Dalacin T

Clindamycin phosphate

1% Topical Lotion

Reference market: UK

AfME markets using the same LPD: Saudi Arabia

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Dalacin T 1% Topical Lotion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of Dalacin T Topical Lotion contains the equivalent of 10 mg clindamycin.

Excipients with known effect:
Cetostearyl alcohol 25 mg/ml.
Methyl parahydroxybenzoate (E218) 3 mg/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Topical lotion

White to off-white aqueous emulsion.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Dalacin T Topical Lotion is indicated for the treatment of acne vulgaris.

4.2. Posology and method of administration

Apply a thin film of Dalacin T Topical Lotion twice daily to the affected area.

Shake well before use.

4.3. Contraindications

Topical clindamycin is contraindicated in individuals with a history of hypersensitivity to clindamycin, lincomycin or to any of the excipients listed in section 6.1.

Clindamycin topical is contraindicated in individuals with a history of inflammatory bowel disease or a history of antibiotic-associated colitis.

4.4. Special warnings and precautions for use

Oral and parenteral clindamycin, as well as most other antibiotics, have been associated with severe diarrhoea and pseudomembranous colitis (see section 4.8). Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skin surface. Diarrhoea and colitis have been reported infrequently with topical clindamycin. Therefore, the physician should, nonetheless, be alert to the development of antibiotic-associated diarrhoea or colitis. If significant or prolonged diarrhoea occurs, the drug should be discontinued and appropriate diagnostic procedures and treatment provided as necessary.

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

Studies indicate a toxin(s) produced by *Clostridium difficile* is the major cause of antibiotic-associated colitis. Colitis is usually characterized by persistent, severe diarrhoea and abdominal cramps.

Endoscopic examination may reveal pseudomembranous colitis. Stool culture for *C. difficile* and/or assay for *C. difficile* toxin may be helpful to diagnosis.

Vancomycin is effective in the treatment of antibiotic-associated colitis produced by *C. difficile.* The usual dose is 125 - 500 mg orally every 6 hours for 7 - 10 days. Additional supportive medical care may be necessary.

Mild cases of colitis may respond to discontinuance of clindamycin alone. Colestyramine and colestipol resins have been shown to bind *C. difficile* toxin *in vitro,* and cholestyramine has been effective in the treatment of some mild cases of antibiotic-associated colitis. Colestyramine resins have been shown to bind vancomycin; therefore, when both colestyramine and vancomycin are used concurrently, their administration should be separated by at least two hours.

The lotion has an unpleasant taste and caution should be exercised when applying medication around the mouth.

Topical clindamycin should be prescribed with caution to atopic individuals.

4.5. Interaction with other medicinal products and other forms of interaction

Systemic 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.

4.6. Fertility, pregnancy and lactation

Pregnancy

There are no adequate and well-controlled studies in pregnant women during the first trimester. A moderate amount of data from clinical trials in pregnant women (between 300-1000 pregnancy outcomes) during the second and third trimesters indicates systemic administration of clindamycin has not been associated with an increased frequency of congenital abnormalities or feto/neonatal toxicity. Oral and subcutaneous reproductive toxicity studies in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus due to clindamycin, except at doses that caused maternal toxicity (see section 5.3). Animal reproduction studies are not always predictive of human response.

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.
should be used during the first trimester of pregnancy only if clearly needed. There are no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy.

Breast-feeding

It is not known whether clindamycin is excreted in human breast milk following use of Dalacin T Topical Lotion. Clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8 μg/mL following systemic use.

Clindamycin has the potential to cause adverse effects on the breastfed infant's gastrointestinal flora such as diarrhoea or blood in the stool, or rash. If oral or intravenous clindamycin is required by a nursing mother, it is not a reason to discontinue breastfeeding, but an alternate drug may be preferred. The developmental and health benefits of breastfeeding should be

considered along with the mother's clinical need for clindamycin and any potential adverse effects on the breastfed child from clindamycin or from the underlying maternal condition.

Fertility
Fertility studies in rats treated orally with clindamycin revealed no effects on fertility or mating ability.

4.7. Effects on ability to drive and use machines

Clindamycin has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. Adverse reactions identified from post-marketing experience are included in italics. The frequency grouping is defined using the following convention: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very Rare (<1/10,000) and Not known (frequency cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

	Very Common (≥1/10)	**Common** (≥1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Not Known** (cannot be estimated from available data)
Infections and Infestations				*Folliculitis,* Pseudomembranous colitis
Eye Disorders				*Stinging of the eye, Eye pain*
Gastrointestinal Disorders			*Gastrointestinal disorder*	*Abdominal pain, Pseudomembranous colitis* (see section 4.4)
Skin and Subcutaneous Tissue Disorders	Seborrhoea, Skin irritation Urticaria, Dry Skin			*Dermatitis contact*

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after marketing authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via local requirements.

To Report side effects

- **Saudi Arabia:**

National Pharmacovigilance Center (NPC)
Call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

- **Other GCC States**

- *Please contact the relevant competent authority.*

4.9. Overdose

Topically applied clindamycin can be absorbed in sufficient amounts to produce systemic effects.

In the event of overdosage, general symptomatic and supportive measures are indicated as required.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Anti-infectives for treatment of acne, ATC Code: DA10AF01.

Mechanism of action
Clindamycin is a lincosamide antibiotic that inhibits bacterial protein synthesis. It binds to the 50S ribosomal subunit and affects both ribosome assembly and the translation process. Although clindamycin phosphate is inactive in vitro, rapid in vivo hydrolysis converts this compound to the antibacterially active clindamycin.

Clindamycin has been shown to have in vitro activity against isolates of the following organisms;

Anaerobic gram positive non spore forming bacilli, including:
Propionibacterium acnes.

Pharmacodynamic effects
Efficacy is related to the time period that the agent level is above the minimum inhibitory concentration (MIC) of the pathogen (%T/MIC).

Resistance
Resistance to clindamycin in *Propionibacterium acnes* can be caused by mutations at the rRNA antibiotic binding site or by methylation of specific nucleotides in the 23S RNA of the 50S ribosomal subunit. These alterations can determine cross resistance to macrolides and streptogramins B (MLSB phenotype). Macrolide-resistant isolates should be tested for inducible resistance to clindamycin using the D zone test.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable. Particularly in severe infections or therapy failure microbiological diagnosis with verification of the pathogen and its susceptibility to clindamycin is recommended.

Resistance is usually defined by susceptibility interpretive criteria (breakpoints) established by EUCAST for systemically administered antibiotics. These breakpoints may be less relevant for topically administered clindamycin. Although clindamycin is not specifically cited, EUCAST has suggested that, for topically applied antimicrobials, resistance might be better defined by epidemiological cut-off values (ECOFFS) rather than the clinical breakpoints determined for systemic administration. However, MIC distributions and ECOFFS have not been published by EUCAST for P. acnes. Based on correlations between clinical results in acne patients and the clindamycin MICs for their *P. acnes* isolates, values as high as 256 mg/L are considered susceptible for topically administered clindamycin.

A Belgian surveillance study (2011-2012) of anaerobic bacteria included 22 *P. acnes* isolates; 95.5% were susceptible to clindamycin. An earlier European surveillance study, which included 304 isolates of *P. acnes*, had reported a resistance rate of 15% to clindamycin. However, this study used a breakpoint of 0.12 mg/L; using the current breakpoint of 4 mg/L, there were no resistant isolates.

Breakpoints
EUCAST breakpoints for Gram-positive anaerobes are listed below. these breakpoints are based on use in systemic infections.

EUCAST Breakpoints for Systemically Administered Clindamycin

Pathogen	Susceptible	Resistant
Gram-positive anaerobes (excluding Clostridium difficile)	≤4 mg/L	>4 mg/L

In a U.S. surveillance study, clindamycin MICs were ≤4 mg/L for 97% of *P. acnes* isolates tested.

In some bacterial species, cross resistance has been demonstrated *in vitro* among lincosamides, macrolides, and streptogramins B.

Clinical efficacy and safety

P. acnes produces an extracellular lipase that hydrolyses sebum triglycerides to glycerol, used by the organism as a growth substrate, and free fatty acids, which have pro-inflammatory and comedogenic properties. A double-blind study had been conducted to examine the effect of topical 1% clindamycin hydrochloride hydrate in a hydroalcoholic vehicle as compared to the effect of the vehicle alone. Fourteen patients applied clindamycin or vehicle alone twice daily for eight weeks. Free fatty acid surface lipid percentages, quantitative bacterial counts, and clinical response were assessed every two weeks. A significant reduction (88%) in the percentage of free fatty acids in the surface lipids was seen in the clindamycin-treated group and not in the vehicle-treated group. Free fatty acids on the skin surface have been decreased from approximately 14% to 2% following application of clindamycin solution in a hydroalcoholic base to 9 patients (average age 22.3 years) with acne vulgaris. There was no significant change in the surface microflora. Despite the short duration of treatment, objective clinical improvement was seen in three of nine treated patients, while none was observed in the placebo-treated patients.

5.2. Pharmacokinetic properties

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 concentrations has been demonstrated in comedones from acne patients. The mean (±SD) concentration of clindamycin in extracted comedones after application of clindamycin topical solution for 4 weeks was 0.60±0.11 mcg.

Older people
Clinical studies for topical clindamycin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

5.3 Preclinical safety data

Impairment of fertility

Fertility studies in rats treated orally with up to 300 mg/kg/day (72-fold the human exposure based on mg/m2) revealed no effects on fertility or mating ability.

Pregnancy

In oral embryo foetal development studies in rats and subcutaneous embryo fetal development studies in rats and rabbits, embryo-fetal toxicity was observed at doses that produced maternal toxicity. In rats, maternal death occurred with an exposure ratio of approximately 3000 relative to patient exposure. In rabbits, maternal toxicity, including abortions, occurred at exposure ratio of approximately 400. Embryo-fetal toxicity, including post-implantation loss and decreased viability, occurred in rabbits at an exposure ratio of 1000.

Carcinogenesis
Long term studies in animals have not been performed with clindamycin to evaluate carcinogenic potential.

Mutagenesis
Genotoxicity tests performed included a rat micronucleus test and an Ames test. Both tests were negative.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium Lauroyl Sarcosinate, Methylparahydroxybenzoate, Glycerol, Stearic Acid, Lexemul T, Cetostearyl Alcohol, Isostearyl Alcohol, and Purified Water.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months.
Do not use Dalacin T Lotion after the expiry date which is stated on the Bottle label after EXP:. The expiry date refers to the last day of that month.

6.4. Special precautions for storage

Keep out of the sight and reach of children.
Store below 25°C
Protect from freezing

6.5. Nature and contents of container

Dalacin T Topical Lotion containing clindamycin phosphate equivalent to 10 mg clindamycin per milliliter is available in the following size:
30 mL plastic squeeze bottle

6.6. Special precautions for disposal and other handling

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. MARKETING AUTHORISATION HOLDER

Marketing Authorisation Holder
Pfizer Inc, United States

Manufacutred By
Pharmacia and Upjohn company – Kalamazoo, USA

8. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 14-07-2013
Date of renewal of authorisation: 11-03-2020

9. DATE OF REVISION OF THE TEXT

March 2021