

CLINDOXYL GEL (logo)

(Clindamycin 1% and benzoyl peroxide 5%)

TOPICAL ACNE THERAPY

CLINDOXYL® Gel (clindamycin phosphate and benzoyl peroxide)

ACTION AND CLINICAL PHARMACOLOGY

Clindamycin Phosphate

Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the active antibiotic clindamycin. Like other macrolides, clindamycin inhibits bacterial protein synthesis by binding to the 50S subunit of ribosomes.

Clindamycin *in vitro* inhibits *Propionibacterium acnes*.

Bacterial resistance may develop to macrolides, such as clindamycin, especially when used alone and cross resistance between macrolides has been demonstrated.

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

Benzoyl Peroxide

The effectiveness of benzoyl peroxide in the treatment of acne vulgaris is primarily attributable to its antibacterial activity, especially with respect to *Propionibacterium acnes*, the predominant organism in sebaceous follicles and comedones. The antibacterial activity of this compound is presumably due to the release of active or free-

radical oxygen capable of oxidizing bacterial proteins. This action, combined with mild keratolytic effect, is believed to be responsible for its usefulness in acne. *P. acnes* resistance has not been reported with benzoyl peroxide. In acne patients treated topically with benzoyl peroxide, resolution of the acne usually coincides with the reduction in the level of *P. acnes* and free fatty acids. Benzoyl peroxide has been shown to be absorbed by the skin, where it is metabolized to benzoic acid and then excreted as benzoate in the urine.

INDICATIONS AND CLINICAL USE

CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide) is indicated in the topical treatment of moderate acne vulgaris characterised by the presence of comedones, papules and pustules. CLINDOXYL Gel is not indicated for the treatment of cystic acne.

CONTRAINDICATIONS

CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide) is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, benzoyl peroxide, or any other component of the preparation, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.

WARNINGS

FOR EXTERNAL USE ONLY. NOT FOR OPHTHALMIC USE. Avoid contact with eyes and mucous membranes. In the event of accidental contact with sensitive surfaces

(eyes, abraded skin, mucous membranes), bathe with copious amounts of cool tap water.

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 that a toxin(s) produced by *Clostridia* is one primary cause of antibiotic-associated pseudomembranous colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucous. 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.**

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

Concomitant topical acne treatments are not recommended because a possible cumulative irritancy effect may occur, especially with peeling, or abrasive agents. If severe irritation develops, discontinue use and institute appropriate therapy.

Use in Pregnancy

Animal reproductive studies have not been performed with benzoyl peroxide.

Reproductive 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.

Animal reproduction studies have not been conducted with CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide). It is not known whether CLINDOXYL Gel can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. CLINDOXYL Gel should not be given to a pregnant woman unless the potential benefits to the mother outweigh the possible risks to the fetus.

Use in Nursing Mothers

It is not known whether benzoyl peroxide or clindamycin are excreted in human milk following the topical use of CLINDOXYL Gel. However, orally and parenterally administered, clindamycin have 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 potential benefits to the mother and the potential risks to the fetus.

Pediatric Use

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

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. Benzoyl peroxide inactivates tretinoin when used concomitantly.

ADVERSE REACTIONS

In controlled clinical trials where a total of 172 patients received CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide), the reported adverse events considered to have a relationship to CLINDOXYL Gel were comprised mainly of reactions at the site of application such as peeling (16.3%), erythema (7.6%), dryness (7.0%), burning (2.3%) and pruritus (1.7%). Mild paraesthesia and worsening of acne were noted in one patient each.

Orally and parenterally administered clindamycin has been associated with severe colitis which may end fatally. Cases of diarrhea, bloody diarrhea and colitis (including,

rarely, pseudomembranous colitis) have been infrequently reported as adverse reactions in patients treated 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.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms

Topically applied clindamycin phosphate formulations can be absorbed in sufficient amounts to produce systemic effects (see WARNINGS). If medication is applied excessively, marked redness and peeling may occur. There are no reports of human ingestion overdosage with CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide).

Treatment

If ingested orally, no specific antidote is available. Simple gastric lavage should be performed. Treatment should be symptomatic.

DOSAGE AND ADMINISTRATION

CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide) should be applied to affected areas once daily before bed time, after the skin has been thoroughly washed, rinsed with warm water and gently patted dry.

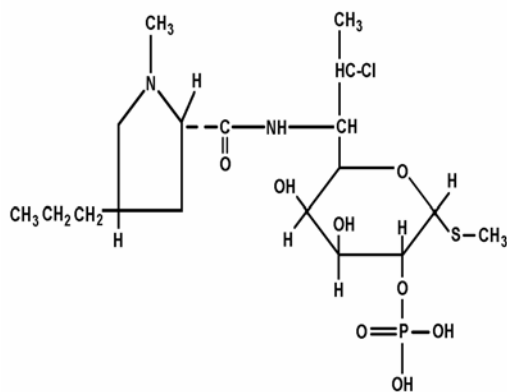
PHARMACEUTICAL INFORMATION

Drug Substance

Clindamycin phosphate

Chemical name: L-threo- α -D-galacto-octopyranoside, methyl 7-chloro- 6, 7, 8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidiny) carbonyl] - amino]-1-thio-,2-(dihydrogen phosphate), 2S-trans)-.

Structural formula:



Molecular formula: $C_{18}H_{34}ClN_2O_8PS$

Molecular weight: 504.97

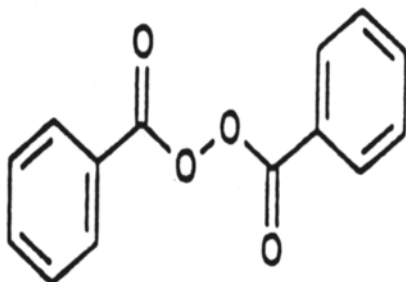
Description:

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. It occurs as a white to off-white, hygroscopic, crystalline powder. It is freely soluble in water, slightly soluble in dehydrated alcohol, very slightly soluble in acetone and practically odourless and has a bitter taste.

Benzoyl Peroxide

Chemical name: Dibenzoyl peroxide

Structural formula:



Molecular formula: $C_{14}H_{10}O_4$

Molecular weight: 242.2

Description:

Benzoyl peroxide is a white amorphous or granular powder. It loses water rapidly on exposure to air. Benzoyl peroxide is sparingly soluble in water or alcohol; soluble in benzene, chloroform and ether.

Composition

Each gram of CLINDOXYL Gel contains clindamycin phosphate equivalent to 1% (10 mg) clindamycin in combination with 5% (50 mg) benzoyl peroxide in a base consisting of carbomer 940, dimethicone, disodium lauryl sulfosuccinate, edetate disodium, glycerin, hydrated silica, methylparaben, poloxamer, purified water and sodium hydroxide.

Stability and Storage Recommendations

Prior to dispensing, CLINDOXYL Gel should be stored in a cold environment, preferably a refrigerator between 2° and 8°C. Do not freeze.

To the Pharmacist: Dispense with a 120 day expiration date and specify "Store at room temperature (15° - 25°C). Keep tube tightly closed. Keep out of the reach of children."

AVAILABILITY OF DOSAGE FORMS

CLINDOXYL Gel (clindamycin phosphate and benzoyl peroxide) is available in a 30 g tube and a 5 g sample tube.

PRODUCT MONOGRAPH AVAILABLE UPON REQUEST

® Registered trade-mark
Patent pending
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