AUSTRALIAN PRODUCT INFORMATION - DALACIN® C (Clindamycin phosphate) Injection

1. NAME OF THE MEDICINE

Clindamycin phosphate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL of DALACIN C contains clindamycin phosphate equivalent to 150 mg clindamycin base; 9.45 mg benzyl alcohol; 0.5 mg disodium edetate; and Water for Injections q.s. When necessary, pH is adjusted with sodium hydroxide and/or hydrochloric acid.

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

For the full list of excipients, see Section 6.1 - List of excipients.

3. PHARMACEUTICAL FORM

Solution for Injection.

DALACIN C (clindamycin phosphate injection) is a sterile solution of a water soluble ester of clindamycin and phosphoric acid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DALACIN C is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

DALACIN C is also indicated in the treatment of serious infections due to susceptible strains of streptococci, pneumococci and staphylococci.

Its use should be reserved for penicillin-allergic patients or other patients for whom, in the judgement of the physician, a penicillin is inappropriate.

Anaerobes

Serious respiratory tract infections such as empyema, anaerobic pneumonitis and lung abscess; serious skin and skin structure infections; septicaemia; intra-abdominal infections such as peritonitis and intra-abdominal abscess (typically resulting from anaerobic organisms resident in the normal gastrointestinal tract) and infections of the female pelvis and genital tract such as endometritis, non-gonococcal tubo-ovarian abscess, pelvic cellulitis and post-surgical vaginal cuff infection, all when given in conjunction with an antibiotic of appropriate gram-negative aerobic spectrum.

Streptococci

Serious respiratory tract infections; serious skin and skin structure infections; septicaemia.

Staphylococci

Serious respiratory tract infections; serious skin and skin structure infections; septicaemia; acute haematogenous osteomyelitis.

Pneumococci

Serious respiratory tract infections.

Adjunctive Therapy

In the surgical treatment of chronic bone and joint infections due to susceptible organisms.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy. Bacteriological studies should be performed to determine the causative organisms and their susceptibility to clindamycin.

4.2 Dose and method of administration

For Intramuscular and Intravenous Use.

Dosage and route of administration should be determined by the severity of the infection, the condition of the patient and the susceptibility of the causative micro-organism.

DALACIN C IM administration should be used undiluted.

DALACIN C IV administration should be diluted (see Dilution for IV use and IV infusion rates below).

Adults (IM or IV Administration)

The usual daily adult dosage of clindamycin phosphate for infections of the intra-abdominal area, female pelvis and other complicated or serious infections is 1200 - 2700 mg given in 2, 3 or 4 equal doses. Doses of up to 4800 mg daily have been used successfully. Less complicated infections due to more susceptible organisms may respond to lower doses such as 600-1200 mg/day administered in 3 or 4 equal doses.

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

Children over one month of age (IM or IV Administration)

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

Serious infections: 15-25 mg/kg/day in 3 or 4 equal doses

More severe infections: 25-40 mg/kg/day in 3 or 4 equal doses

As an alternative to dosing on a body weight basis, children may be dosed on the basis of square metres of body surface.

Serious infections: 350 mg/m^2/day

More severe infections: 450 mg/m^2/day

In severe infections it is recommended that children be given no less than 300 mg per day regardless of body weight.

Parenteral therapy may be changed to oral clindamycin (DALACIN C Capsules) when the condition warrants and at the discretion of the physician.

In cases of β-haemolytic streptococcal infections, treatment should be continued for at least 10 days.

Dilution for IV Use and IV Infusion Rates

DALACIN C must be diluted prior to IV administration. The concentration of clindamycin in diluent for infusion should not exceed 12 mg per mL AND INFUSED AT A RATE OF NOT MORE THAN 30 MG PER MINUTE AS INDICATED BELOW:

Table 1. Dilution and Infusion Rates in Relation to Total Infusion Dose

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

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

Directions for use

The neck of the ampoule is pre-scored at the point of constriction (no ampoule file is needed to open the ampoules). A coloured dot on the ampoule head helps to orientate the ampoule. Take the ampoule and face the coloured dot. The ampoule opens easily by placing the thumb on the coloured dot and gently pressing downwards.

Compatibility

DALACIN C has been known to be physically and chemically compatible for at least 24 hours in glucose 5% water and sodium chloride injection solutions containing the following antibiotics in usually administered concentrations: amikacin sulfate, aztreonam, cefamandole nafate, cefazolin sodium, cefotaxime sodium, cefoxitin sodium, ceftazidime sodium, ceftizoxime sodium, gentamicin sulfate, netilmicin sulfate, piperacillin and tobramycin. The compatibility and duration of stability of drug mixtures will vary depending on concentration and other conditions.

No incompatibility has been demonstrated with the antibiotics cefalotin, kanamycin, gentamicin, penicillin or carbenicillin.

4.3 Contraindications

This drug is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin, lincomycin or any of the ingredients listed under Section 6.1 – List of excipients.

4.4 Special warnings and precautions for use

SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH ADRENALINE. OXYGEN, COLLOID INFUSION, ANTIHISTAMINES AND INTRAVENOUS CORTICOSTEROIDS SHOULD ALSO BE ADMINISTERED AS INDICATED.

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 generalised 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 (Adverse effects (undesirable effects)).

The use of clindamycin can lead to the development of severe colitis. Fatalities have been reported. Therefore, DALACIN C should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in Section 4.1 –Therapeutic indications. It should not be used in patients with non-bacterial infections such as most upper respiratory tract infections.

A toxin produced by *Clostridioides 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 parenteral clindamycin. 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 suitable oral antibacterial agents effective against *C. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Antibiotic-associated colitis and diarrhoea (due to *C. difficile*), occur more frequently and may be more severe in debilitated and/or elderly patients (> 60 years). When clindamycin is indicated in these patients, they should be carefully monitored for change in bowel frequency.

C. difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, and may range in severity from mild diarrhoea 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 diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

DALACIN C should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

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

DALACIN C should be prescribed with caution in atopic individuals.

During prolonged therapy periodic liver function tests and blood counts 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.

Patients with very severe renal disease and/or very severe hepatic disease accompanied by severe, metabolic aberrations should be dosed with caution, and serum clindamycin levels monitored during high-dose therapy.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy. The use of DALACIN C may result in overgrowth of non-susceptible organisms - particularly yeasts. Should superinfections occur, appropriate measures should be taken as indicated by the clinical situation.

DALACIN C 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 – Dose and method of administration. Drugs which delay peristalsis (e.g. opiates and diphenoxylate with atropine [LOMOTIL®]) may prolong and/or worsen the condition and should not be used.

Rare instances of cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration (see Section 4.2 – Dose and method of administration).

Local irritation, pain, induration and sterile abscess have been reported after intramuscular injection and thrombophlebitis after intravenous infusion (see Section 4.8 – Adverse effects (undesirable effects)). Reactions can be minimised by giving deep intramuscular injections and avoiding prolonged use of indwelling intravenous catheters.

Usage in Meningitis

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

Use in the Elderly

No data available.

Paediatric Use

When DALACIN C is administered to newborns and infants, appropriate monitoring of organ system functions is desirable.

This product contains benzyl alcohol which is associated with severe adverse effects, including fatal "gasping syndrome", in paediatric patients. The minimum amount of benzyl alcohol at which toxicity may occur is unknown. 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.

Effects on Laboratory Tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

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.

Antagonism has been demonstrated between DALACIN C and erythromycin *in vitro*. Because of possible clinical significance these two drugs should not be administered concurrently.

In vitro studies of human liver and intestinal microsomes showed that clindamycin is metabolised 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.

See Section 4.2 – Dose and method of administration, Compatibility and Section 6.2 Incompatibilities for physicochemical interactions.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in Pregnancy – Pregnancy Category A

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

Clindamycin should be used in pregnancy only if clearly needed.

Benzyl alcohol can cross the placenta (see Section 4.4 – Special warnings and precautions for use).

Use in Lactation

Clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8 micrograms/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. Therefore, clindamycin is not recommended for nursing mothers.

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 effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (undesirable effects)

The adverse effects listed in the table below are presented by system organ class. Within each frequency category, the adverse effects are presented in the order of frequency and then by decreasing medical seriousness.

System organ class	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10000 to <1/1000)	Frequency not known (cannot be estimated from available data)
Infections and infestations	Pseudomembranous colitis			Vaginal infection
Blood and lymphatic system disorders	Eosinophilia			Agranulocytosis, neutropenia, thrombocytopenia, leucopenia
Immune system disorders				Anaphylactoid reaction
Nervous system disorders		Dysgeusia		
Cardiac disorders		Cardio-respiratory arrest§†		
Vascular disorders	Thrombophlebitis†	Hypotension §†		
Gastrointestinal disorders	Diarrhoea, abdominal pain	Vomiting, nausea		
Hepatobiliary disorders				Jaundice
Skin and subcutaneous tissue disorders	Rash maculo-papular	Urticaria	Erythema multiforme, pruritus	Toxic epidermal necrolysis (TEN), Steven Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), dermatitis exfoliative, dermatitis bullous, rash morbilliform

System organ class	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10000 to <1/1000)	Frequency not known (cannot be estimated from available data)
Musculoskeletal and connective tissue disorders				Polyarthritis
General disorders and administration site conditions		Pain†, injection site abscess†		Injection site irritation†
Investigations	Liver function test abnormal			
CIOMS III categories: Very Common ≥1/10 (≥10%); Common ≥1/100 to <1/10 (≥1% and <10%); Uncommon ≥1/1000 to <1/100 (≥0.1% and <1%); Rare ≥1/10,000 to <1/1000 (≥0.01% and <0.1%); Very Rare <1/10,000 (<0.01%)				

† Adverse reactions apply only to injectable formulations.
§ Rare instances have been reported following too rapid intravenous administration (see Section 4.2 – Dose and method of administration).

Post-Marketing Experience

The following additional adverse reactions have been reported during post-marketing experience.

Infections and infestations

Frequency not known: *C. difficile* colitis.

Immune system disorders

Frequency not known: Anaphylactic shock, anaphylactic reaction, hypersensitivity.

Skin and subcutaneous tissue disorders

Frequency not known: Angioedema.

Renal and urinary disorders

Frequency not known: Acute kidney injury.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

Signs and symptoms

The minimal toxic or lethal dose is not well established. At therapeutic doses, the primary toxic effects may involve the gastrointestinal tract and may include severe diarrhoea and pseudomembranous colitis that may result in death. Rapid administration of large doses has resulted in ventricular dysrhythmias, hypotension and cardiac arrest. Dermatitis, nephrotoxicity, hepatotoxicity, and various haematological abnormalities are toxic effects that occur less frequently.

Recommended treatment

No specific antidote is known. Support respiratory and cardiac function. In cases of overdose, drug levels of clindamycin are not clinically useful. However, monitoring serum concentrations in patients with markedly reduced renal and hepatic function, may be indicated during high-dose therapy. Monitor full blood count in patients with significant exposure as clindamycin may produce abnormalities of the haematopoietic system. Because clindamycin may cause hepatotoxicity, monitor liver function tests in patients with significant exposure.

Neither haemodialysis nor peritoneal dialysis appear to be effective in reducing clindamycin levels significantly.

Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen and intravenous corticosteroids should also be administered as indicated.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

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

Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

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-haemolytic streptococci groups A, B, C, and G
- Viridans group streptococci
- *Corynebacterium* spp.

Gram-negative bacteria

- *Chlamydia trachomatis*

Anaerobic bacteria

Gram-negative bacteria:

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

Gram-positive bacteria:

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

Fungi

- *Pneumocystis jirovecii*

Protozoans

- *Toxoplasma gondii*
- *Plasmodium falciparum*

Breakpoints

Dilution or diffusion techniques – either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility testing procedures require the use of laboratory control microorganisms to control the technical aspects of laboratory procedures.

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 2. 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 high dosage of drug can be used. This category also provides a buffer zone, which 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.

Standardised 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 3. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 3 should be achieved.

Table 3. 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
Streptococcuspneumoniae 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.
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[a]MIC ranges for anaerobes are based on agar dilution methodology.

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

Table 4. 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 5. 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

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5.2 Pharmacokinetic properties

Biologically inactive clindamycin phosphate is rapidly converted to active clindamycin.

By the end of short-term intravenous infusion, peak serum levels of active clindamycin are reached.

In vitro studies in human liver and intestinal microsomes indicated that clindamycin is predominantly oxidised by CYP3A4, with minor contribution from CYP3A5, to form clindamycin sulfoxide and a minor metabolite, N-desmethylclindamycin.

Biologically-inactive clindamycin phosphate disappears rapidly from the serum, the average disappearance half-life is 6 minutes; however, the serum disappearance half-life of active clindamycin is about 3 hours in adults and 2.5 hours in children.

After intramuscular injection of DALACIN C, peak levels of active clindamycin are reached within 3 hours in adults and 1 hour in children. Serum level curves may be constructed from IV peak serum levels as given in Table 6 by application of the disappearance half-lives listed above.

Serum levels of clindamycin can be maintained above the *in vitro* minimum inhibitory concentrations for most indicated organisms by administration of DALACIN C every 8-12 hours in adults and every 6-8 hours in children, or by continuous intravenous infusion. An equilibrium state is reached by the third dose.

The disappearance half-life of clindamycin is increased slightly in patients with markedly reduced renal or hepatic function; dosage schedules need not be modified in the presence of mild to moderate renal or hepatic disease. No significant levels of clindamycin are attained in the cerebrospinal fluid even in the presence of inflamed meninges.

Table 6: Average Peak Serum Concentrations After Dosing with DALACIN C

Dosage Regimen	Clindamycin (micrograms/mL)	Clindamycin Phosphate (micrograms/mL)
Healthy Adult Males (Post Equilibrium)		
300 mg IV in 10 min q 8 h	7	15
600 mg IV in 20 min q 8 h	10	23
900 mg IV in 30 min q 12 h	11	29
1200 mg IV in 45 min q 12 h	14	49
300 mg IM q 8 h	6	3

Table 6: Average Peak Serum Concentrations After Dosing with DALACIN C

Dosage Regimen	Clindamycin (micrograms/mL)	Clindamycin Phosphate (micrograms/mL)
600 mg IM q 12 h*	9	3
Children (first dose)*		
5-7 mg/kg in 1 h	10	
3-5 mg/kg IM	4	
5-7 mg/kg IM	8	

* Data in this group from patients being treated for infection

Serum assays for active clindamycin require an inhibitor to prevent *in vitro* hydrolysis of clindamycin phosphate.

Obese paediatric patients aged 2 to less than 18 years and obese adults aged 18 to 20 years

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

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Disodium edetate
Hydrochloric acid
Sodium hydroxide
Water for Injections.

6.2 Incompatibilities

The following drugs are physically incompatible with DALACIN C: ampicillin, phenytoin sodium, barbiturates, aminophylline, calcium gluconate, magnesium sulfate, ceftriaxone sodium and ciprofloxacin.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

The following sizes are available:

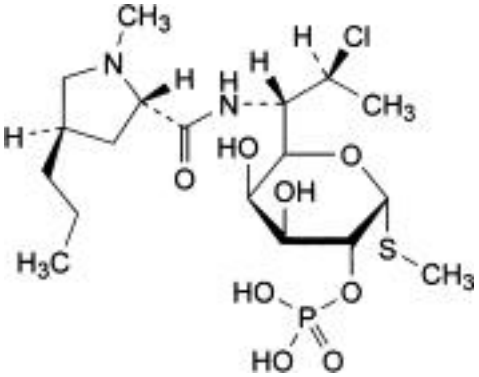
2 mL ampoule (300 mg) – 10's
4 mL ampoule (600 mg) – 10's

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

Chemical structure



The MW of clindamycin phosphate is 504.96.

CAS number

CAS Number: 24729-96-2

7. MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 (Prescription Only Medicine).

8. SPONSOR

Pfizer Australia Pty Ltd
Level 17, 151 Clarence Street
Sydney NSW 2000
Toll Free Number: 1800 675 229
www.pfizer.com.au

9. DATE OF FIRST APPROVAL

2 August 1991

10. DATE OF REVISION

19 August 2022

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Summary Table of Changes

Section changed	Summary of new information
4.2, 5.2	To add new information regarding PK and PD data for clindamycin in obese children.
6.5	Removed information on oral dosage form.