PRODUCT INFORMATION
DALACIN® V Cream 2%
(Clindamycin phosphate Intravaginal Cream)

NAME OF THE MEDICINE

DALACIN V clindamycin 2% (20 mg/g) (as phosphate) cream.

Clindamycin is a semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent compound lincomycin. The MW of clindamycin phosphate is 504.96 and its structure is represented below:

![Clindamycin Structure]

DESCRIPTION

DALACIN V Cream 2% contains the equivalent of 2% (20 mg/g) free clindamycin as a water soluble ester of clindamycin and phosphoric acid (clindamycin phosphate). Each unit dose of DALACIN V Cream 2% (approximately 5 grams) represents 100 mg of clindamycin.

DALACIN V Cream 2% also contains: sorbitan monostearate, polysorbate 60, propylene glycol, stearic acid, cetostearyl alcohol, cetyl ester wax, paraffin liquid and purified water. Each 5 g contains 50 mg benzyl alcohol as preservative.

PHARMACOLOGY

Microbiology

Clindamycin is an antimicrobial agent which has been shown to be effective in the treatment of infection caused by susceptible anaerobic bacteria or susceptible strains of Gram positive aerobic bacteria. Biological activity of clindamycin from this formulation is inferred from the efficacy demonstrated in the clinical studies of the treatment of Bacterial Vaginosis. Clindamycin has been shown to have in vitro activity against the following organisms which

**Pharmacokinetics**

Following a once a day (for seven days) dosing of approximately 5 grams of DALACIN V Cream, containing the equivalent of 100 mg clindamycin, peak serum clindamycin levels averaged 20 ng/mL (range 3 to 93 ng/mL) in normal volunteers. Approximately 3% (range 0.1 to 11.3%) of the administered dose was absorbed systemically.

In women with Bacterial Vaginosis, being treated with DALACIN V Cream once daily (5 grams) for seven days, the amount of clindamycin absorbed was 4% (range 0.8 to 8.2%), which approximates results seen in normal volunteers.

The levels of clindamycin absorbed following the intravaginal administration of DALACIN V Cream reached steady state within four days of the seven day regimen.

**INDICATIONS**

DALACIN V Cream 2% is indicated for the treatment of symptomatic Bacterial Vaginosis.

**Note:** For the purposes of this indication Bacterial Vaginosis is usually defined by positive results to at least three of the four following criteria:

1. Vaginal discharge with pH > 4.5,
2. Vaginal discharge demonstrating an amine ("fishy") odour with the addition of 10% potassium hydroxide,
3. Vaginal discharge with "clue cells" on microscopy, and
4. A gram stain consistent with a diagnosis of Bacterial Vaginosis (*Lactobacillus* morphotype absent or markedly decreased; *Gardnerella* morphotype predominant flora; white blood cells absent or few; *Mobiluncus* morphotype may or may not be present).

Other pathogens which may be associated with genital infection such as *Trichomonas vaginalis, Candida albicans, Chlamydia trachomatis* and *Neisseria gonorrhoeae* should be ruled out by appropriate laboratory means.

**CONTRAINDICATIONS**

Clindamycin phosphate cream is contraindicated in patients with a history of hypersensitivity to clindamycin, lincomycin or other components of the cream (see DESCRIPTION). Clindamycin phosphate cream is also contraindicated in individuals with a history of inflammatory bowel disease or history of antibiotic-associated colitis.
PRECAUTIONS

FOR INTRAVAGINAL USE ONLY. NOT FOR OPHTHALMIC, DERMAL OR ORAL USE.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics, including clindamycin. A toxin produced by Clostridium difficile appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with the use of antibiotics, including vaginally administered clindamycin (approximately 4% of the administered dose is absorbed systemically; see PHARMACOKINETICS). Symptoms may occur up to several weeks after cessation of antibiotic therapy.

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

Drugs which delay peristalsis (eg. opiates and diphenoxylate with atropine [Lomotil]) may prolong and/or worsen the condition and should not be used.

DALACIN V Cream 2% should be used with caution in patients with a history of regional enteritis, ulcerative colitis or antibiotic associated colitis.

The use of intravaginal clindamycin phosphate may result in the localised overgrowth of non-susceptible organisms, particularly yeasts. Clindamycin has shown in vitro activity against Lactobacilli species which are the predominant bacteria in normal vaginal flora. In clinical trials approximately 14% of patients treated with DALACIN V Cream 2% developed symptomatic cervicitis/vaginitis predominantly due to C. albicans (see ADVERSE EFFECTS).

The persistence of symptoms following treatment with DALACIN V Cream 2% should alert the clinician to the possibility of concomitant infection with organisms such as Trichomonas vaginalis, Candida albicans, Chlamydia trachomatis and Neisseria gonorrhoeae. Appropriate microbiological investigations and therapy directed at such organisms should be considered.

The patient should be instructed not to engage in vaginal intercourse or use other vaginal products (such as tampons or douches) during treatment with clindamycin vaginal cream.

This cream contains mineral oil. As mineral oil may weaken latex or rubber products such as condoms or vaginal contraceptive diaphragms the use of these contraceptive devices is not recommended within 72 hours following treatment with DALACIN V Cream 2%.

DALACIN V Cream 2% contains ingredients that will cause burning and irritation of the eyes. In the event of accidental contact with the eyes, rinse the eye with copious quantities of cool tap water.

Use in Pregnancy

CATEGORY A where the fetal membranes are intact.
Studies of DALACIN V Cream 2% have not been conducted in women during the first trimester.

Use in Lactation
It is not known if clindamycin is excreted in breast milk following the use of vaginally administered clindamycin phosphate. Clindamycin has however been reported to appear in breast milk following both orally and parenterally administered clindamycin. Therefore a full assessment of benefit-risk should be made when consideration is given to using DALACIN V Cream in the treatment of nursing mothers.

Paediatric Use
The safety and effectiveness of DALACIN V Cream 2% has not been established in children.

Use in the Elderly
Clinical studies for clindamycin phosphate vaginal cream 2% did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Effect on Ability to Drive and Use Machines
The effect of clindamycin on the ability to drive or operate machinery has not been systematically evaluated.

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

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

Effects on Fertility
Fertility studies in rats treated orally with up to 300 mg/kg/day (31 times the human exposure based on mg/m²) revealed no effects on fertility or mating

INTERACTIONS WITH OTHER MEDICINES
Cross resistance has been demonstrated between clindamycin, erythromycin and lincomycin.

No systemic drug interactions are known or anticipated with DALACIN V Cream. Antagonism has been demonstrated between clindamycin and erythromycin in vitro however
this potential interaction would not appear to be applicable unless erythromycin was also applied intravaginally.

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.

As the studies involving DALACIN V Cream did not allow concurrent intravaginal medication to be administered there are no data regarding the concomitant use of other intravaginal medications.

**ADVERSE EFFECTS**

**Clinical Trials**

*Non-pregnant women*

In clinical trials involving non-pregnant women, medical events judged to be related, probably related, possibly related or of unknown relationship to DALACIN V Cream 2% were reported in 20.7% of the patients receiving treatment for 3 days and 21.3% of the patients receiving treatment for 7 days. Events occurring in ≥1% of patients receiving 3-day or 7-day DALACIN V Cream 2% are shown in Table 1.

**Table 1. Events Occurring in ≥1% of Non-Pregnant Patients Receiving DALACIN V Cream 2%**

<table>
<thead>
<tr>
<th>SOC MedDRA PT</th>
<th>DALACIN V Cream 2%</th>
<th>3-Day (N = 600)</th>
<th>7-Day (N = 1325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulvovaginal candidiasis</td>
<td>7.7%</td>
<td>10.4%</td>
<td></td>
</tr>
<tr>
<td>Vulvovaginitis</td>
<td>6.0%</td>
<td>4.4%</td>
<td></td>
</tr>
<tr>
<td>Vulvovaginitis trichomonal</td>
<td>0</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Candida infection</td>
<td>1.3%</td>
<td>0.2%</td>
<td></td>
</tr>
<tr>
<td><strong>Reproductive system and breast disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulvovaginal disorder</td>
<td>3.2%</td>
<td>5.3%</td>
<td></td>
</tr>
</tbody>
</table>

MedDRA = Medical Dictionary for Regulatory Activities; N = number of patients; PT = Preferred Term; SOC = System Organ Class.

The following ADRs were reported in <1% (uncommon) of the patients receiving clindamycin vaginal cream application during clinical trials.

**Infections and infestations:** fungal infection, bacterial infection, skin candida, urinary tract infection, vaginal infection

**Immune system disorders:** hypersensitivity

**Endocrine disorders:** hyperthyroidism

**Nervous system disorders:** headache, dizziness
Ear and labyrinth disorders: vertigo

Respiratory, thoracic and mediastinal disorders: epistaxis

Gastrointestinal disorders: abdominal pain, constipation, diarrhoea, nausea, vomiting, breath odour, dyspepsia, flatulence, gastrointestinal disorder

Skin and subcutaneous tissue disorders: pruritus (non-application site), rash, rash maculopapular, urticaria, erythema

Reproductive system and breast disorders: menstrual disorder, metrorrhagia, vaginal discharge, vulvovaginal pain, endometriosis

General disorder and administration site conditions: inflammation

Investigations: microbiology test abnormal

Special senses: taste perversion

Pregnant women:

In clinical trials involving women during the second trimester of pregnancy, medical events judged to be related, probably related, possibly related or of unknown relationship to DALACIN V Cream 2% were reported in 22.8% of pregnant patients. Events occurring in ≥1% of patients receiving DALACIN V Cream 2% or placebo are shown in Table 2.

Table 2.  Events Occurring in ≥1% of Pregnant Patients Receiving DALACIN V Cream 2% or Placebo

<table>
<thead>
<tr>
<th>SOC MedDRA PT</th>
<th>7-Day N = 180</th>
<th>7-Day (Placebo) N = 184</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Vulvovaginal candidiasis</td>
<td>13.3%</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>1.7%</td>
<td>0</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Vulvovaginal disorder</td>
<td>6.7%</td>
</tr>
<tr>
<td>Pruritus (non-application site)</td>
<td>1.1%</td>
<td>0</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Abnormal labour</td>
<td>1.1%</td>
</tr>
<tr>
<td>Pregnancy, puerperium and perinatal conditions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MedDRA = Medical Dictionary for Regulatory Activities; N = number of patients; PT = Preferred Term; SOC = System Organ Class.

Events occurring in <1% of the patients receiving DALACIN V CREAM 2% with a frequency of “Uncommon” include:

Infections and infestations: candida infection, upper respiratory tract infection, vulvovaginitis trichomonal

Gastrointestinal disorders: diarrhoea

Skin and subcutaneous tissue disorders: erythema
Renal and urinary disorders: glycosuria, proteinuria, dysuria

Reproductive system and breast disorders: metrorrhagia, vulvovaginal pain

Post-Marketing Experience
Post-marketing experience of the patients receiving DALACIN V Cream 2% with a frequency category of “Frequency not known” include:

Gastrointestinal disorders: pseudomembranous colitis, abdominal distension

Musculoskeletal and connective tissue disorders: back pain

Reproductive system and breast disorders: pelvic pain

General disorder and administration site conditions: pain

DOSAGE AND ADMINISTRATION

The recommended dose of DALACIN V Cream 2% is one applicator-full (approximately 5 grams) of cream intravaginally at bedtime for seven (7) consecutive days.

OVERDOSAGE

Clindamycin from DALACIN V Cream 2% may be absorbed in sufficient amounts to produce systemic effects. Acute ingestion of clindamycin has not been associated with significant toxicity. Gastrointestinal decontamination is probably not necessary in most cases.

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

PRESENTATION AND STORAGE CONDITIONS

DALACIN® V Cream 2% is supplied in a 40 g collapsible laminate tube. Each 40 gram pack also contains seven (7) single-use disposable applicators, intended to be used once nightly for seven (7) days.

Storage Conditions
Store below 25ºC.

NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
ABN 50 008 422 348
38-42 Wharf Road
West Ryde NSW 2114
Australia
POISON SCHEDULE OF THE MEDICINE

S4 (Prescription Only Medicine)

DATE OF FIRST INCLUSION IN THE ARTG

8 April 1994

DATE OF MOST RECENT AMENDMENT

10 June 2016

© Registered Trademark