

## **PRODUCT MONOGRAPH**

**Pr DALACIN\* T**

**(Clindamycin Phosphate Topical Solution USP)**

**Topical Solution 1%**

**Pre-Moistened Pads**

**Antibiotic**

Pfizer Canada Inc  
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# PRODUCT MONOGRAPH

**DALACIN\* T**

**Topical Solution**

**Pre-Moistened Pads**

**Clindamycin Phosphate Topical Solution USP**

**1%**

## **THERAPEUTIC CLASSIFICATION**

**Antibiotic**

## **ACTIONS**

Clindamycin phosphate is inactive in vitro but in vivo hydrolysis converts this compound to the antibacterially active clindamycin. Clindamycin has been shown to have in vitro activity against isolates of Propionibacterium acnes which may account for its usefulness in acne. Clindamycin activity has been demonstrated in serum, urine and in comedonal extracts from acne patients.

The mean concentration of antibiotic activity in extracted comedones after application of DALACIN T (clindamycin phosphate) for 4 weeks was 597 µg/gram of comedonal material (range 60-1490). Clindamycin in vitro inhibits Propionibacterium acnes cultures tested.

## **INDICATIONS AND CLINICAL USE**

DALACIN T (clindamycin phosphate) is indicated for the treatment of acne vulgaris.

## **CONTRAINDICATIONS**

DALACIN T (clindamycin phosphate) is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of inflammatory bowel disease (including regional enteritis and ulcerative colitis), or a history of antibiotic - associated colitis.

## **WARNINGS**

### **Gastrointestinal**

#### **Clostridium difficile-associated disease:**

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including DALACIN T (clindamycin phosphate topical solution USP 1%). CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of Clostridium difficile. C. difficile produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against Clostridium difficile. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against Clostridium difficile. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases. (see ADVERSE REACTIONS).

## **PRECAUTIONS**

DALACIN T (clindamycin phosphate) contains an alcohol base which will cause burning and irritation of the eye. In the event of accidental contact with sensitive surfaces (eye, abraded skin, mucous membranes), bathe with copious amounts of cool tap water.

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

DALACIN T should be prescribed with caution in atopic individuals.

#### **Use in Pregnancy:**

Safety for use in pregnancy has not been established.

**Use by Nursing Mothers:**

It is not known whether DALACIN T when topically applied is excreted in human milk. However, oral and parenteral clindamycin have been reported to appear in breast milk and therefore nursing should not be undertaken while a patient is on the drug.

**Drug Interactions:**

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

Clindamycin (oral and parenterally administered) has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, Dalacin T should be used with caution in patients receiving such agents.

**ADVERSE REACTIONS**

In a large U.S. postmarketing surveillance study among 1298 patients treated only with topical clindamycin phosphate solution, skin dryness/irritation, diarrhea or gastrointestinal symptoms were the most commonly reported medical events. Of those, 258 (19.9%) reported one or more of the following dermatological events. Among patients treated with oral antibiotics only, or no antibiotics, the percentage of patients reporting dermatologic event(s) was 20.8% and 25.4% respectively.

- |                |                    |
|----------------|--------------------|
| Dry skin       | Irritation         |
| Acne worse     | Itching            |
| Rash/redness   | New Acne           |
| Peeling        | Sunburn            |
| Discolouration | Contact Dermatitis |
| Urticaria      |                    |

The following new gastrointestinal problems were reported in this surveillance study by 18.7% of the DALACIN T treated patients, 22.9% of the oral antibiotic treated patients, and 18.4% of the patients with no antibiotic exposure.

- |                       |                   |
|-----------------------|-------------------|
| Abdominal Pain/cramps | "Nervous" stomach |
| Nausea                | Ulcers            |
| Flu/Virus             | Vomiting          |
| Indigestion           | Colon problems    |
| Gas/Bloating          | (not colitis)     |

Cases of diarrhea, bloody diarrhea and colitis (including pseudomembranous colitis) have been reported as adverse reactions in patients treated with topical formulations of clindamycin. Diarrhea was reported by 55 of the 1298 (5%) DALACIN T patients, compared to 3.9% of control patients. (See WARNINGS, Gastrointestinal, CDAD)

In addition to the above, the following side effects have also been occasionally reported during drug treatment with DALACIN T: oily skin, and gram-negative folliculitis.

### **OVERDOSAGE**

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

For management of a suspected drug overdose, contact your regional Poison Control Center.

### **DOSAGE AND ADMINISTRATION**

Apply a thin film of DALACIN T (clindamycin phosphate) twice daily to the clean and dry skin in the area to be treated. Patients responding to DALACIN T should show improvement in 8 weeks. Treatment beyond 12 weeks may call for evaluation by the physician.

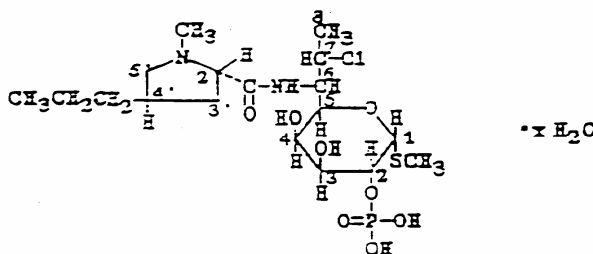
## PHARMACEUTICAL INFORMATION

### Drug Substance:

Proper Name: Clindamycin phosphate

Chemical name: (1) Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-trans(1-methyl-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-threo-a-D-galacto-,2-(dihydrogen phosphate), hydrate;  
(2) Lincomycin, 7(S)-chloro-7-deoxy-,2-phosphate, hydrate;  
(3) Clindamycin 2-phosphate hydrate

Structural formula:



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

Molecular Weight: 505

Description: Clindamycin phosphate is a water soluble ester of clindamycin and phosphoric acid. The intact ester is essentially inactive as an antibacterial agent.

Chemical or enzymatic hydrolysis of clindamycin phosphate is necessary to obtain the antibiotic activity of the clindamycin base.

Clindamycin phosphate is a white to off-white, hygroscopic, crystalline powder which melts at about 175°C with decomposition. It has two acidic protons with  $pK_1 = 0.964$  and  $pK_2 = 6.081$ . The partition coefficient is 0.03. The pH of a solution of 10 mg/mL in water is between 3.5 and 4.5.

### Composition:

Each mL contains clindamycin phosphate equivalent to 10 mg clindamycin. The solution also contains isopropyl alcohol 50% v/v, propylene glycol and purified water. When needed, the pH of the solution is adjusted with hydrochloric acid and/or sodium hydroxide.

**Stability and Storage Recommendations:** Store at controlled room temperature (15E - 30EC)

### **AVAILABILITY OF DOSAGE FORMS**

DALACIN T (clindamycin phosphate topical solution) is available in 30 and 60 mL bottles. A dab-o-matic applicator and cap is provided external to each bottle for placement into the bottle.

To assist the patient, the pharmacist may assemble the bottle upon dispensing as follows:

- 1) remove cap from bottle and discard,
- 2) firmly press applicator into bottle,
- 3) seal firmly by tightening domed-cap.

DALACIN T is also available in cartons of 60 pre-moistened pads. Each pre-moistened pad is intended for single use and should be discarded after each use.

## **INFORMATION FOR THE CONSUMER**

### DALACIN\* T

(clindamycin phosphate topical solution USP)

DALACIN T (clindamycin phosphate) belongs to the family of antibiotics. When applied to the skin in a solution it helps to control acne (pimples commonly seen in teenagers and young adults). This medicine is available on a doctor's prescription only. With any questions concerning this medicine consult your doctor, or pharmacist.

#### **Proper Use of this Medicine**

Before applying this medicine, the area to be treated should be washed thoroughly but gently with warm water and bland soap, rinsed well and patted dry. Unless skin is oily, washing 2 or 3 times a day is enough. The face should not be washed for at least two hours after applying this medicine.

The medicine should be used for the full time of treatment recommended by your doctor even if the symptoms clear up after a few days. If the medicine is stopped too soon, the symptoms may return.

After shaving, it is best to wait 30 minutes before applying the medicine because the alcohol in it may irritate freshly shaven skin.

The medicine is available in bottles as well as pre-moistened pads.

The medicine that comes in a bottle has a separate applicator and cap. To use the applicator: 1) remove cap from bottle and discard, 2) firmly press applicator into bottle, 3) seal firmly by tightening domed-cap.

The pharmacist may have assembled the bottle for you, in which case the applicator top will already be attached to the bottle. The applicator top may then be used to apply the medicine directly to the skin. The bottle should be tilted and pressed firmly against the skin using a dabbing rather than a rolling motion. Reducing the pressure will decrease the flow.

The medicine that comes in the pre-moistened pad is enough for one application. Throw away the pre-moistened pad after using one time. Do not use if the seal is broken.

When using either the bottle or the pre-moistened pad, a thin film of the medicine is to be applied to the whole area affected by acne, not just to the pimples themselves.

In order to prevent this medicine from getting in the eyes, nose, or mouth, it should be spread away from these areas on application. If the medicine does get in the eyes, they must be washed out immediately but carefully using large amounts of cool tap water. If the eyes still burn or are painful, a doctor should be consulted.

This medicine should not be used more often than prescribed by your doctor because it may cause dryness or irritation of the skin.

The bottle contains approximately a 4 week (30 mL size) or an 8 week supply (60 mL).

The carton of pre-moistened pads contains a 4 week (60 pre-moistened pads) supply.

#### How to Store this Medicine

Keep out of the reach of children.

Store away from heat and direct light.

Keep medicine from freezing.

Store the bottle in an upright fashion.

#### **When Dalacin T should not be used:**

Do not use Dalacin T if:

- You have a history of hypersensitivity (allergies) to preparations including clindamycin or lincomycin
- You have a history in inflammatory bowel disease (including regional enteritis and ulcerative colitis, or a history of antibiotic-associated colitis (inflamed bowel).

#### **Precautions While Using this Medicine**

- Safety in pregnancy has not been established.
- If frequent diarrhea occurs it should not be treated without first checking with your doctor.
- If you experience stomach upset, nausea or diarrhea while using DALACIN T, check with your doctor.

#### **Use in Pregnancy:**

Safety for use in pregnancy has not been established. If you are pregnant (or become pregnant), check with your doctor before using DALACIN T.

### **Use by Nursing Mothers:**

It is not known whether DALACIN T when topically applied is excreted in breast milk. If you are currently nursing (or planning on nursing), check with your doctor before using DALACIN T.

### **Side effects of this Medicine**

Check with your doctor immediately if any of the following very rare side effects occur:

- Abdominal or stomach cramps, pain or bloating is severe
- Diarrhea (watery and severe) which may also be bloody
- Nausea or vomiting

Also check with your doctor as soon as possible if any of the following side effects occur:

Skin rash, itching, redness or other signs or irritation not present before using this medicine.

Other side effects that do not normally require medical attention may occur. These include the following:

- Dry or scaly skin
- Peeling of skin
- Stinging or burning feeling

If any other unusual or unexpected effects occur, check with your doctor.

### **DRUG INTERACTIONS**

Tell your doctor if you are taking or being administered any other topical or oral medication, including erythromycin or neuromuscular blocking agents.

### **OVERDOSAGE**

In case of overdose, particularly accidental oral ingestion, contact your doctor, hospital emergency department or regional poison control centre.

## PHARMACOLOGY AND TOXICOLOGY

### Human Studies

In vitro studies using human skin from leg amputations indicated that approximately 5 to 10% of a single application of 1% <sup>3</sup>H-clindamycin solution penetrated the epidermis. Twice daily applications increased the total amount of clindamycin penetrating the skin but three times a day applications did not.

Clindamycin plasma concentrations were detectable ( $\geq 0.5$  ng/ml) in 5 of 6 patients when 1% clindamycin phosphate was applied to approximately 300 cm<sup>2</sup> of the face every 12 hours for 6 doses. Peak concentrations in plasma ranged from 0 to 3.0 ng/ml which represent levels 1000 times lower than peak levels after 600 mg clindamycin phosphate given intravenously or 300 mg of clindamycin hydrochloride given orally.

Clindamycin phosphate was detected in the urine of all 6 patients in amounts from less than 1 ng/ml to 53 ng/ml. Since the total cumulative dose of clindamycin phosphate applied to the skin was 60 mg, the percent of dose recovered in the urine was 0.156% (range 0.08 to 0.34%).

The penetration of clindamycin into comedones has been demonstrated. When 9 patients were treated with topical 1% clindamycin phosphate twice daily for 16 weeks, all patients had one or more comedones containing clindamycin bioactivity. In addition, quantitative cultures of acne comedones were performed on 5 clindamycin and 8 vehicle-treated patients. Clindamycin produced significantly reduced P. acnes colony counts at weeks 6, 12 and 14.

Thirty-five P. acnes isolates from the clindamycin-treated patients were tested for their clindamycin susceptibility. No stepwise increases in MIC were encountered in specimens collected over the observation period (16 weeks treatment, 12 weeks post-treatment). The largest MIC observed was 0.39  $\mu$ g/ml.

Four patients treated with topical clindamycin phosphate developed resistant strains of Staphylococcus aureus and enterococci during treatment. Two thirds of these strains had disappeared 8 weeks after treatment. All strains of Propionibacteria acnes were sensitive to clindamycin and remained so through an 8 week treatment period.

There were no changes in the colonic flora when patients received topical clindamycin phosphate treatment. No increased resistance to clindamycin was detected in the colon.

A comparative irritancy study showed retinoic acid most irritating, followed by 1% clindamycin hydrochloride and benzoyl peroxide. No irritancy was found for clindamycin phosphate or a 3% sulfur cream.

An evaluation for potential to cause allergic contact dermatitis was performed in 102 patients using 1% and 3% clindamycin phosphate. On rechallenge all were negative.

Clindamycin phosphate 1% solution was tested for sensitization potential by the Draize test with the addition of ultraviolet irradiation. No evidence of photoallergic or allergic contact sensitization was found in any subject.

### **Animal Studies**

A 1% solution of clindamycin phosphate was applied once a day and a 3% solution was applied three times a day to rats for 21 days. No inflammation, hyperplasia, parakeratosis, hemorrhage or edema was noted in the treated area of the skin. In the 3% solution study, females grew in weight slightly more, had slightly lower leukocyte and heterophil counts, and had a lower proportion of liver: body weight (21 day) when compared to control animals. Bioactivity was present in serum immediately after last application in the 1% and 3% studies, however in the 3% study, bioactivity was present in the skin, urine and trace amounts in the long bones 5 days after the last application. There was no difference in absorption between animals with intact or abraded skin.

A 1% clindamycin hydrochloride topical solution was applied daily to dogs for 21 days. There was no skin damage and no evidence of absorption in the dog.

A 3% clindamycin hydrochloride solution was applied three-times-a-day to pigs for 21 days. There was no skin irritation and five days post-therapy, there was residual bioactivity present in the treated skin, which was largely confined to the epidermis.

### **Ocular Application**

Rats were administered 1% clindamycin hydrochloride or phosphate formulations to the eyes for 20 days. There was no evidence of ocular irritation or inflammation. A single administration of 1% clindamycin hydrochloride to the eyes of rabbit produced mild to moderate irritation similar to that for the vehicle control.

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