to be effective in the treatment of antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. The usual adult dosage is 500 milligrams to 2 grams of vancomycin orally per day in three to four divided doses administered for 7 to 10 days. Cholestyramine or other resin binders bind vancomycin *in vitro*. If both a resin and vancomycin are to be administered concurrently, it may be advisable to separate the time of administration of each drug.

Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin.

PRECAUTIONS

General

Clindamycin Phosphate Topical Solution contains an alcohol base which will cause burning and irritation of the eye. In the event of accidental contact with sensitive surfaces (eye, abraded skin, mucous membranes), bathe with copious amounts of cool tap water. The solution has an unpleasant taste and caution should be exercised when applying medication around the mouth.

Clindamycin Phosphate Topical Solution should be prescribed with caution in atopic individuals.

Drug Interactions

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore it should be used with caution in patients receiving such agents.

Pregnancy: Teratogenic effects—Pregnancy Category B

Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin ranging from 100 to 600 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to clindamycin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of Clindamycin Phosphate Topical Solution. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients under the age of 12 have not been established.

ADVERSE REACTIONS

In 18 clinical studies of various formulations of topical Clindamycin Phosphate using placebo vehicle and/or active comparator drugs as controls, patients experienced a number of treatment emergent adverse dermatologic events [see table below].

Number of Patients Reporting Events

Treatment Emergent Adverse Event	Solution n=553 (%)	Gel n=148 (%)	Lotion n=168 (%)
Burning	62 (11)	15 (10)	17 (11)
Itching	38 (7)	15 (10)	17 (11)
Burning/itching	60 (11)	# (-)	# (-)
Dryness	105 (19)	34 (23)	29 (18)
Erythema	88 (16)	10 (7)	22 (14)
Oiliness/Oily Skin	8 (1)	26 (18)	12* (10)
Peeling	61 (11)	# (-)	11 (7)

not recorded

* of 126 subjects

Orally and parenterally administered clindamycin has been associated with severe colitis which may end fatally.

Cases of diarrhea, bloody diarrhea and colitis (including pseudomembranous colitis) have been reported as adverse reactions in patients treated with oral and parenteral formulations of clindamycin and rarely with topical clindamycin (see WARNINGS).

Abdominal pain and gastrointestinal disturbances as well as gram-negative folliculitis have also been reported in association with the use of topical formulations of clindamycin.

OVERDOSAGE

Topically applied Clindamycin Phosphate Topical Solution can be absorbed in sufficient amounts to produce systemic effects. (See WARNINGS.)

DOSAGE AND ADMINISTRATION

Apply a thin film of Clindamycin Phosphate Topical Solution or use a Clindamycin Phosphate Topical Solution pledget for the application of Clindamycin Phosphate twice daily to affected area. More than one pledget may be used. Each pledget should be used only once and then be discarded.

Pledget: Remove pledget from jar just before use. Do not use if the seal under the cap is broken. Discard after single use. Keep all liquid dosage forms in containers tightly closed.

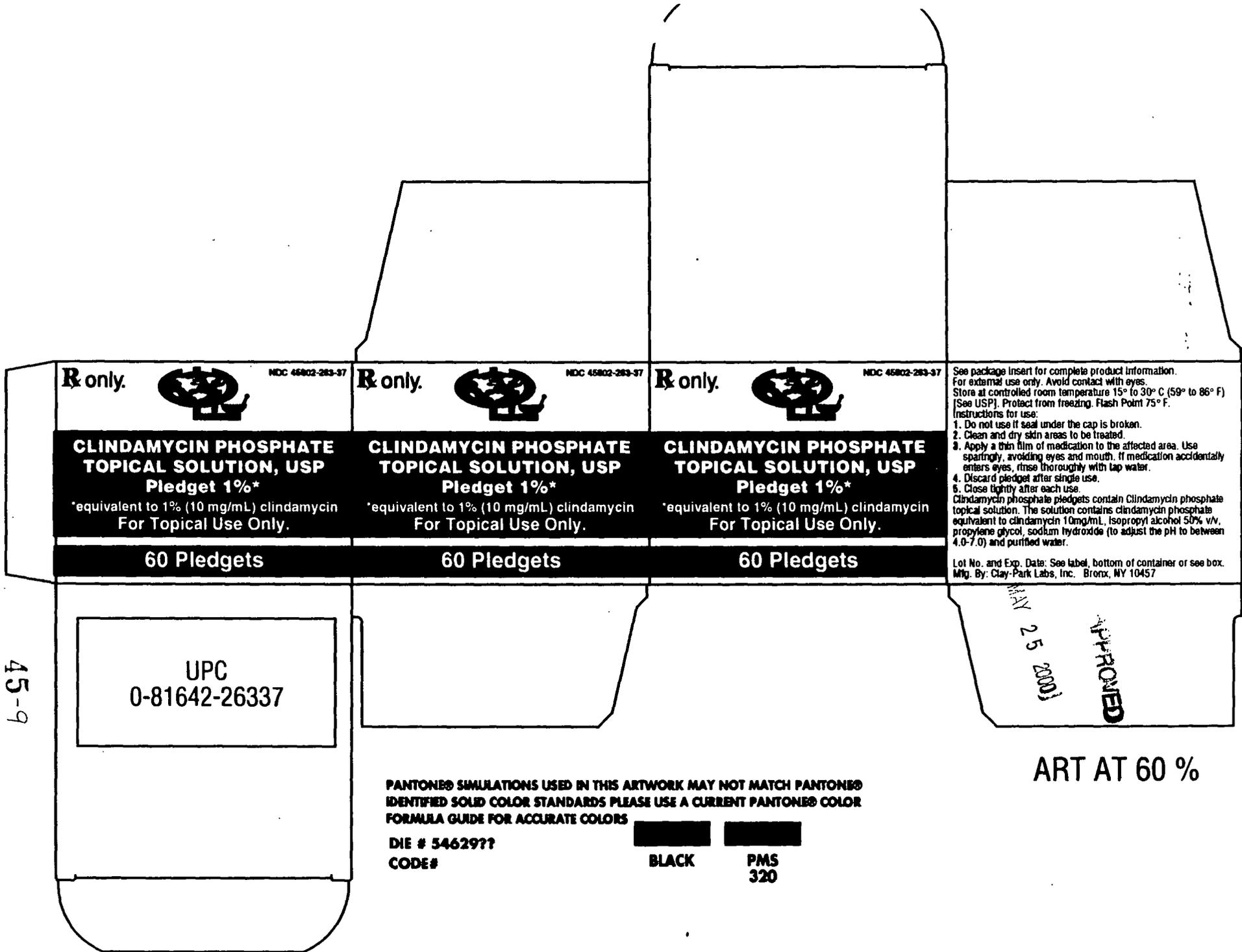
HOW SUPPLIED

Clindamycin Phosphate Topical Solution containing clindamycin phosphate equivalent to 10 mg clindamycin per milliliter is available in the following sizes: 30 mL applicator bottle, 60 mL applicator bottle.

Clindamycin Phosphate Pledgets contains Clindamycin Phosphate Topical Solution. The solution contains Clindamycin Phosphate equivalent to 10 mg clindamycin per milliliter. Clindamycin Phosphate Pledgets is available in a Jar of 60 single-use pledget applicators. Store at controlled room temperature 15° to 30° C (59° to 86° F) [See USP]. Protect from freezing. Flash Point 75° F.

Rx only

Mfg. By: Clay-Park Labs, Inc., Bronx, NY 10457



R only.



NDC 45802-263-37

See package insert for complete product information.

For external use only. Avoid contact with eyes.

Store at controlled room temperature 15° to 30° C (59° to 86° F) [See USP]. Protect from freezing. Flash Point 75° F.

Instructions for use:

1. Do not use if seal under the cap is broken.
2. Clean and dry skin areas to be treated.
3. Apply a thin film of medication to the affected area. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
4. Discard pledget after single use.
5. Close tightly after each use.

Clindamycin phosphate pledgets contain Clindamycin phosphate topical solution. The solution contains clindamycin phosphate equivalent to clindamycin 10mg/mL, isopropyl alcohol 50% w/v, propylene glycol, sodium hydroxide (to adjust the pH to between 4.0-7.0) and purified water.

Lot No. and Exp. Date: See label, bottom of container or see box.

Mfg. By: Clay-Park Labs, Inc. Bronx, NY 10457

CLINDAMYCIN PHOSPHATE TOPICAL SOLUTION, USP

Pledget 1%*

*equivalent to 1% (10 mg/mL) clindamycin
For Topical Use Only.

60 Pledgets

RECEIVED
MAY 25 2000

44-5

4 OZ LABEL 1 1/2 X 8 3/4

PANTONE® SIMULATIONS USED IN THIS ARTWORK MAY NOT MATCH PANTONE® IDENTIFIED SOLID COLOR STANDARDS PLEASE USE A CURRENT PANTONE® COLOR FORMULA GUIDE FOR ACCURATE COLORS



BLACK



**PMS
320**

Wg