

DALACIN C

Clindamycine phosphate

300 mg/2 ml solution for injection
600 mg/4 ml solution for injection

Reference market: Belgium

AfME markets using the same LPD: Saudi Arabia

SUMMARY OF PRODUCT CHARACTERISTICS

WARNING

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including CLEOCIN PHOSPHATE 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*.

Because CLEOCIN PHOSPHATE therapy has been associated with severe colitis which may end fatally, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in the **INDICATIONS AND USAGE** section. It should not be used in patients with nonbacterial infections such as most upper respiratory tract infections. *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.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

1. NAME OF THE MEDICINAL PRODUCT

Dalacin C 300 mg/2 ml solution for injection
Dalacin C 600 mg/4 ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dalacin C 300 mg/2 ml - 600 mg/4 ml 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.

Excipients with known effect:
Dalacin C solution for injection
The solution for injection contains benzyl alcohol (9.45 mg/ml) (see section 4.4).

For the 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 is indicated in the treatment of serious infections, when caused by clindamycin susceptible strains of gram-positive aerobes such as streptococci, pneumococci and staphylococci, or by susceptible anaerobic bacteria (see section 5.1) :

1. Upper respiratory tract infections: chronic sinusitis caused by anaerobic strains. Clindamycin can be used for selected cases of chronic suppurative otitis media or as adjunctive therapy along with an antibiotic active against aerobic gram-negative organisms. Infections caused by *H. influenzae* are not an indication (see section 5.1). Clindamycin can also be used in cases of recurrent pharyngotonsillitis.
2. Lower respiratory tract infections including infectious exacerbation of chronic bronchitis and pneumonia.
3. Serious skin and soft tissue infections caused by susceptible organisms.
4. Bone and joint infections including osteomyelitis and septic arthritis.
5. Serious gynaecological infections of the pelvis including pelvic inflammatory disease (PID). Clindamycin can also be used in a single therapy in cases of cervicitis due to *Chlamydia trachomatis*.
6. Intra-abdominal infections including peritonitis and abdominal abscess.
7. Septicaemia and endocarditis.
   Selected cases of septicaemia and/or endocarditis due to susceptible organisms have responded well to clindamycin. However, bactericidal drugs are often preferred for these infections.
8. Dental infections including periodontal abscess and periodontitis.
9. Toxoplasmic encephalitis in patient with AIDS. In patients who cannot tolerate the usual treatment, clindamycin may be used in combination with pyrimethamine.
10. *Pneumocystis jirovecii* pneumonia in patients with AIDS. In patients who cannot tolerate the usual treatment, clindamycin may be used in combination with primaquine.

Like other antibiotics information regarding the prevention of local resistance as well as the official recommendations regarding prescription of antibiotics must be reviewed before prescribing clindamycin.

4.2 Posology and method of administration

Posology

The posology and the mode of administration should be determined by the seriousness of the infection, the patient's condition and the sensitivity of the disease causing germ.

Clindamycin phosphate IM administration should be used undiluted.

Clindamycin phosphate IV administration should be diluted (see dilution for IV use and IV infusion rate below).

Adults:

Clindamycin phosphate solution for injection (IM or IV administration):
Parenteral (IM or IV administration). Dalacin C Phosphate must be diluted prior to IV administration and should be infused over at least 10-60 minutes.
Serious infections: 600 mg - 1.2 g/day in two, three or four equal doses.
More severe infections: 1.2 - 2.7 g/day in two, three or four equal doses.

Adults were successfully treated with doses up to 4800 mg daily.
Intramuscular administration of more than 600 mg in one administration is not recommended.

Treatment of Pelvic Inflammatory Disease (PID): clindamycin phosphate I.V. 900 mg every 8 hours, associated to a suitable Gram negative spectre antibiotic (e.g. gentamicin 2 mg/kg, followed by 1.5 mg/kg every 8 hours) in patients with a normal renal function. This treatment should be administered for at least 4 days. From the moment clinical improvement occurs, the treatment should be continued for another 2 days. Then 1800 mg of clindamycin hydrochloride per day should be administered orally, divided over several administrations, up to a total treatment duration of 10 to 14 days.

Paediatric population (in children older than 1 month):
Clindamycin should be dosed based on total body weight regardless of obesity (see section 5.2).

Clindamycin phosphate (IM or IV administration):
Serious infections: 15-25 mg/kg/day in three or four equal doses.

More severe infections: 25-40 mg/kg/day in three or four equal doses. In severe infections it is recommended that children be given no less than 300 mg/day regardless of body weight.

Elderly patients:

The half-life, volume of distribution and clearance, and extent of absorption after administration of clindamycin phosphate are not altered by increased age. Analysis of data from clinical studies has not revealed any age-related increase in toxicity. Dosage requirements in elderly patients should not be influenced, therefore, by age alone. See *Precautions* for other factors which should be taken into consideration

Treatment for infections caused by beta-haemolytic streptococci should be continued for at least 10 days to guard against subsequent rheumatic fever or glomerulonephritis.

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

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

Posology in cases of renal and/or liver function impairment:

Dose adjustment is not necessary in patients with an impaired renal function. Haemodialysis and peritoneal dialysis are not effective to remove clindamycin from the blood.

In patients with moderately to seriously reduced liver function, a prolonged half-life of clindamycin was seen. Accumulation is rare if clindamycin is administered every 8 hours. A dose reduction is, therefore, not considered necessary.

Dosage in specific indications:

Toxoplasmic encephalitis in patients with AIDS:
Dalacin C solution for injection or Dalacin C hard capsules in a dose of 600-1200 mg every 6 hours for 2 weeks, followed by oral administration of 300-600 mg every 6 hours. The total treatment usually lasts 8 to 10 weeks. Oral administration of 25 mg to 75 mg of pyrimethamine per day for 8 to 10 weeks is necessary. With higher doses of pyrimethamine one should administer 10 to 20 mg of folic acid per day.

Pneumocystis jirovecii pneumonia in patients with AIDS:
Dalacin C solution for injection in intravenous infusion in a dose of 600 to 900 mg every 6 hours or Dalacin C solution for injection in intravenous infusion in a dose of 900 mg every 8 hours or Dalacin C hard capsules in a dose of 300 to 450 mg every 6 hours for 21 days, combined with 15 to 30 mg of oral primaquine per day for 21 days.

4.3 Contraindications

– Hypersensitivity to the active substance, to lincomycin, to any component of the formulation, or to any of the excipients listed in section 6.1.

– Clindamycin phosphate solution for injection must not be given to premature babies or neonates because of the benzyl alcohol content.

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 sections 4.3 and 4.8).

  The clindamycin phosphate injectable formulation contains benzyl alcohol (9.45 mg/mL). Benzyl alcohol may cause anaphylactoid reactions. Intravenous administration of the preservative benzyl alcohol has been associated with serious adverse events, and death in paediatric patients including neonates characterized by central nervous system depression, metabolic acidosis, gasping respirations, cardio-vascular failure and haematological anomalies ("gasping syndrome"). 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. Use only if it is necessary and if there are no alternatives possible. If given in high volumes, should be used with caution and preferably for short term treatment in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).
- Premature and low-birth weight infants may be more likely to develop toxicity. Benzyl alcohol containing products should not be used in pre-term or full-term neonates unless strictly necessary.

- Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *Clostridioides difficile*. This has been reported with use of nearly all antibacterial agents, including clindamycin, and may range in severity from mild diarrhoea to fatal colitis. *C. difficile* produces toxins A and B which contribute to the development of *Clostridioides difficile* associated diarrhoea (CDAD) and is a primary cause of "antibiotic-associated colitis". Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. This form of colitis is characterized by mild, watery diarrhoea that may develop to serious, chronic diarrhoea, leukocytosis, fever, serious abdominal cramps that may be accompanied by loss of blood and mucus. Without further treatment peritonitis, shock and toxic megacolon may develop. Antibiotic induced colitis can occur with clindamycin up to 2 to 3 weeks after discontinuation of the treatment. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

- It is important to consider the diagnosis of CDAD in patients who present with diarrhoea during or after the administration of antibacterial agents. This may progress to colitis, including pseudomembranous colitis (see section 4.8), which may range from mild to fatal colitis. If antibiotic-associated diarrhoea or antibiotic-associated colitis is suspected or confirmed, ongoing treatment with antibacterial agents, including clindamycin, should be discontinued and adequate therapeutic measures should be initiated immediately. 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. Drugs inhibiting peristalsis are contraindicated in this situation. The diagnosis of an antibiotic induced colitis is usually made based on clinical symptoms. The diagnosis can be confirmed by endoscopic demonstration of pseudomembranous colitis or by demonstrating the presence of *Clostridioides difficile* and toxins in the faeces.

- Medicinal products which slow intestinal motility must be avoided.

- Clindamycin should be prescribed with caution to individuals with a history of gastro-intestinal conditions, particularly colitis. Antibiotic induced colitis and diarrhoea occur more frequently and in more serious forms in debilitated and/or older patients.

- Since clindamycin does not diffuse adequately in the cerebrospinal fluid, this drug should not be used to treat meningitis (see section 4.3).

- If therapy is prolonged, liver and kidney functions tests should be performed.

- Acute kidney injury, including acute renal failure, has been reported infrequently. In patients receiving prolonged therapy, suffering from pre-existing renal dysfunction or taking concomitant nephrotoxic drugs, monitoring of renal function should be considered (see section 4.8).

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

- **Intravenous administration: Clindamycin phosphate should not be injected intravenously undiluted as a bolus, but should be infused over at least 10 - 60 minutes (see section 4.2).**

- Clindamycin appears to have neuromuscular blocking properties that can enhance the effects of other neuromuscular blocking drugs. In patients that are treated with these drugs, clindamycin should, therefore, be used with caution (see section 4.5).

- In patients with hypersensitivity, clindamycin phosphate should be administered with caution.

- In patients with serious renal and/or serious liver disorders associated to serious metabolic conditions, clindamycin should be administered cautiously. The serum levels of clindamycin should be monitored if high doses are required (see section 4.2).

- The solution for injection contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Antagonism (inducible resistance) can be demonstrated *in vitro* between clindamycin and erythromycin against a subset of macrolide resistant bacterial strains. Due to a possible clinical significance both agents should not be used concomitantly unless adequate susceptibility testing has been performed.

Clindamycin administered by injection has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, clindamycin must be used cautiously in patient taking medication such as vecuronium, rocuronium, gentamicin, rapacuronium (with magnesium) or pancuronium. Synergistic effects of other antibiotics together with clindamycin on neuromuscular blocking agents have been described. Careful attention is therefore needed when using antibiotics together with muscle relaxants, because the synergy effect triggered by the combination could cause deeper muscle relaxation and delay recovery.

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 (such as ritonavir, lopinavir, indinavir, cobicistat, ketoconazole, itraconazole, voriconazole, posaconazole, clarithromycin, telithromycin, grapefruit juice, nefazodone) 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.

Vitamin K antagonists
Increased coagulation tests (PT/INR) and/or bleeding, have been reported in patients treated with clindamycin in combination with a vitamin K antagonist (e.g. warfarin, acenocoumarol and fluindione). Coagulation tests, therefore, should be frequently monitored in patients treated with vitamin K antagonists.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data on the use of clindamycin in pregnant women during the first trimester of pregnancy. Clindamycin crosses the placenta. In clinical trials, the use of Dalacin C in pregnant women and the systemic administration of clindamycin during the second and third trimesters, have not been associated with an increased incidence of congenital abnormalities. Animal studies did not reveal any direct or indirect deleterious effects on reproduction (see section 5.3).

The following statement only applies to the *solution for injection*: Benzyl alcohol can cross the placenta (see section 4.4).

As a precautionary measure, it is preferable to avoid the use of Dalacin C during the first trimester of pregnancy. The use of Dalacin C during the second and third trimester of pregnancy may be considered after establishing the proper diagnosis by the doctor.

Breastfeeding

Orally and parenterally administered clindamycin has been reported to appear in human breast milk in ranges from < 0.5 to 3.8 µg/mL (50 to 100% of the serum level is attained in the breast milk (see section 5.2)).

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. The developmental and health benefits of breastfeeding for the child 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. If possible Dalacin C should not be used during breastfeeding. If a breast-feeding mother needs oral or intravenous clindamycin, it may be considered to temporarily interrupt breastfeeding for the duration of the mother's treatment.
If oral clindamycin is used during breastfeeding, the infant should be closely monitored for adverse drug reactions. If these occur, breastfeeding should be discontinued.

Fertility

Fertility studies in rats treated orally with clindamycin revealed no effects on fertility or mating ability (see section 5.3). No data are available on man fertility.

4.7 Effects on ability to drive and use machines

Clindamycin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. Adverse reactions identified from post-marketing experience are included in italics. The frequency grouping is defined using the following convention: Very common (≥ 1/10), Common (≥ 1/100, < 1/10), Uncommon (≥ 1/1000, < 1/100), Rare (≥ 1/10000, < 1/1000), Very rare (< 1/10000) and Not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Adverse Reactions Table

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Rare ≥ 1/10000 to < 1/1000	Very Rare < 1/10000	Frequency not known (cannot be estimated from available data)
Infections and infestations	*Pseudomembranous colitis* (see section 4.4), *Clostridioides difficile colitis*				*Vaginal infection*
Blood and lymphatic system disorders	Eosinophilia[2]				*Agranulocytosis, Neutropenia, Thrombocytopenia, Leukopenia*
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[5], Abdominal pain[2]	Vomiting[2], Nausea		Colitis	*Oesophageal ulcer*, Oesophagitis**
Hepatobiliary disorders	Liver function test abnormal				*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 symptom (DRESS), Acute Generalised Exanthematous Pustulosis (AGEP), Angioedema, Dermatitis exfoliative, Dermatitis bullous, Rash morbilliform*
Renal and urinary disorders					*Acute kidney injury*[#]
General disorders and administration site conditions[†]		Pain[†‡], Injection site abscess[†‡]			*Injection site irritation*[†‡]

System Organ Class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Rare ≥ 1/10000 to < 1/1000	Very Rare < 1/10000	Frequency not known (cannot be estimated from available data)
Musculoskeletal					Cases of polyarthritis have been reported.

[2] Frequency for solution for injection: not known
[5] Frequency for solution for injection: uncommon
† Only applicable for solution for injection
* Only applicable for oral formulations
§ Rare instances have been reported following too rapid intravenous administration (see section 4.2).
‡ These reactions can be reduced to a minimum by deep administration of IM injections and by avoiding prolonged catheterisation in the same vein.
[#] See section 4.4.

- If diarrhoea occurs during treatment, the therapy should be discontinued.
- In cases of serious anaphylactoid reactions, immediate measures should be taken with the administration of epinephrine (adrenaline), oxygen and intravenous steroids. Mechanical ventilation, possibly with intubation, should also be applied if necessary.
- The use of clindamycin phosphate can cause overgrowth of insensitive germs, particularly yeasts.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after marketing authorisation 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 according to their local country requirements.

To Report side effects:

- **Saudi Arabia:**

National Pharmacovigilance Center (NPC)
Call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

- **Other GCC States**

- *Please contact the relevant competent authority.*

4.9 Overdose

The toxicity of clindamycin is not linked to the dose. An overdose does not cause specific symptoms. Haemodialysis and peritoneal dialysis are not effective to remove clindamycin from the serum.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterials for systemic administration - lincosamides
ATC code: J01F F 01

The active substance is clindamycin, a semi-synthetic antibiotic obtained by 7-(S)-chloro-substitution of the 7-(R)-hydroxyl group of lincomycin.

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 and clindamycin palmitate HCl are inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin. At usual doses, clindamycin exhibits bacteriostatic activity *in vitro*.

PK-PD relationship

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.Clindamycin may still be used for short-term therapy of less serious skin and soft tissue infections as constitutive resistance is unlikely to develop during such therapy.

Antibacterial activity in combination with other antibacterial agents

An antagonism was demonstrated between clindamycin, erythromycin and chemically related macrolides. Clindamycin does not demonstrate any antagonism with penicillins.

Clinical efficacy against specific pathogens

Commonly susceptible organisms
Aerobic gram-positive microorganisms
Actinomyces israelii
Staphylococcus aureus (methicillin-susceptible)
Streptococcus agalactiae
Viridans group *streptococci*
Anaerobic microorganisms
Bacteroides spp. (excluding *B. fragilis*)
Fusobacterium spp.
Peptococcus spp.
Prevotella spp.
Veillonella spp.
Other microorganisms
Chlamydia trachomatis
Clamydophila pneumoniae
Gardnerella vaginalis
Mycoplasma hominis
Fungi
Pneumocystis jirovecii
Protozoans
Plasmodium falciparum

Toxoplasma gondii
Organisms for which acquired resistance may be a problem
Aerobic gram-positive microorganisms
Staphylococcus aureus (methicillin-resistant)
Staphylococcus epidermidis
Staphylococcus haemolyticus
Staphylococcus hominis
Streptococcus pneumoniae
Anaerobic microorganisms
Bacteroides fragilis
Clostridium perfringens
Peptostreptococcus spp.
Propionibacterium spp.
Inherently resistant organisms
Aerobic gram-positive microorganisms
Enterococcus spp.
Listeria monocytogenes
Nocardia spp.
Aerobic gram-negative microorganisms
Enterobacterales
Pseudomonas aeruginosa
Haemophilus influenzae
Moraxella catarrhalis
Neisseria spp.
Anaerobic microorganisms
Clostridioides difficile
Other microorganisms
Mycoplasma pneumoniae
Ureaplasma urealyticum

Susceptibility testing breakpoints
MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for Clindamycin and are listed here: https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

Prevalence of acquired resistance
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.

5.2 Pharmacokinetic properties

Absorption
1 to 3 hours following intramuscular injection of 600 mg of clindamycin phosphate, serum peak levels of clindamycin of 9 µg/ml were observed. Following intravenous infusion of 300 mg in 10 min. and 600 mg in 20 min. respectively serum peak levels of 7 µg/ml and 10 µg/ml respectively are reached at the end of the infusion.

Table 1 gives the mean serum levels after the administration of clindamycin phosphate. Clindamycin serum levels can be maintained above the *in vitro* MIC's for most sensitive organisms by administering clindamycin phosphate every 8 to 12 hours in adults or every 6 to 8 hours in children by continuous I.V. infusion. Steady state levels are reached after the third dose.

Table 1

Dose	Clindamycin µg/ml	Clindamycin phosphate µg/ml
Adults (after the steady state)		
300 mg I.V. in 10 min. every 8 u.	7	15
600 mg I.V. in 20 min. every 8 u.	10	23
600 mg I.V. in 30 min. every 6 u.	10.9	
600 mg I.V. in 30 min. every 8 u.	10.8	
900 mg I.V. in 30 min. every 8 u.	14.1	
900 mg I.V. in 30 min. every 12 u.	11	29
1200 mg I.V. in 45 min. every 12 u.	14	49
300 mg I.M. every 8 u.	6	3
600 mg I.M. every 12 u.	9	3

Dose	Clindamycin µg/ml
Children (first dose) (1)	
5-7 mg/kg I.V. in 1 hour	10
3-6 mg/kg I.M.	4
5-7 mg/kg I.M.	8

(1) Patients in this group were treated for existing infections.

Distribution

The protein binding is between 40 and 90 % of the administered dose. No accumulation could be demonstrated with oral administration.

Clindamycin easily penetrates in most body fluids and tissues. In bone tissue a level of approx. 40 % (20-75 %) of the serum level is reached, in the mother's milk 50-100 %, in synovial fluid 50 %, in the sputum 30-75 %, in the peritoneal fluid 50 %, in foetal blood 40 %, in pus 30 %, in pleural fluid 50-90 %. Clindamycin does not penetrate however in the cerebrospinal fluid, not even in the event of meningitis.

Biotransformation

Clindamycin has a half-life of approx. 1 1/2 - 3 1/2 hours. This is somewhat longer in patients with a significantly reduced function of the liver or of the kidneys. The dose regimen should however not be adjusted in cases of moderately seriously reduced function of the kidneys or of the liver.

Clindamycin is relatively extensively metabolised.

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**.**

Elimination

The excretion in the urine is 10-20 % and in the faeces some 4 % in microbiologically active form. The remainder is excreted as biologically inactive metabolites.
The excretion is mainly via the bile and the faeces.

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 normalized by total body weight are comparable regardless of obesity.

5.3 Preclinical safety data

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 foetal development studies in rats and subcutaneous embryo foetal 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 Solution for injection:
Benzyl alcohol, disodium edetate, Sodium Hydroxide, water for injection.

6.2 Incompatibilities

The following drugs are physically incompatible with the solution for injection of clindamycin phosphate: ampicillin, sodium phenytoin, barbiturates, aminophyllin, calcium gluconates, magnesium sulphate, sodium ceftriaxon and ciprofloxacin.

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

Do not use Dalacin C after the expiry date which is stated on the carton after EXP:. The expiry date refers to the last day of that month.

Shelf life: 24 months.

6.4 Special precautions for storage

Store between (2°C – 8°C). Do not freeze.

6.5 Nature and contents of container

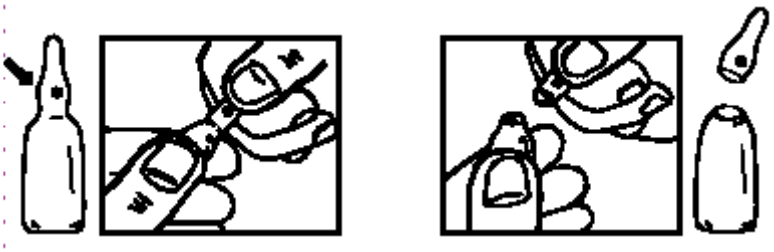
DALACIN C 300 mg/2 ml:
– Pack containing 1 ampoule of 2 ml.
DALACIN C 600 mg/4 ml:
– Pack containing 1 ampoule of 4 ml.

6.6 Special precautions for disposal and other handling

Keep out of the sight and reach of children.

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.

INDICATIONS FOR OPENING THE AMPOULE – SOLUTION FOR INJECTION
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. MARKETING AUTHORISATION HOLDER

Marketing Authorisation Holder
Pfizer SA, Belgium

Manufactured Packed and Released By:
Pfizer Manufacturing Belgium NV, Belgium

8. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01-May-1987

9. DATE OF REVISION OF THE TEXT

September 2024