Dalacin C®

Clindamycin

Capsules

CDS

AfME Markets using same as LPD:  Ethiopia, Ghana, Kenya, Nigeria, Tanzania, Uganda

## 1. NAME OF THE MEDICINAL PRODUCT

DALACIN C

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient: clindamycin hydrochloride

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

Clindamycin hydrochloride is the hydrated hydrochloride salt of clindamycin. Each capsule contains clindamycin hydrochloride equivalent to 150 mg or 300 mg of clindamycin.

DALACIN C 150 mg, capsule :
Clindamycin hydrochloride, hydrated form
Quantity corresponding to clindamycin base 150.00 mg
For one capsule.

DALACIN C 300 mg, capsule :
Clindamycin hydrochloride, hydrated form
Quantity corresponding to clindamycin base 300.00 mg
For one capsule.

## 3. PHARMACEUTICAL FORM

Capsules

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

Clindamycin 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 including tonsillitis, pharyngitis, sinusitis, otitis media and scarlet fever.

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

(c) Skin and soft tissue infections including 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 clindamycin therapy.

(d) Bone and joint infections including osteomyelitis and septic arthritis.

(e) Gynecological infections including 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 clindamycin has been shown to be effective in eradicating the organism.

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

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

(h) Dental infections such as periodontal abscess and periodontitis.

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

(j) *Pneumocystis jirovecii* (previously classified as *Pneumocystis carinii*) pneumonia in patients with AIDS. In patients who are intolerant to, or do not respond adequately to conventional treatment, clindamycin may be used in combination with primaquine.

(k) Malaria, including multi-resistant *Plasmodium falciparum*, in combination with quinine.

(l) Prophylaxis of endocarditis in patients sensitive/allergic to penicillin(s).

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

### 4.2. Posology and method of administration

*Dosage in Adults*

Clindamycin hydrochloride capsules (oral administration):

600-1800 mg/day divided in 2, 3 or 4 equal doses. To avoid the possibility of oesophageal irritation, clindamycin HCl capsules should be taken with a full glass of water and no less than 30 minutes before lying down.

*Dosage in Children (over 1 month of age)*

Clindamycin should be dosed based on total body weight regardless of obesity.

Clindamycin hydrochloride capsules *(for children who are able to swallow capsules)*:

To avoid the possibility of oesophageal irritation, clindamycin HCl capsules should be taken with a full glass of water and no less than 30 minutes before lying down.

Doses of 8-25 mg/kg/day in 3 or 4 equal doses.

Clindamycin capsules are not suitable for children who are unable to swallow them whole. The capsules do not provide exact mg/kg doses therefore it may be necessary to use the clindamycin palmitate oral solution in some cases.

*Dosage in Elderly*

Pharmacokinetic studies with clindamycin 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 5.2 Pharmacokinetic properties).

*Dosage in Renal Impairment*

Clindamycin dosage modification is not necessary in patients with renal insufficiency.

*Dosage in Hepatic Impairment*

Clindamycin 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 Dosage in Adults and Dosage in Children. Treatment should be continued for at least 10 days.

(b) Inpatient Treatment of Pelvic Inflammatory Disease

Clindamycin phosphate 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 clindamycin hydrochloride 450-600 mg q6h daily to complete 10-14 days total therapy.

(c) Treatment of *Chlamydia trachomatis* Cervicitis

Clindamycin hydrochloride capsules orally 450-600 mg 4 times daily for 10-14 days.

(d) Treatment of Toxoplasmic Encephalitis in Patients with AIDS

Clindamycin hydrochloride orally 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

Clindamycin hydrochloride 300 to 450 mg orally every 6 hours for 21 days.

and

Primaquine 15 to 30 mg dose orally once daily for 21 days.

(f) Treatment of Acute Streptococcal Tonsillitis/Pharyngitis

Clindamycin hydrochloride capsules 300 mg orally twice daily for 10 days.

(g) Treatment of Malaria

Clindamycin hydrochloride capsules or clindamycin palmitate solution (oral administration).

Uncomplicated Malaria/*P falciparum*

*Adults:*

Quinine sulfate: 650 mg orally three times daily for 3 or 7 days plus clindamycin: 20 mg base/kg/day orally divided three times daily for 7 days.

*Children:*

Quinine sulfate: 10 mg/kg orally three times daily for 3 or 7 days plus clindamycin: 20 mg base/kg/day orally divided three times daily for 7 days.

Severe malaria

*Adults:*

Quinidine gluconate: 10 mg/kg loading dose IV over 1-2 hrs, then 0.02 mg/kg/min continuous infusion for at least 24 hours (for alternative dosing regimen please refer to quinidine label). Once parasite density <1% and patient can take oral medication, complete treatment with oral quinine, dose as above, plus clindamycin: 20 mg base/kg/day orally divided three times daily for 7 days. If patient not able to take oral medication, give 10 mg base/kg clindamycin loading dose IV followed by 5 mg base/kg IV

every 8 hours. Avoid rapid IV administration. Switch to oral clindamycin (oral dose as above) as soon as patient can take oral medication. Treatment course = 7 days.

*Children:*

Quinidine gluconate: Same mg/kg dosing and recommendations as for adults plus clindamycin: 20 mg base/kg/day orally divided three times daily for 7 days. If patient not able to take oral medication, give 10 mg base/kg clindamycin loading dose IV followed by 5 mg base/kg IV every 8 hours. Avoid rapid IV administration. Switch to oral clindamycin (oral dose as above) as soon as patient can take oral medication. Treatment course = 7 days.

(h) Prophylaxis of Endocarditis in Patients Sensitive to Penicillin

Clindamycin hydrochloride capsules or clindamycin palmitate solution (oral administration). Adults: 600 mg 1 hour before procedure; children: 20 mg/kg 1 hour before procedure. Alternatively, when parenteral administration is required: clindamycin phosphate 600 mg IV 1 hour before procedure.

**Dilution for IV use 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 | 100mL | 40 min |

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

### 4.3. Contraindications

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

### 4.4. Special warnings and precautions for use

Severe hypersensitivity reactions, including severe skin reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), toxic

epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP) have been reported in patients receiving clindamycin therapy. If a hypersensitivity or severe skin reaction occurs, clindamycin should be discontinued and appropriate therapy should be initiated (see Section 4.3 Contraindications and Section 4.8 Undesirable effects).

The clindamycin phosphate injectable formulation contains benzyl alcohol. The preservative benzyl alcohol has been associated with serious adverse events, including the "gasping syndrome", and death in pediatric patients. Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the "gasping syndrome", the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low birth weight infants may be more likely to develop toxicity.

Pseudomembranous 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 *Clostridioides 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 *Clostridioides difficile* colitis.

*Clostridioides 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 *Cdifficile*.

*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.

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 function tests should be performed.

Clindamycin is potentially nephrotoxic. Acute kidney injury including acute renal failure has been reported. Therefore, monitoring of renal function should be considered during therapy of

patients with pre-existing renal dysfunction or taking concomitant nephrotoxic drugs and monitoring of renal function should be performed if therapy is prolonged.

Oral capsules: Due to the risk of oesophagitis and oesophageal ulcer, it is important to ensure compliance with administration guidance (see Sections 4.2 and 4.8).

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

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.

Clindamycin is metabolized predominantly by CYP3A4, and to a lesser extent by CYP3A5, to the major metabolite clindamycin sulfoxide and minor metabolite N-desmethylclindamycin. Therefore inhibitors of CYP3A4 and CYP3A5 may reduce clindamycin clearance and inducers of these isoenzymes may increase clindamycin clearance. In the presence of strong CYP3A4 inducers such as rifampicin, monitor for loss of effectiveness.

*In* vitro studies indicate that clindamycin does not inhibit CYP1A2, CYP2C9, CYP2C19, CYP2E1 or CYP2D6 and only moderately inhibits CYP3A4. Therefore, clinically important interactions between clindamycin and co-administered drugs metabolized by these CYP enzymes are unlikely.

## 4.6. Fertility, pregnancy and lactation

Use in Pregnancy

Benzyl alcohol can cross the placenta. See Section 4.4 Special warnings and precautions for use.

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. Animal reproduction studies are not always predictive of human response.

Clindamycin crosses the placenta in humans. After multiple doses, amniotic fluid concentrations were approximately 30% of maternal blood concentrations.

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. There are no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy**.**

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 ≤0.5 to 3.8 μg/mL.

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.

### 4.7. 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.

### 4.8. Undesirable effects

All undesirable effects listed in the label are presented by MedDRA system organ class (SOC). Within each SOC, the undesirable effects are presented in the order of decreasing medical seriousness.

**Adverse Drug Reaction Table**

| System Organ Class | Adverse Drug Reactions |
|---|---|
| Infections and infestations | pseudomembranous colitis*, *Clostridioides difficile* colitis*, vaginal infection* |
| Blood and lymphatic system disorders | agranulocytosis*, neutropenia*, thrombocytopenia*, leukopenia*, eosinophilia |
| Immune system disorders | anaphylactic shock*, anaphylactoid reaction*, anaphylactic reaction*, hypersensitivity* |
| Nervous system disorders | Dysgeusia |
| Cardiac disorders | cardio-respiratory arrest§ |
| Vascular disorders | thrombophlebitis†, hypotension§ |
| Gastrointestinal disorders | diarrhoea, abdominal pain, oesophageal ulcer*‡≠, oesophagitis*‡≠, vomiting, nausea |
| Hepatobiliary disorders | jaundice* |
| Skin and subcutaneous tissue disorders | toxic epidermal necrolysis*(TEN), Stevens-Johnson syndrome (SJS)*, drug reaction with eosinophilia and systemic symptoms (DRESS)*, acute generalised exanthematous pustulosis (AGEP)*, angioedema*, dermatitis exfoliative*, dermatitis bullous*, rash maculo-papular*, urticaria*, erythema multiforme, pruritus, rash morbilliform* |

**Adverse Drug Reaction Table**

| System Organ Class | Adverse Drug Reactions |
|---|---|
| Renal and urinary disorders | acute kidney injury* |
| General disorders and administration site conditions | pain†, injection site abscess†, injection site irritation†‡ |
| Investigations | liver function test abnormal |

*ADR identified post-marketing
†ADRs apply only to injectable formulations
‡ADRs apply only to oral formulations
§Rare instances have been reported following too rapid intravenous administration (see **Section 4.2 Posology and method of administration**).
≠Possible occurrence of oesophagitis and oesophageal ulcer, particularly if taken in a lying position and/or with a small amount of water.

### 4.9. Overdose

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

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

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. At usual doses, clindamycin exhibits bacteriostatic activity *in* vitro.

Pharmacodynamic effects

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

Resistance

Resistance to clindamycin is most often due to mutations at the rRNA antibiotic binding site or methylation of specific nucleotides in the 23S RNA of the 50S ribosomal subunit. These alterations can determine *in* vitro cross resistance to macrolides and streptogramins B ($MLS_B$ phenotype). Resistance is occasionally due to alterations in ribosomal proteins. Resistance to clindamycin may be inducible by macrolides in macrolide-resistant bacterial isolates. Inducible resistance can be demonstrated with a disk test (D-zone test) or in broth. Less frequently encountered resistance mechanisms involve modification of the antibiotic and active efflux. There is complete cross resistance between clindamycin and lincomycin. As with many antibiotics, the incidence of resistance varies with the bacterial species and the geographical area. The incidence

of resistance to clindamycin is higher among methicillin-resistant staphylococcal isolates and penicillin-resistant pneumococcal isolates than among organisms susceptible to these agents.

Antimicrobial activity

Clindamycin has been shown to have *in* vitro activity against most isolates of the following organisms:

Aerobic bacteria

Gram-positive bacteria

- *Staphylococcus aureus* (methicillin-susceptible isolates)
- Coagulase-negative staphylococci (methicillin-susceptible isolates)
- *Streptococcus pneumoniae* (penicillin-susceptible isolates)
- Beta-hemolytic streptococci groups A, B, C, and G
- Viridans group streptococci
- *Corynebacterium* spp.

Gram-negative bacteria

- *Chlamydia trachomatis*

Anaerobic bacteria

Gram-positive bacteria

- *Actinomyces* spp.
- *Clostridioides* spp. (except *Clostridioides difficile*)
- *Eggerthella* (*Eubacterium*) spp.
- *Peptococcus* spp.
- *Peptostreptococcus* spp. (*Finegoldia magna, Micromonas micros*)
- *Propionibacterium acnes*

Gram-negative bacteria

- *Bacteroides* spp.
- *Fusobacterium* spp.
- *Gardnerella vaginalis*
- *Prevotella* spp.

Fungi

- *Pneumocystis jirovecii*

Protozoans

- *Toxoplasma gondii*
- *Plasmodium falciparum*

Breakpoints

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 Clinical and Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST) for systemically administered antibiotics.

Clinical and Laboratory Standards Institute (CLSI) breakpoints for relevant organisms are listed below.

**Table 1. CLSI Susceptibility Interpretive Criteria for Clindamycin**

| ***Pathogen*** | **Minimal Inhibitory Concentrations (mcg/mL)** | | | **Disk Diffusion (Zone Diameters in mm)[a]** | | |
|---|---|---|---|---|---|---|
| | **S** | **I** | **R** | **S** | **I** | **R** |
| *Staphylococcus* spp. | ≤0.5 | 1–2 | ≥4 | ≥21 | 15–20 | ≤14 |
| *Streptococcus* spp. | ≤0.25 | 0.5 | ≥1 | ≥19 | 16–18 | ≤15 |
| Anaerobic bacteria[b] | ≤2 | 4 | ≥8 | NA | NA | NA |

NA=not applicable; S=susceptible; I=intermediate; R=resistant.
[a]Disk content 2 micrograms of clindamycin
[b]MIC ranges for anaerobes are based on agar dilution methodology.

A report of "Susceptible" (S) indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of "Intermediate" (I) indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" (R) indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the usually achievable concentrations; other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the

techniques of the individuals performing the test. Standard clindamycin powder should provide the MIC ranges in Table 2. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 2 should be achieved.

**Table 2. CLSI Acceptable Quality Control (QC) Ranges for Clindamycin to be Used in Validation of Susceptibility Test Results**

| QC Strain | Minimum Inhibitory Concentration Range (mcg/mL) | Disk Diffusion Range (Zone Diameters in mm) |
|---|---|---|
| *Staphylococcus aureus* ATCC 29213 | 0.06–0.25 | NA |
| *Staphylococcus aureus* ATCC 25923 | NA | 24–30 |
| *Streptococcus pneumoniae* ATCC 49619 | 0.03–0.12 | 19–25 |
| *Bacteroides fragilis* ATCC 25285 | 0.5–2[a] | NA |
| *Bacteroides thetaiotaomicron* ATCC 29741 | 2–8[a] | NA |
| *Eggerthella lenta* ATCC 43055 | 0.06–0.25[a] | NA |

NA=Not applicable.
ATCC® is a registered trademark of the American Type Culture Collection
[a]MIC ranges for anaerobes are based on agar dilution methodology.

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints are presented below.

**Table 3. EUCAST Susceptibility Interpretive Criteria for Clindamycin**

| | MIC breakpoints (mg/L) | | Zone diameter breakpoints (mm)[a] | |
|---|---|---|---|---|
| **Organism** | **S ≤** | **R >** | **S ≥** | **R <** |
| *Staphylococcus* spp. | 0.25 | 0.5 | 22 | 19 |
| *Streptococcus* Groups A, B, C and G | 0.5 | 0.5 | 17 | 17 |
| *Streptococcus pneumoniae* | 0.5 | 0.5 | 19 | 19 |
| *Viridans group streptococci* | 0.5 | 0.5 | 19 | 19 |
| Gram-positive anaerobes | 4 | 4 | NA | NA |
| Gram-negative anaerobes | 4 | 4 | NA | NA |
| *Corynebacterium* spp. | 0.5 | 0.5 | 20 | 20 |

[a]Disk content 2 µg of clindamycin
NA=not applicable; S=susceptible; R=resistant

EUCAST QC ranges for MIC and disk zone determinations are in the table below.

**Table 4. EUCAST Acceptable Quality Control (QC) Ranges for Clindamycin to be Used in Validation of Susceptibility Test Results**

| QC Strain | Minimum Inhibitory Concentration Range (mcg/mL) | Disk Diffusion Range (Zone Diameters in mm) |
|---|---|---|
| *Staphylococcus aureus* ATCC 29213 | 0.06–0.25 | 23-29 |
| *Streptococcus pneumoniae* ATCC 49619 | 0.03–0.125 | 22-28 |

## 5.2. Pharmacokinetic properties

Serum level studies with a 150 mg oral dose of clindamycin hydrochloride in 24 normal adult volunteers showed that clindamycin was rapidly absorbed after oral administration. An average peak serum level of 2.50 mcg/mL was reached in 45 minutes; serum levels averaged 1.51 mcg/mL at 3 hours and 0.70 mcg/mL at 6 hours. Absorption of an oral dose is virtually complete (90%), and the concomitant administration of food does not appreciably modify the serum concentrations; serum levels have been uniform and predictable from person to person and dose to dose. Serum level studies following multiple doses of clindamycin hydrochloride for up to 14 days show no evidence of accumulation or altered metabolism of drug. 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). *In* vitro studies in human liver and intestinal microsomes indicated that clindamycin is predominantly oxidized by CYP3A4, with minor contribution from CYP3A5, to form clindamycin sulfoxide and a minor metabolite, N-desmethylclindamycin. 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.

*Obese Pediatric Patients Aged 2 to Less than 18 Years and Obese Adults Aged 18 to 20 Years*

An analysis of pharmacokinetic data in obese pediatric patients aged 2 to less than 18 years and obese adults aged 18 to 20 years demonstrated that clindamycin clearance and volume of distribution normalized by total body weight are comparable regardless of obesity.

### 5.3. Preclinical safety data

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 Salmonella reversion test. Both tests were negative.

Impairment of Fertility:

Fertility studies in rats treated orally with up to 300 mg/kg/day (approximately 1.1 times the highest recommended adult human dose based on $mg/m^2$) revealed no effects on fertility or mating ability.

In oral embryo fetal development studies in rats and subcutaneous embryo fetal development studies in rats and rabbits, no developmental toxicity was observed except at doses that produced maternal toxicity.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

DALACIN C 150 mg hard capsules:
Maize starch, talc, magnesium stearate, lactose.
Composition of the capsule shell: gelatin, titanium dioxide.

DALACIN C 300 mg hard capsules:
Maize starch, talc, magnesium stearate, lactose.
Composition of the capsule shell: titanium dioxide, gelatin.

### 6.2. Incompatibilities

Not applicable

### 6.3. Shelf life

**Keep out of the sight and reach of children.**
**Do not use DALACIN C capsules after the expiry date which is stated on the Carton/Blister after EXP:. The expiry date refers to the last day of that month.**

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.

### 6.4. Special precautions for storage

Store below 30°C

### 6.5. Nature and contents of container

DALACIN C 150 mg, capsule : 16 or 100 capsules in heat-formed blister packs (Aluminium foil/PVC).
DALACIN C 300 mg, capsule : 16 capsules in heat-formed blister packs (Aluminium foil/PVC).

Not all strength/pack sizes may be marketed.

### 6.6. Special precautions for disposal and other handling

Not applicable

## 7. FURTHER INFORMATION

**MANUFACTURED BY**

FAREVA AMBOISE
Zone Industrielle,
29 route des Industries,
37530 Pocé Sur Cisse,
France

## 8. PRESCRIPTION STATUS

Medicinal product subject to medical prescription.

## 9. DATE OF REVISION OF THE TEXT

November 2023