Dalacin C®

Clindamycin

Solution for Injection

CDS

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

1. NAME OF THE MEDICINAL PRODUCT

DALACIN C

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient: clindamycin phosphate.

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 300 mg solution for injection

The active substance is clindamycin. This is present in the form of clindamycin phosphate (178.23 mg), equivalent to 150 mg clindamycin per ml. Each mL also contains 0.5 mg disodium edetate and 9.45 mg benzyl alcohol added as preservative.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection -A clear, colourless solution

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).

(m) Prophylaxis of infection in neck and head surgery. Clindamycin phosphate, diluted in normal saline, is used as an intraoperative irrigant of the surgical field.

Clindamycin phosphate, 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 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

Clindamycin phosphate IM administration should be used undiluted.

Clindamycin phosphate IV administration should be diluted (See **Dilution for IV use and IV infusion rates** below**)**.

Dosage in Adults

Clindamycin phosphate (IM or IV administration):

The usual daily adult dosage of clindamycin phosphate for infections of the intraabdominal 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 microorganisms 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.

Dosage in Children (over 1 month of age)

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

Clindamycin phosphate (IM or IV administration):

20-40 mg/kg/day in 3 or 4 equal doses.

Dosage in Neonates (under 1 month of age)

Clindamycin phosphate (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 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, Dosage in Children, and Dosage in Neonates. 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 phosphate IV or 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 phosphate IV 600 to 900 mg every 6 hours or 900 mg IV every 8 hours or 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.

(i) Prophylaxis of Infection in Head and Neck Surgery

Clindamycin phosphate 900 mg diluted in 1000 mL normal saline for use as an intraoperative irrigant in contaminated head and neck surgery prior to wound closure.

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), acute generalized exanthematous pustulosis (AGEP), Kounis syndrome 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 *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.

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.

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

Intravenous: 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 4.2 Posology and method of administration.

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*, Kounis syndrome, hypersensitivity*
Nervous system disorders	dysgeusia
Cardiac disorders	cardio-respiratory arrest§
Vascular disorders	thrombophlebitis†, hypotension§

Adverse Drug Reaction Table

System Organ Class	Adverse Drug Reactions
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*, cutaneous vasculitis*, rash maculo-papular, urticaria, erythema multiforme, pruritus, rash morbilliform*, symmetrical drug-related intertriginous and flexural exanthema*
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 (MLSB 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

ATCC® is a registered trademark of the American Type Culture Collection

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

Benzyl alcohol, Disodium edentate Water for injection.

6.2. Incompatibilities

(This list may not be all-inclusive due to the multiple factors influencing drug compatibility data.)

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

COMPATIBILITIES:

Solutions of clindamycin phosphate in 5 % dextrose in water and in sodium chloride solutions, to which one of the following antibiotics are added in the usual concentration remain stable for at least 24 hours: amikacin sulphate, aztreonam, cefamandole nafate, cefazolin sodium, cefotaxime sodium, cefoxitin sodium, ceftazidime sodium, ceftizoxime sodium, gentamicin sulphate, netilmicin sulphate, piperacillin and tobramycin.

The compatibility and the stability of these mixtures can vary depending on the concentration and other conditions.

6.3. Shelf life

Keep out of the sight and reach of children.

Do not use DALACIN C INJECTION after the expiry date which is stated on the Carton/Vial Label after EXP:. The expiry date refers to the last day of that month.

6.4. Special precautions for storage

Store at 2 to 8°C (Refrigerate. Do not freeze).

6.5. Nature and contents of container

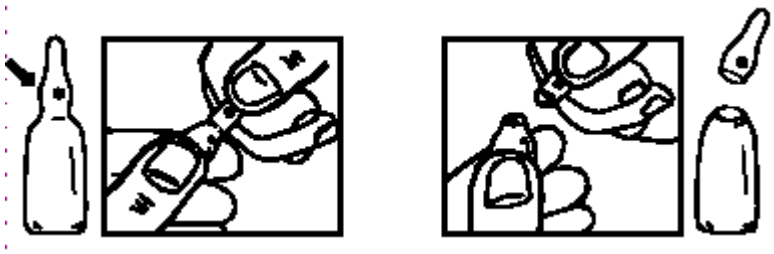
Solution for injection

DALACIN C 300 mg:
– Pack containing 1 ampoule of 2 ml.

6.6. Special precautions for disposal and other handling

INDICATIONS FOR OPENING THE AMPOULE

Exert pressure on the ampoule with the point towards you, as indicated on the graph.



Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. FURTHER INFORMATION

MANUFACTURED BY

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

8. PRESCRIPTION STATUS

Medicinal product subject to medical prescription.

9. DATE OF REVISION OF THE TEXT

September 2025