Clindacin Phosphate Topical Solution

USP, 1% (Pledgets)

For External Use

DESCRIPTION
Clindacin® ETZ contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per milliliter. Each Clindacin® ETZ pledget 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)-hydroxy group of the parent antibiotic, lincomycin.

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

The structural formula is represented below:

The chemical name for clindamycin phosphate is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-β-D-galacto-octopyranoside 2-(dihydrogen phosphate).

CLINICAL PHARMACOLOGY
Although clindamycin phosphate is inactive in vivo; 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.

The mean concentration of antibiotic activity in extracted comedones after application of clindamycin topically for 4 weeks was 597 mcg/g comedonal material (range = 0.490). Clindamycin in vivo inhibits all Propionibacterium acne strains except those resistant (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
Clindacin® ETZ 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
Clindacin® ETZ 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 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.

Steel culture for Clostridium difficile and stool assay for C. difficile toxin may be helpful diagnostically.

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

Antispasmodic agents such as aprepitant and diphenoxylate with atropine may prolong and/or worsen the condition. Vancomycin 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 - In clinical trials with pregnant women, the systemic administration of clindamycin during the second and third trimesters has not been associated with an increased frequency of congenital abnormalities. There are no adequate studies in pregnant women during the first trimester of pregnancy. Clindacin should be used during the first trimester of pregnancy only if clearly needed.

Nursing Mothers - It is not known whether clindamycin is excreted in human milk following use of Clindacin® ETZ. 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.

Garlic Oil - Clinical studies for clindamycin phosphate topical solution USP, 1% did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses in the elderly and younger patients.

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).

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Event</th>
<th>Solution (n=563)</th>
<th>Gel (n=148)</th>
<th>Lotion (n=160)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burning</td>
<td>62 (11)</td>
<td>15 (10)</td>
<td>17 (11)</td>
</tr>
<tr>
<td>Itching</td>
<td>36 (7)</td>
<td>15 (10)</td>
<td>17 (11)</td>
</tr>
<tr>
<td>Burning/Itching</td>
<td>60 (11)</td>
<td># (-)</td>
<td># (-)</td>
</tr>
<tr>
<td>Erythema</td>
<td>105 (19)</td>
<td>34 (23)</td>
<td>22 (14)</td>
</tr>
<tr>
<td>Peeling</td>
<td>86 (16)</td>
<td>10 (7)</td>
<td>22 (14)</td>
</tr>
<tr>
<td>Oily/Usk/ Skin</td>
<td>8 (1)</td>
<td>26 (18)</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>* 128 subjects</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Number of treatment emergent adverse dermatologic events

Orally and parenterally administered clindamycin has been associated with severe colitis which may result in death. 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, gastrointestinal disturbances, gram-negative folliculitis, eye pain and contact dermatitis have also been reported in association with the use of topical formulations of clindamycin.

OVERDOSAGE
Topically applied Clindacin® ETZ can be absorbed in sufficient amounts to produce systemic effects (see WARNINGS).

DOSEAGE AND ADMINISTRATION
Do not use the unit-dose pack seal is broken. Remove pledget just before use. Use pledget to apply a thin film of Clindamycin Topical Solution to the affected area twice daily. More than one pledget may be used. Each pledget should be used only once and then discarded.

HOW SUPPLIED
Clindacin® ETZ (Clindamycin Phosphate Topical Solution USP, 1% (Pledgets)) is available as follows:
A carton containing 60 individually wrapped single-use pledget applicators (NDC 04358-172-60)

STORAGE
Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature] Protect from freezing.

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