Pfizer

ڈالاسین سی

Dalacin C®
(Clindamycin)

DESCRIPTION

Clindamycin is a semisynthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent compound lincomycin.

Clindamycin phosphate is a water-soluble ester of clindamycin and phosphoric acid. Each mL contains the equivalent of 150 mg clindamycin, 0.5 mg disodium edetate and 9.45 mg benzyl alcohol added as preservative in each mL.
Dalacin C® Sterile Solution 300 mg: Each 2 mL contains; Clindamycin (Clindamycin phosphate) 300 mg
Dalacin C® Sterile Solution 600 mg: Each 2 mL contains; Clindamycin (Clindamycin phosphate) 600 mg
Dalacin C® Capsules 150 mg: Each capsule contains; Clindamycin (Clindamycin Hydrochloride) 150 mg
Dalacin C® Capsules 300 mg: Each capsule contains; Clindamycin (Clindamycin Hydrochloride) 300 mg

THERAPEUTIC INDICATIONS

Dalacin C® has been shown to be effective in the treatment of the following infections when caused by susceptible anaerobic bacteria; susceptible strains of gram positive aerobic bacteria such as streptococci, staphylococci and pneumococci; and susceptible strains of *Chlamydia trachomatis*.

(a) **Upper respiratory infections:** tonsillitis, pharyngitis, sinusitis, otitis media and scarlet fever.

(b) **Lower respiratory infections:** bronchitis, pneumonia, empyema and lung abscess.

(c) **Skin and soft tissue infections:** acne, furuncles, cellulitis, impetigo, abscesses, and wound infections. For specific skin and soft tissue infections like erysipelas and paronychia (panaritium), it would seem logical that these conditions would respond very well to Dalacin C® therapy.

(d) **Bone and joint infections:** osteomyelitis and septic arthritis.

(e) **Gynecological infections:** endometritis, cellulitis, vaginal cuff infection and tubo-ovarian abscess, salpingitis, and pelvic inflammatory disease when given in conjunction with an antibiotic of appropriate gram negative aerobic spectrum. In cases of cervicitis due to Chlamydia trachomatis, single drug therapy with Dalacin C® has been shown to be effective in eradicating the organism.

(f) **Intra-abdominal infections:** peritonitis and abdominal abscess when given in conjunction with an antibiotic of appropriate gram negative aerobic spectrum.

(g) **Septicemia and endocarditis:** The effectiveness of Dalacin C® in the treatment of selected cases of endocarditis has been documented when Dalacin C® is determined to be bactericidal to the infecting organism by in vitro testing of appropriate achievable serum concentrations.

(h) **Dental infections:** periodontal abscess and periodontitis.

(i) **Toxoplasmic encephalitis in patients with AIDS.** In patients who are intolerant to conventional treatment, clindamycin in combination with pyrimeth-amine has been shown to be efficacious.

(j) **Pneumocystis *jiroveci* (previously classified as *Pneumocystis carinii*) pneumonia in patients with AIDS:** In patients who are intolerant to, or do not respond adequately to conventional treatment, Dalacin C® may be used in combination with primaquine.
(k) **Malaria:** Including multi-resistant Plasmodium falciparum, alone or in combination with quinine or chloroquine.

(l) **Prophylaxis of endocarditis:** In patients sensitive-/allergic to penicillin(s).

(m) **Prophylaxis of infection in neck and head surgery:** Dalacin C®, diluted in normal saline, is used as an intraoperative irrigant of the surgical field.
Dalacin C®, when used concurrently with an aminoglycoside antibiotic such as gentamicin or tobramycin, has been shown to be effective in preventing peritonitis or intra-abdominal abscess after bowel perforation and bacterial contamination secondary to trauma.

In-vitro susceptibility to Dalacin C® has been shown for the following organisms: B. melaninogenicus, B. disiens, B. bivius, Peptostreptococcus spp., G. vaginalis, M. mulieris, M. curtisii, and Mycoplasma hominis.

POSOLOGY AND METHOD OF ADMINISTRATION

Dosage in Adults

Dalacin C® (IM or IV administration):
The usual daily adult dosage of Dalacin C® for infections of the intra-abdominal area, female pelvis, and other complicated or serious infections is 2400-2700 mg given in 2, 3, or 4 equal doses. Less complicated infections due to more susceptible micro-organisms may respond to lower doses such as 1200-1800 mg/day administered in 3 or 4 equal doses.
Doses of up to 4800 mg daily have been used successfully.

Single IM doses of greater than 600 mg are not recommended.

Dalacin C® capsules (oral administration):
600-1800 mg/day divided in 2, 3 or 4 equal doses.
To avoid the possibility of esophageal irritation, Dalacin C® capsules should be taken with a full glass of water.

Dosage in Children (over 1 month of age)

Dalacin C® (IM or IV administration): 20-40 mg/kg/day in 3 or 4 equal doses.

Dalacin C® capsules (oral administration):
To avoid the possibility of esophageal irritation, Dalacin C® capsules should be taken with a full glass of water.
Doses of 8-25 mg/kg/day in 3 or 4 equal doses.

Dosage in Neonates (under 1 month of age)

Dalacin C® (IM or IV administration): 15-20 mg/kg/day in 3 or 4 equal doses. The lower dosage may be adequate for small premature infants.

Dosage in Elderly: Pharmacokinetic studies with Dalacin C® have shown no clinically important differences between young and elderly subjects with normal hepatic function and normal (age-adjusted) renal function after oral or intravenous administration. Therefore, dosage adjustments are not necessary in the elderly with normal hepatic function and normal (age-adjusted) renal function (see Section Pharmacokinetic Properties).

Dosage in Renal Impairment: Dalacin C® dosage modification is not necessary in patients with renal insufficiency.

Dosage in Hepatic Impairment: Dalacin C® dosage modification is not necessary in patients with hepatic insufficiency.

Dosage in Specific Indications

(a) Treatment of Beta-Hemolytic Streptococcal Infections

Refer to the dosage recommendations above under 1, 2, and 3. Treatment should be continued for at least 10 days.

(b) Inpatient Treatment of Pelvic Inflammatory Disease

Dalacin C® 900 mg (IV) every 8 hours daily plus an antibiotic with an appropriate gram negative aerobic spectrum administered IV, e.g., gentamicin 2.0 mg/kg followed by 1.5 mg/kg every 8 hours daily in patients with normal renal function. Continue (IV) drugs for at least 4 days and at least 48 hours after the patient improves. Then continue oral Dalacin C® 450-600 mg q6h daily to complete 10-14 days total therapy.

(c) Treatment of Chlamydia trachomatis Cervicitis

Dalacin® capsules orally 450-600 mg 4 times daily for 10-14 days

(d) Treatment of Toxoplasmic Encephalitis in Patients with AIDS

Dalacin C® IV 600-1200 mg every 6 hours for 2 weeks followed by 300-600 mg orally every 6 hours. The usual total duration of therapy is 8 to 10 weeks. The dose of pyrimethamine is 25 to 75 mg orally each day for 8 to 10 weeks. Folinic acid 10 to 20 mg/day should be given with higher doses of pyrimethamine.

(e) Treatment of Pneumocystis carinii Pneumonia in Patients with AIDS: Dalacin C®, IV 600 to 900 mg every 6 hours or 900 mg IV every 8 hours for 21 days. And Primaquine 15 to 30 mg dose orally once daily for 21 days.

(f) Treatment of Acute Streptococcal Tonsillitis/ Pharyngitis

Dalacin C® capsules 300 mg orally twice daily for 10 days

(g) Treatment of Malaria

Dalacin C® capsules (oral administration). Adults: 10 to 20 mg/kg/day and children 10 mg/kg/day administered in equal doses every 12 hours for 7 days, alone, or in combination with quinine (12 mg/kg every 12 hours), or chloroquine (15 to 25 mg every 24 hours), for 3-5 days.

(h) Prophylaxis of Endocarditis in Patients Sensitive to Penicillin: Dalacin C® 600 mg IV 1 hour before procedure.

(i) Prophylaxis of Infection in Head and Neck Surgery: Dalacin C® 900 mg diluted in 1000 mL normal saline for use as an intra-operative irrigant in contaminated head and neck surgery prior to wound closure.

Dilution and IV Infusion rates

The concentration of clindamycin in diluent for infusion should not exceed 18 mg per mL and INFUSION RATES SHOULD NOT EXCEED 30 MG PER MINUTE. The usual infusion rates are as follows:

Dose	Diluent	Time
300 mg	50 mL	10 min
600 mg	50 mL	20 min
900 mg	50-100 mL	30 min
1200 mg	100 mg	40 min

Administration of more than 1200 mg in a single 1-hour infusion is not recommended.

CONTRAINDICATIONS

Clindamycin is contraindicated in patients previously found to be sensitive to clindamycin or lincomycin or to any component of the formulation.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

The clindamycin phosphate injectable formulation contains benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants.

Pseudomembraneous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider the diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis". After the primary diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate-to-severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Since clindamycin does not diffuse adequately into cerebrospinal fluid, the drug should not be used in the treatment of meningitis.

If therapy is prolonged, liver and kidney function tests

should be performed.
The use of clindamycin phosphate may result in overgrowth of non-susceptible organisms, particularly yeasts.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C *difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Clindamycin phosphate should not be injected intravenously undiluted as a bolus, but should be infused over at least 10-60 minutes as directed in Section Posology and Method of Administration.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION
Antagonism has been demonstrated between clindamycin and erythromycin in vitro. Because of possible clinical significance, these two drugs should not be administered concurrently.

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.

Pregnancy and Lactation
Use in Pregnancy: Clindamycin crosses the placenta in humans. After multiple doses, amniotic fluid concentrations were approximately 30% of maternal blood concentrations. Clindamycin should be used in pregnancy only if clearly needed.

Use in Nursing Mothers: Clindamycin has been reported to appear in human breast milk in ranges from 0.7 to 3.8 µg/mL.

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.

UNDESIRABLE EFFECTS
- *Blood and Lymphatic System Disorders:* Transient neutropenia (leukopenia) and eosinophilia have been reported. Reports of agranulocytosis and thrombocytopenia have been made. No direct etiologic relationship to concurrent clindamycin therapy could be made in any of the foregoing.
- *Immune System Disorders:* A few cases of anaphylactoid reactions have been reported.
- *Nervous System Disorders:* Dysgeusia
- *Cardiac Disorders:* Rare instances of cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration (see section **Posology and Method of Administration**).
- *Vascular Disorders:* Thrombophlebitis has been reported with IV injection. These reactions can be minimized by deep IM injection and avoidance of indwelling intravenous catheters.
- *Hepatobiliary Disorders:* Jaundice and abnormalities in liver function tests have been observed during clindamycin therapy.
- *Skin and Subcutaneous Tissue Disorders:* Maculopapular rash and urticaria have been observed during drug therapy. Generalized mild to moderate morbilliform-like skin rashes are the most frequently reported reactions. Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with clindamycin. Pruritus, vaginitis and rare instances of exfoliative and vesiculo-bullous dermatitis have been reported. Rare cases of toxic epidermal necrolysis have been reported during post-marketing surveillance.
- *General Disorders and Administration Site Conditions:* Local irritation, pain, abscess formation have been seen with IM injection.

OVERDOSE
Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Microbiology: Clindamycin has been shown to have in vitro activity against isolates of the following organisms:

Aerobic gram-positive cocci, including:
- *Staphylococcus aureus;*
- *Staphylococcus epidermidis (penicillinase and nonpenicillinase producing strains);*
- When tested by in vitro methods some staphylococcal strains originally resistant to erythromycin rapidly develop resistance to clindamycin;
- Streptococci (except Streptococcus faecalis);
- Pneumococci.

Anaerobic gram-negative bacilli, including:
- Bacteroides species (including Bacteroides fragilisgroup and Bacteroides melaninogenicus group);
- Fusobacterium species.

Anaerobic gram-positive non-sporeforming bacilli, including:
- Propionibacterium
- Eubacterium
- Actinomyces species

Anaerobic and microaerophilic gram-positive cocci, including:
- Peptococcus species;
- Peptostreptococcus species;
- Microaerophilic streptococci.

Clostridia: Clostridia are more resistant than most anaerobes to clindamycin. Most *Clostridium perfringens* are susceptible, but other species, e.g., *Clostridium sporogenes* and *Clostridium tertium* are frequently resistant to clindamycin.

Susceptibility testing should be done.

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

PHARMACOKINETIC PROPERTIES
Serum half-life of clindamycin is increased slightly in patients with markedly reduced renal function. Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.
Concentrations of clindamycin in the serum increased linearly with increased dose. Serum levels exceed the MIC (minimum inhibitory concentration) for most indicated organisms for at least six hours following administration of the usually recommended doses. Clindamycin is widely distributed in body fluids and tissues (including bones). The average biological half-life is 2.4 hours. Approximately 10%of the bioactivity is excreted in the urine and 3.6% in the feces; the remainder is excreted as bioinactive metabolites. Doses of up to 2 grams of clindamycin per day for 14 days have been well tolerated by healthy volunteers, except that the incidence of gastrointestinal side effects is greater with the higher doses. No significant levels of clindamycin are attained in the cerebrospinal fluid, even in the presence of inflamed meninges.
Pharmacokinetic studies in elderly volunteers (61-79 years) and younger adults (18-39 years) indicate that age alone does not alter clindamycin pharmacokinetics (clearance, elimination half-life, volume of distribution, and area under the serum concentration time curve) after IV administration of clindamycin phosphate. After oral administration of clindamycin hydrochloride, elimination half-life is increased to approximately 4.0 hours (range 3.4 –5.1 h) in the elderly compared to 3.2 hours (range 2.1 - 4.2 h) in younger adults. The extent of absorption, however, is not different between age groups and no dosage alteration is necessary for the elderly with normal hepatic function and normal (age-adjusted) renal function.

PHARMACEUTICAL PARTICULARS
Incompatibilities
When combined with Dalacin C® in an infusion solution, ampicillin, phenytoin sodium, barbiturates, aminophyllin, calcium gluconate, magnesium sulfate, ceftriaxone sodium, and ciprofloxacin are each physically incompatible with clindamycin phosphate.

IMPORTANT
No ampoule file is needed to open the ampoules. The neck of the ampoule is prescored at the point of constriction. A colored dot on the ampoule head helps to orientate the ampoule. Take the ampoule and face the colored dot. The ampoule opens easily by placing the thumb on the colored dot and gently pressing downwards as shown.

SHELF-LIFE
Injectable solution: 24 months
Capsules: 36 months

HOW SUPPLIED
Dalacin C®
Injectable solution
- 300 mg/2 mL: Package of 1 ampoule at a dose of 2 mL
- 600 mg/4 mL: Package of 1 ampoule at a dose of 4 mL

Capsules
- 150 mg: Package of 16's capsules
- 300 mg: Package of 16's capsules

DOSAGE
Use as directed by the physician.

INSTRUCTIONS
Storage:
Dalacin C® Capsules
Store below 30°C.

Dalacin C® Sterile Solution
Do not store above 25°C.
Do not refrigerate or freeze.
Avoid exposure to heat & sunlight.
Keep out of the reach of children.

CAUTION
To be sold on the prescription of a registered medical practitioner only.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

کیپسولز: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

انجکشن: ۲۵ ڈگری سینٹی گریڈ سے زیادہ پر نہ رکھیں۔
ریفریجریٹر یا فریزر میں نہ رکھیں۔
دوا کو گرمی اور سورج کی روشنی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔

تاکید: صرف رجسٹرڈ میڈیکل پریکٹشنر کے نسخہ پر فروخت کریں۔

Dalacin C® Capsules
Manufactured by:
Pfizer Pakistan Ltd.
B-2, S.I.T.E., Karachi, Pakistan.

Dalacin C® Phosphate Sterile Solution
Manufactured by:
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B-2870 Puurs,Belgium.

Packed by:
Pfizer Pakistan Ltd.
B-2, S.I.T.E., Karachi, Pakistan.

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