PRODUCT INFORMATION
DALACIN® T TOPICAL LOTION

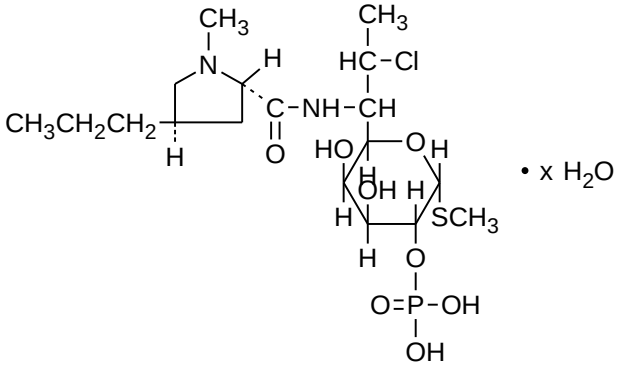
NAME OF THE MEDICINE

DALACIN T clindamycin 1% (10 mg/mL) (as phosphate) lotion.

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-2-0-dihydrogen phosphate. It has a molecular weight of 504.96, and the molecular formula is $C_{18}H_{34}C1N_20_8PS$.

CAS Registry Number: 24729-96-2.

The structural formula is represented below:



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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 is a white to off-white, odourless, hygroscopic, crystalline powder, found to be soluble in water, slightly soluble in dehydrated alcohol, sparingly soluble in dehydrated alcohol, sparingly soluble in acetone, and practically insoluble in chloroform and ether.

PHARMACOLOGY

Pharmacodynamics

Clindamycin phosphate is a prodrug which is converted to its biologically active form, clindamycin, by phosphate hydrolysis.

Cross resistance has been demonstrated between clindamycin and lincomycin. Antagonism has been demonstrated between clindamycin and erythromycin.

Pharmacokinetics

Following multiple topical applications of clindamycin phosphate lotion 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 serum (Cmax 2.7 ng/mL) and about 0.23% of the dose is recovered in urine as clindamycin.

Clindamycin in the serum is extensively metabolised. Approximately 10% of an oral dose is excreted as biologically active clindamycin in urine. Inactive metabolites are also excreted in urine.

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 μg eq/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 a 1% clindamycin solution containing alcohol.

CLINICAL TRIALS

Five randomised, controlled clinical trials have been performed to evaluate the efficacy and safety of clindamycin phosphate topical lotion in patients with moderate to severe acne vulgaris (defined in the studies as 12 to 70 inflammatory pustules and no more than 6 cystic lesions on the face). All studies were either double-blind or investigator blind studies. Four studies compared the lotion with placebo and two of these studies also included clindamycin phosphate solution (an alcohol based formulation) as a comparator. Efficacy was based upon the reduction in numbers of acne lesions (including papules, pustules and open and closed comedones).

A total of 362 patients were enrolled in these comparative studies, and 276 patients were evaluable for efficacy. Patients were evaluated at 3, 6, 9 and 12 weeks.

A statistically significant change ($p<0.05$) in mean acne lesion scores from baseline favouring DALACIN T lotion (n = 47) over placebo (n = 48) was seen in one study. There was a trend for DALACIN T (n = 56) to produce a superior response to placebo (n = 55) in three other studies in the observation period. The adverse events recorded during treatment with the lotion in these studies were minor and unrelated to therapy.

INDICATIONS

DALACIN T topical lotion is indicated in the treatment of acne vulgaris, particularly forms in which comedones, papules and pustules predominate.

CONTRAINDICATIONS

DALACIN T topical lotion is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

DALACIN T topical lotion is also contraindicated in individuals with a history of inflammatory bowel disease or a history of antibiotic-associated colitis.

PRECAUTIONS

Oral and parenteral clindamycin have been associated with severe diarrhoea and pseudomembraneous colitis which may result in patient death. Use of the clindamycin phosphate topical lotion (DALACIN T) results in absorption of the antibiotic from the skin surface. Diarrhoea, bloody diarrhoea and pseudomembraneous colitis have been reported with the use of topical and systemic clindamycin.

It is important to consider the diagnosis of antibiotic-associated colitis in patients who develop diarrhoea or colitis associated with antibiotic use. Antibiotic-associated colitis (whether pseudomembraneous or not) appears to result from a toxin produced by *Clostridium difficile* in the alimentary tract. The severity of the colitis may range from mild watery diarrhoea to severe, persistent, life-threatening bloody diarrhoea. The diagnosis is usually made by recognition of the clinical symptoms. The symptoms may occur during therapy or up to several weeks after cessation of therapy. Additional confirmatory signs of antibiotic-associated colitis include pseudomembrane formation seen with colonoscopy, *C. difficile* culture from the stool, or assay of the stool for *C. difficile* toxin.

Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *C. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (LOMOTIL®), may prolong and/or worsen the condition and should not be used.

DALACIN T should be prescribed with caution in atopic individuals.

For external use only. Avoid contact with sensitive surfaces such as the eyes, lips and mucous membranes.

DALACIN T is not generally effective in severe (nodulocystic) acne.

Use of topical clindamycin (DALACIN T) has been associated with the development of strains of *Propioniibacterium acnes* resistant to clindamycin in some patients. If there is evidence of the development of clinical resistence during treatment, consideration should be given to discontinuation of treatment with topical antibiotics.

Effects on fertility

Fertility was not impaired in rats given 300 mg/kg/day in the diet.

Use in pregnancy Category A

Reproductive studies have been performed in rats and mice using oral and parenteral doses of clindamycin phosphate up to 300 mg/kg/day and have revealed no evidence of harm to the fetus due to clindamycin. There are however, no adequate and well-controlled studies in pregnant women.

Use in lactation

It is not known if clindamycin is excreted in human milk following the use of topically administered clindamycin phosphate. However, after oral or parenteral administration, clindamycin has been detected in human milk. Therefore, use of DALACIN T in lactating mothers is not recommended.

Carcinogenicity

Long-term studies in animals to evaluate the carcinogenic potential of clindamycin phosphate have not been performed.

Genotoxicity

Clindamycin phosphate was negative in assays evaluating the potential to cause gene mutations and chromosomal damage.

Use in the elderly

Clinical studies for Dalacin T did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Effects on ability to drive and use machines

The effect of clindamycin on the ability to drive or operate machinery has not been systematically evaluated.

INTERACTIONS WITH OTHER MEDICINES

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

Antagonism has been demonstrated in between clindamycin and erythromycin *in vitro*. Because of possible clinical significance, these two drugs should not be administered concurrently.

ADVERSE EFFECTS

The tables below list the adverse effects identified through clinical study experience and post-marketing surveillance. The most common adverse reactions are abdominal pain, gastrointestinal disorders, skin irritation, urticaria, dry skin and seborrhoea.

Clinical trial data

Table 1. Adverse events reported with DALACIN T topical lotion, solution and placebo in 5 USA comparative clinical studies. Included are all adverse events with an incidence ≥ 1% in any treatment group.[1]

	Number of patients that experienced an adverse event					
	Lotion		Solution		Placebo	
System organ class	(N=121)		(N=52)		(N=103)	
	n	**%**	**n**	**%**	**n**	**%**
Total number of patients with adverse events	29	24.0	16	30.8	31	30.1
General disorders and administration site conditions						
Cold/flu	6	5.0	-	-	3	2.9
Dental procedure	1	0.8	1	1.9	-	-
Renal and urinary tract disorders						
Urinary tract infection	3	2.5	-	-	1	1.0
Gastrointestinal disorders						
Diarrhoea	5	4.1	5	9.6	5	4.9
Vomiting	1	0.8	1	1.9	1	1.0
Abdominal cramps, pain	-	-	3	5.8	1	1.0
Nausea	-	-	1	1.9	2	1.9
Reproductive system and breast disorders						
Vaginitis	-	-	1	1.9	-	-
Respiratory, thoracic and mediastinal disorders						
Sore throat/tonsillitis/ Laryngitis	3	2.5	-	-	5	4.9
Upper respiratory tract infection/cough/tracheitis	1	0.8	-	-	3	2.9
Sinusitis/congestion	-	-	2	3.8	-	-
Psychiatric disorders						
Anxiety	-	-	-	-	2	1.9
Musculo-skeletal and connective tissue disorders						
Fracture	1	0.8	2	3.8	-	-
Skin and subcutaneous tissue disorders						
Skin problems	3	2.5	1	1.9	1	1.0

1. Note that a causal relationship to the study treatment has not been determined.

Post-marketing experience

Table 2. The following adverse events have been reported since marketing of Dalacin T lotion in spontaneous post-marketing surveillance:[1,2]

Immune system disorders	
Rare	Allergic reaction.
General disorders and administration site conditions	
Very rare	Oedema.
Cardiovascular system	
Very rare	Rapid heartbeat, chest tightness.

Gastrointestinal disorders	
Common	Diarrhoea, nausea.
Rare	Abdominal pain.
Very rare	Acute colitis, bloating, constipation, coloured tongue, dyspepsia, flatulence, gastrointestinal distress, gastrointestinal reflux, heartburn, pseudomembraneous colitis, rectal bleeding, vomiting.
Metabolism and nutrition disorders	
Very rare	Weight loss.
Blood and lymphatic system disorders	
Very rare	Leukopenia.
Nervous system disorders	
Very rare	Headache, dizziness, facial numbness, metallic taste, voice loss.
Reproductive system and breast disorders	
Very rare	Fertility disorders.
Respiratory, thoracic and mediastinal disorders	
Very rare	Epistaxis, sore throat.
Skin and subcutaneous tissue disorders	
Very common	Skin irritation, dry skin, urticaria.
Common	Seborrhoea.
Uncommon	Burning sensation, rash, erythema.
Rare	Pruritis, contact dermatitis, facial swelling.
Very rare	Blisters, hair loss, papular pruritic skin rash, skin inflammation, scaling, skin discolouration.
Eye disorders	
Very rare	Eye irritation.
Frequency not known	Eye pain.
Infections and infestations	
Very rare	Fungal infection, bladder infection, folliculitis.
Investigations	
Very rare	Elevated liver enzymes.

1. Note that a causal relationship to DALACIN T topical lotion has not been determined.
2. Frequencies estimated from spontaneous reporting.
   Very Common (≥ 10%), Common (≥1% and <10%), Uncommon (≥0.1% and <1%), Rare (≥0.01% and <0.1%) and Very Rare (<0.01%), Frequency not known (cannot be estimated from available data).

DOSAGE AND ADMINISTRATION

Apply a thin film of DALACIN T topical lotion twice daily to the affected area.

DALACIN T topical lotion should be shaken immediately before using.

The efficacy of DALACIN T lotion has not been demonstrated beyond 12 week's duration. Please refer to the Clinical Trials section.

OVERDOSAGE

Topically applied DALACIN T can be absorbed in sufficient amounts to produce systemic effects. In the event of overdosage, general symptomatic and supportive measures are indicated as required.

Contact the Poisons Information Centre on 13 11 26 for advice on the management of an overdose.

PRESENTATION AND STORAGE CONDITIONS

DALACIN T topical lotion: White to off-white emulsion containing clindamycin phosphate equivalent to clindamycin 10 mg/mL, in an aqueous base containing glycerol, sodium lauroyl sarcosinate, stearic acid, glyceryl monostearate, mono- and di- glycerides, water - purified, potassium hydroxide, cetostearyl alcohol, isostearyl alcohol and methyl hydroxybenzoate.

DALACIN T topical lotion is available in 60 mL bottles.

Storage conditions

Store below 25C.

NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
38-42 Wharf Road
West Ryde NSW 2114
Australia

POISON SCHEDULE OF THE MEDICINE

Schedule 4 (Prescription Only Medicine).

DATE OF FIRST INCLUSION IN THE ARTG

22 February 1999

DATE OF MOST RECENT AMENDMENT

10 May 2016

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