SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF THE MEDICINAL DRUG
DALACIN C®
Clindamycin

QUALITATIVE AND QUANTITATIVE COMPOSITION
DALACIN C® 150 mg - 300 mg Capsules
Clindamycin. (clindamycin. hydrochlorid.) 150 mg - 300 mg - Amyl. mayd. - Lactos. - Talc. - Magnes. stear. - q.s. pro capsul. gelatin. una - cum Erythrosin. - Natr. indigotinedisulfon. - Gelatin. De capsules à 150 mg en à 300 mg bevatten additioneel nog Titan. dioxyd.

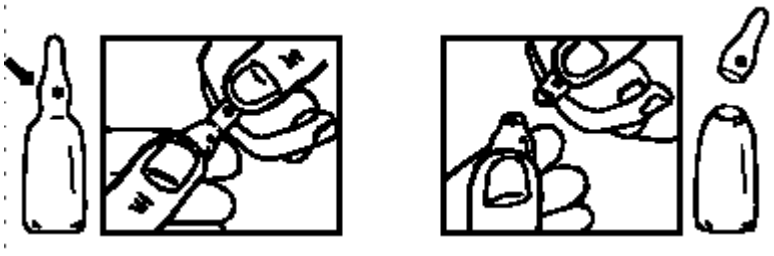
DALACIN C® 300 mg - 600 mg - Solution for injection
Clindamycin. (clindamycin. phosph.) 300 mg - 600 mg Alcohol benzylic. - Dinatr. edetas - Aqua ad iniectabil. q.s. ad 2 ml - 4 ml - 6 ml.

PHARMACEUTICAL FORMS, MODE OF ADMINISTRATION AND PACKAGING
ORAL ADMINISTRATION
Capsules:
- Packaging containing 16 capsules with 150 mg.
- Packaging containing blisters of 10 capsules with 300 mg.

INTRAVENOUS OR INTRAMUSCULAR ADMINISTRATION
Solution for injection
DALACIN C® 300 mg:
- Packaging containing 1ampoule of 2 ml.

DALACIN C® 600 mg:
- Packaging containing 1 ampoules of 4 ml.

INDICATIONS FOR OPENING THE AMPOULE
Exert pressure on the ampoule with the point towards you, as indicated on the graph.



CLINICAL PARTICULARS
Therapeutic indications
Clindamycin is indicated in the treatment of serious infections due to clindamycin sensitive micro-organisms (including *Staphylococcus aureus*) in patients who are allergic for penicillins. In cases of aerobic infections clindamycin is an alternative if other antimicrobial drugs are inactive

or contraindicated. In cases of anaerobic infections clindamycin can be considered as a first choice drug.
Upper airway infections: chronic sinusitis due to anaerobic germs. Clindamycin can be used in certain cases of chronic suppurative otitis media or as a supportive therapy in combination with an antibiotic active against Gram negative aerobic organisms. Infections due to *H. influenzae* are not an indication (see under Properties).
Clindamycin can also be used in cases of recurrent pharyngotonsillitis when other antimicrobial drugs are inactive or are contraindicated (penicillins, erythromycin and chemical related macrolides, cephalosporins).
Lower airway infections such as:

- aspiration pneumonia, lung abscess, necrotising pneumonia and empyema
- bacterial lung infection. DALACIN C® can also be used as an adjuvant in the treatment of Gram negative lung infection in order to suppress Gram positive cocci and anaerobic organisms.

1. Serious infections of the skin and of the soft tissues.
2. Bone- and joint infections such as osteomyelitis and septic arthritis.
3. Serious gynaecological infections of the pelvis (PID) including endometritis, subcutaneous infections, perivaginal infections, tubo-ovarial abscesses and salpingitis with simultaneous administration of an antibiotic with adequate activity against Gram negative aerobic organisms. Single therapy with clindamycin in cases of cervicitis due to *Chlamydia trachomatis*.
4. In intra-abdominal infections, including peritonitis and abdominal abscess, the choice treatment is clindamycin associated with an antibiotic with adequate activity against Gram negative aerobic organisms.
   In simultaneous administration associated with a suitable Gram negative antibiotic such as an aminoside, clindamycin appears to be effective in preventing peritonitis or intra-abdominal abscesses after intestinal perforation and bacterial contamination following trauma.
5. Septicaemia and endocarditis. The effectiveness of clindamycin in the treatment of selected cases of endocarditis is documented (after the bactericidal effect of clindamycin against the causal germ was demonstrated in *in vitro* tests with adequate, obtainable serum levels).
6. Dental infections such as peridental abscess and parodontitis.
7. Limited clinical research suggests that clindamycin can be used for the treatment of encephalitis due to *Toxoplasma* in patients with AIDS. In patients who do not tolerate the usual treatment, clindamycin associated to pyrimethamine was found to be effective.
8. Limited clinical research suggests that clindamycin can be used for the treatment of *Pneumocystis carinii* pneumonia in patients with AIDS. In patients who do not tolerate the usual treatment (with sulfadiazine) or who do not adequately respond to this treatment, clindamycin can be used in association with primaquine.
9. Clinical studies show that clindamycin can be an alternative therapy alone or associated to quinine or amodiaquine for the treatment of malaria due to drug resistant *P. falciparum.*

As for all antibiotics, *in vitro* sensitivity tests should be carried out in cases of serious infections.

Dosage and mode of administration

The dose 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. It is recommended to swallow the capsules with a glass of water in order to avoid irritation of the esophagus.

ADULTS (I.M. OR I.V. ADMINISTRATION) (CLINDAMYCIN PHOSPHATE)

The usual daily dose of clindamycin phosphate is 2400-2700 mg in 2, 3 or 4 equal doses for intra-abdominal infections, pelvic infections in women and other serious infections, usually combined with a suitable Gram negative aerobic antibiotic.
Less complicated infections due to more sensitive germs may respond to lower doses of 1200-1800 mg/day, divided in 3 or 4 equal doses.
Adults were successfully treated with doses up to 4800 mg.
Intramuscular administration of more than 600 mg in one administration is not recommended.
Treatment of PID: clindamycin phosphate I.V. 900 mg every 8 hours, associated to a suitable Gram negative 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, divided over several administrations, up to a total treatment duration of 10 to 14 days.

ADULTS (ORAL ADMINISTRATION) (CLINDAMYCIN HYDROCHLORIDE CAPSULES)
The current posology is 600-1800 mg divided in 3 or 4 administrations.
In the exceptional case of a treatment for recurrent infection with β haemolytic streptococcal infection: 300 mg, twice daily for at least 10 days (see limitations in the section Indications).
Cervicitis due to Chlamydia trachomatis: 1800 mg per day, divided over several administrations for 10-14 days.

CHILDREN (OLDER THAN 1 MONTH) (I.V. OR I.M. ADMINISTRATION) (CLINDAMYCIN PHOSPHATE)
20-40 mg/kg/day in 3 or 4 equal administrations.

CHILDREN (OLDER THAN 1 MONTH) (ORAL ADMINISTRATION) CLINDAMYCIN HYDROCHLORIDE CAPSULES)
8-25 mg/kg/day in 3 or 4 equal administrations.

NEONATES (YOUNGER THAN 1 MONTH) (I.V. OR I.M. ADMINISTRATION) (CLINDAMYCIN PHOSPHATE)
15-20 mg/kg/day in 3 or 4 equal doses.
The lowest dose can be indicated for small premature babies.

DOSE IN CASES OF IMPAIRED RENAL AND/OR LIVER FUNCTION
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.

ENCEPHALITIS DUE TO *TOXOPLASMA* IN PATIENTS WITH AIDS
DALACIN C® solution for injection or DALACIN C® 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 CARINII 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® 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.

MALARIA
20 mg/kg/day oral or parenteral treatment for at least 5 days.

DILUTION AND INFUSION RATES
The concentration of clindamycin in the dilution medium should not be more than 18 mg per ml and the infusion rate should not be more than 30 mg per minute (See Side-effects). The normal infusion rates are as follows:

Dose	Dilution agent	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.

Intravenous infusions of more than 1200 mg per hour are not recommended.

Contraindications
Clindamycin is contraindicated in patients who previously were hypersensitive to clindamycin or lincomycin or one of the other constituents of the product and in cases of infectious meningitis.

Special warnings and special precautions for use
The injectable form of this product contains benzyl alcohol (9 mg/ml). It was reported that benzyl alcohol can be associated to the fatal "gasping syndrome" (respiratory disorder characterized by chronic gasping for breath) in premature babies.
The treatment with clindamycin was associated to serious colitis with a possible fatal issue. Toxins, produced by *Clostridium difficile* are the main cause of antibiotic induced colitis. 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 slime. 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.
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 *Clostridium difficile* and toxins in the faeces.
The treatment of antibiotic induced colitis can involve one or more of the following steps:
1) mild antibiotic induced colitis:
   - discontinuation of the treatment with clindamycin
   - administration of colestipol (3 x 5 mg per day recommended) or colestyramine resins (3 x 4 mg per day recommended)

2) serious antibiotic induced colitis:
   - administration of electrolyte solution and protein supplements
   - administration of metronidazole (500 mg, oral, every 8 hours for 10 days)
   - administration of vancomycin (125 to 500 mg, oral, every 6 hours for 7 to 10 days)
   - administration of vancomycin in the event of recurrences
   - simultaneous administration of vancomycin and colestyramine is associated to the risk of binding. It is, therefore, recommended to leave a time interval between the administrations
   - administration of 25 000 units of oral bacitracin, four times daily for 7 to 10 days as an alternative treatment

3) Drugs that inhibit the intestinal motility should be avoided.

Clindamycin should be prescribed with caution to individuals whit 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 penetrate adequately in the cerebrospinal fluid, this drug should not be used to treat meningitis.
Antagonism between clindamycin and erythromycin was demonstrated *in vitro*. Because of the possible clinical significance of this finding, both drugs should not be used simultaneously.
With prolonged treatment, the function of the liver and of the kidneys should be monitored.
The use of clindamycin phosphate can result in an overgrowth of insensitive organisms, mainly yeasts.
Clindamycin phosphate should never be administered in I.V. bolus in undiluted form, but must be infused over a time period of at least 10 - 60 minutes (See Posology and method of administration).

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.
In patients with hypersensitivity, clindamycin phosphate should be administered with caution.
In patients with serious renal disorders and/or serious liver conditions associated to serious metabolic conditions, clindamycin should be administered cautiously. The serum levels of clindamycin should be monitored if high doses are required. See above, under Posology and method of administration.

Interaction with other medicinal products and other forms of interaction
An antagonism was demonstrated between clindamycin, erythromycin and chemically related macrolides.
Clindamycin appears to have neuromuscular blocking properties that can enhance the effect of other neuromuscular blockers. In patients treated with such drugs, clindamycin should, therefore, be used with caution.
Pregnancy and lactation
The safe use during pregnancy was not demonstrated. Clindamycin can pass through the placenta. After multiple doses, the concentrations in the amnionic fluid was approx. 30% of the concentrations in the blood of the mother animal. Clindamycin should only be used during pregnancy if necessary.

Clindamycin was demonstrated in the mother's milk, in doses of 0.7 to 3.8 µg/ml. Because of the possibility of serious side-effects of clindamycin in breastfed children, a decision should be made as to whether to discontinue the breastfeeding or the treatment with the drug, taking into account the importance of the drug for the mother (see "Special warnings and special precautions for use").

Effects on the ability to drive and use machines
There are no indications that clindamycin affects the ability to drive motor vehicles or to operate machinery.**Undesirable effects**
1. Gastrointestinal: abdominal pain, nausea, vomiting and diarrhoea (see Special precautions); oesophagitis for the oral preparations. Nearly all antibiotics can (sometimes after a latency time) cause serious diarrhoea, colitis and pseudomembranous colitis due to the toxins of *Clostridium difficile*. In cases of serious or prolonged cases of diarrhoea during treatment, the therapy should be discontinued. Colitis should be specifically treated, e.g. with oral vancomycin, associated to adequate administration of fluids, electrolytes and proteins. Drugs that inhibit the gastrointestinal peristalsis must be avoided.

2. Hypersensitivity reactions: maculopapular rash and urticaria were observed during drug treatment. The treatment with clindamycin has been associated to measles-like skin rash. Rare cases of erythema multiforme, sometimes similar to the Stevens-Johnson syndrome, were reported. Cases of anaphylactoid reactions were reported. Anaphylactic shock was reported following intravenous administration. In cases of serious anaphylactoid reactions, immediate measures should be taken with the administration of epinephrine, oxygen and intravenous steroids. Mechanical ventilation, possibly with intubation, should also be applied if necessary.
3. Liver: jaundice and abnormal liver function tests were observed during treatment with clindamycin.
4. Skin and mucosae: pruritus, vaginitis and rare cases of exfoliative and vesiculobullous dermatitis.
5. Haematopoiesis: transient neutropenia (leukopenia) and eosinophilia, agranulocytosis and thrombocytopenia. In none of these cases a direct etiological link with the treatment with clindamycin could be observed.
6. Cardiovascular: rare cases of cardiopulmonary arrest and hypotension following rapid intravenous administration (see Posology and method of administration).
7. Local reactions: following I.M. injection: local irritation, pain and abscess; following I.V. injection: thrombophlebitis. These reactions can be reduced to a minimum by deep administration of I.M. injections and by avoiding prolonged catheterisation in the same vein.
8. The use of clindamycin phosphate can cause overgrowth of insensitive germs, particularly yeasts.

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.

PHARMACOLOGICAL PROPERTIESPharmacodynamic properties

MICROBIOLOGY

The active substance is clindamycin, a semi-synthetic antibiotic obtained by 7-(S)-chlorosubstitution of the 7-(R)-hydroxyl group of lincomycin.
Due to its effect on the protein synthesis of the micro-organisms, it has a strong antimicrobial activity. Clindamycin can be either bactericidal or bacteriostatic, depending on the sensitivity of the organisms and the concentration of the antibiotic.

Clindamycin is active *in vitro* against the organisms in the following table:

Organisms	MIC 90 (µg/mL)
Aerobic Gram positive cocci	
Staphylococcus aureus	0,5
Staphylococcus epidermidis (penicillinase and non penicillinase producing colonies)	
Streptococci	0,15 –0,53
Pneumococci	0,23
Anaerobic Gram negative bacilli	
Bacteroides species including:	
B. fragilis group	2-4
P. melaninogenicus (B.melaninogenicus) group	0,07
Fusobacterium species	0,85
Anaerobic Gram positive, non sporulating bacilli	
Propionibacterium	0,16
Eubacterium	4
Actinomyces – including *A. israelii*	0,12
Anaerobic and micro-aerophilic Gram positive cocci	
Peptococcus species	
Peptostreptococcus species	2
Micro-aerophilic streptococci	
Clostridia, including:	
C. perfringens	3,4
Other *Clostridid*a species. *C. sporogenes* and *C. tertium* are often resistent, sensitivity tests should be carried out.	8
Other	
Chlamydia trachomatis	2
Some strains of *Toxoplasma gondii*	MIC_{50} = 1 – 11 ng/mL
Pneumocystis carinii	No data available, not recommended in monotherapy
Some strains of *Plasmodium falciparum* (including chloroquine resistant strains)	
Gardnerella vaginalis	0,3
Mobiluncus spp, including *Mobiluncus mulieris* and *Mobiluncus curtisii*	0,5
Mycoplasma hominis	0,016

Methicilline-sensitive *Staphylococcus aureus* strains are generally sensitive to clindamycin. Clindamycin has a significant activity against many strains of methicilline-resistant staphylococci (MRSA). However, the occurrence of a significant number of clindamycin-resistant MRSA-strains excludes the use of clindamycin for infections due to these organisms without sensitivity tests. *In vitro* some erythromycin-resistant strains of staphylococci rather rapidly developed resistance against clindamycin.

The following germs are usually resistant:

– Aerobic Gram negative bacilli
– *Enterococcus faecalis*
– *Nocardia* species
– *Neisseria meningitidis*
– Some strains of *Haemophilus influenzae* (in places where resistance to antibiotics is frequent).

In vitro cross-reaction was observed between clindamycin and lincomycin. Antagonism was demonstrated between clindamycin and erythromycin and chemically related macrolides. Clindamycin does not demonstrate any antagonism with penicillins.

Although clindamycin hydrochloride is active both *in vivo* and *in vitro*, clindamycin phosphate and clindamycin palmitate are not active *in vitro*. However, both compounds are *in vivo* rapidly hydrolysed to the active base.

5.2 Pharmacokinetic data

– Resorption
After oral administration clindamycin is rapidly and nearly completely (90 %) absorbed. The following table gives the mean plasma levels after oral administration of 150 mg in adults.

Way of administration and dose	**Time/plasma levels in µg/mL**				
	45 min	1 hr.	2 hr.	3 hr.	6 hr.
Oral, 150 mg HCl	2.5	2.48	1.88	1.51	0.7

The serum peak level of clindamycin palmitate is obtained at the same time as for the hydrochloride. In children oral clindamycin palmitate was administered in doses of 2, 3 and 4 mg per kg every 6 hours. 1 hour after the first administration serum levels of 1.2, 2.2 and 2.4 µg/ml respectively were obtained. At the fifth administration a steady state was obtained. Using the above dose regimens serum peak levels of 2.5, 3.0 and 3.8 µg/ml respectively are expected. The oral resorption is quantitatively not significantly affected by the simultaneous administration of food. The absorption can, however, be somewhat slowed down.

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. serum peak levels of 7 µg/ml and 10 µg/ml respectively are reached. Table 1 gives the mean serum levels after the administration of clindamycin phosphate. Clindamycin serum levels can be maintained above the *in vitro* MRC'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 administering a 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 h.	7	15
600 mg I.V. in 20 min. every 8 h.	10	23
600 mg I.V. in 30 min. every 6 h.	10,9	

600 mg I.V. in 30 min. every 8 h.	10,8	
900 mg I.V. in 30 min. every 8 h.	14,1	
900 mg I.V. in 30 min. every 12 h.	11	29
1200 mg I.V. in 45 min. every 12 h.	14	49
300 mg I.M. every 8 h.	6	3
600 mg I.M. every 12 h.	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 in the cerebrospinal fluid, not even in the event of meningitis.
- Biotransformation
  Clindamycin has a half live 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 not be adjusted in cases of a moderately or moderately seriously reduced function of the kidneys or of the liver.
  Clindamycin is relatively extensively metabolised.
- Excretion
  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.

PHARMACEUTICAL PARTICULARS

Incompatibilities

The following drugs are physically incompatible with clindamycin phosphate: ampicillin, sodium phenytoin, barbiturates, aminophyllin, calcium gluconates, magnesium sulfate, sodium ceftriaxon and ciprofloxacin.
COMPATIBILITIES:
Solutions of clindamycin phosphate in 5 % dextrose in water and in sodium chloride solutions, to which at least one of the following antibiotics were 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.

Special precautions for storage

Store at room temperature (15°-25°C).

PROVISION OF THE DRUG
On medical prescription only.

DATE OF THE LAST UPDATE OF THE TEXT
December 2003