CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

64160

DRAFT FINAL PRINTED LABELING

JAN 28 200

APPROVED

fougera

CLINDAMYCIN PHOSPHATE GEL USP, 1%

FOR EXTERNAL USE ONLY **AVOID CONTACT WITH EYES**

℞ only

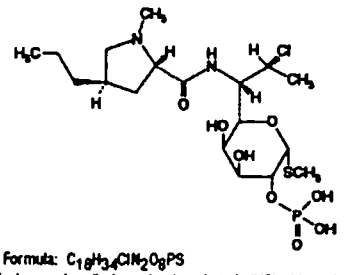
DESCRIPTION

Clindamycin Phosphate Gel, for topical use, contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per gram.

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 gel contains allantoin, carbomer 934P, methylparaben, polyethylene glycol 400, propylene glycol, sodium hydroxide and purified water.

The structural formula is represented below:



Molecular Formula: $C_{18}H_{34}ClN_2O_8PS$ Molecular Weight: 504.97

The chemical name for clindamycin phosphate is 7(S)-chloro-7-deoxylincomycin-2-phosphate.

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 Gel 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 Gel 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 cultures 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 mg to 2 grams of vancomycin orally per day in three to four divided doses administered for 7 to 10 days. Cholestyramine or colestipol resins 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 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. 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 has not been established.

ADVERSE REACTIONS

In 18 clinical studies of various formulations of Clindamycin Phosphate Topical solution 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=160 (%)
Burning	62 (11)	15 (10)	17 (11)
Itching	36 (7)	15 (10)	17 (11)
Burning/Itching	60 (11)	# (–)	# (–)
Dryness	105 (19)	34 (23)	29 (18)
Erythema	86 (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 topical solution can be absorbed in sufficient amounts to product system effects (see **WARNINGS**).

DOSAGE AND ADMINISTRATION

Apply a thin film of Clindamycin Phosphate Gel twice daily to affected area. Keep container tightly closed.

HOW SUPPLIED

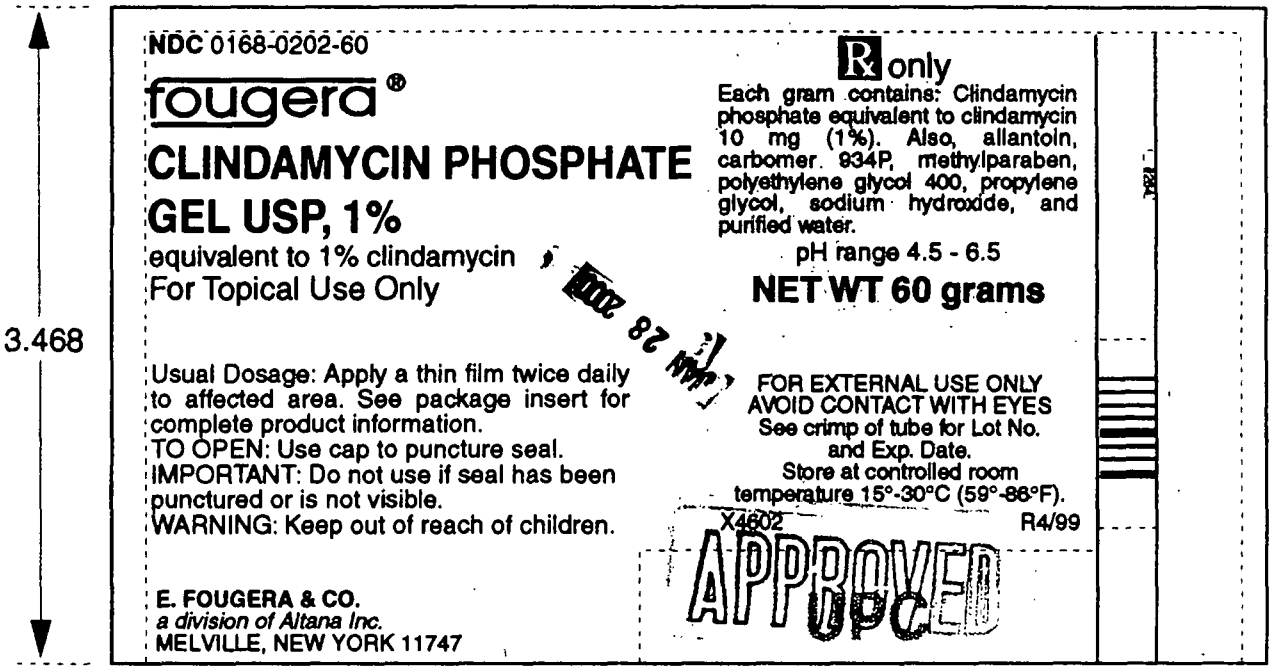
Clindamycin Phosphate Gel containing clindamycin phosphate equivalent to 10 mg clindamycin per gram is available in the following sizes:

30 gram tube NDC 0168-0202-30 60 gram tube NDC 0168-0202-60

Store at controlled room temperature 15°-30°C (59°-86°F). Protect from freezing.

E. Fougera & Co.
a division of Altana Inc.
Melville, NY 11747

I220230A
#88
R4/99



3.468

6.000

Die Size 1 1/8 x 6 circ:3.468
Colors: Black PMS Yellow
Pharma Code: #264

UPC

℞

See crimp of tube for Control No. and Exp. Date.

IX4602
R4/98
#264

NDC 0168-0202-60

fougera®

℞ only

CLINDAMYCIN PHOSPHATE GEL USP, 1%

equivalent to 1% clindamycin
For Topical Use Only

Usual Dosage: Apply a thin film twice daily to affected area.
See package insert for complete product information.
Store at controlled room temperature 15° to 30°C (59° to 86°F).
IMPORTANT: The opening of this product is covered by a metal tamper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.

E. FOUGERA & CO.
a division of Altana Inc., MELVILLE, NEW YORK 11747

FOR EXTERNAL USE ONLY
AVOID CONTACT WITH EYES

NET WT 60 grams

fougera® CLINDAMYCIN PHOSPHATE GEL USP, 1%

pH range 4.5 - 6.5

TO OPEN: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open.

To close, screw the cap back onto the tube.

NDC 0168-0202-60

fougera®

℞ only

CLINDAMYCIN PHOSPHATE GEL USP, 1%

equivalent to 1% clindamycin
For Topical Use Only

Each gram contains: Clindamycin phosphate equivalent to clindamycin 10 mg (1%). Also, allantoin, carbomer 934P, methylparaben, polyethylene glycol 400, propylene glycol, sodium hydroxide, and purified water.

NET WT 60 grams

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405

T545
PRINT SIDE
1-3/8 X 1-3/8 X 6-3/16

Name: Clindamycin Phosphate 60g Cart
Die Size: 1.375 x 1.375 x 6.1875
UPC Code: 0168-0202-60
Pharma Code: #264
Colors: PMS Yellow PMS Black