## 1. NAME(S) OF THE MEDICINAL PRODUCT

Dalacin 150 mg hard capsules
Dalacin 300 mg hard capsules

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dalacin 150 mg hard capsules:
Each capsule contains 150 mg clindamycin (equivalent to 177.515 mg of clindamycin hydrochloride).

Dalacin 300 mg hard capsules:
Each capsule contains 300 mg clindamycin (equivalent to 355.03 mg of clindamycin hydrochloride).

Excipients with known effect
*Dalacin 150 mg hard capsule*
Each capsule contains 209.485 mg lactose-monohydrate.

*Dalacin 300 mg hard capsule*
Each capsule contains 253.97 mg lactose-monohydrate.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

*Dalacin 150 mg hard capsules*
Approximately 440 mg of white powder is filled in each capsule, which is made from hard gelatine that consists of a white upper and lower half designated with black "CLIN 150" and "Pfizer" signs.

*Dalacin 300 mg hard capsules*
Approximately 650 mg of white powder is filled in each capsule, which is made from hard gelatine that consists of a white upper and lower half designated with black "CLIN 300" and "Pfizer" signs.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Treatment of infections caused by susceptible *anaerobic* bacteria or susceptible strains of *Gram positive aerobic* bacteria, for example, streptococci, staphylococci and pneumococci; and susceptible strains of *Chlamydia trachomatis*.
Treatment of patients with penicillin sensitive infections, who are allergic to penicillin.

1. Upper respiratory infections including tonsillitis, pharyngitis, sinusitis, otitis media/chronic suppurative otitis media and scarlet fever.
2. Lower respiratory infections including bronchitis, pneumonia, empyema and lung abscess.
3. 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.
4. Bone and joint infections including osteomyelitis and septic arthritis.
5. Gynecological infections including endometritis, cellulitis, vaginal cuff infection, tuboovarian abscess, salpingitis, and pelvic inflammatory disease when clindamycin should be given in conjunction with an

antibiotic of appropriate Gram negative aerobic spectrum. In cases of cervicitis due to *Chlamydia trachomatis*, clindamycin is effective as monotherapy.

6. Intra-abdominal infections including peritonitis and abdominal abscess. Clindamycin should be given in conjunction with an antibiotic of appropriate *Gram negative* aerobic spectrum.
7. 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.
8. Dental infections such as periodontal abscess and periodontitis.
9. Toxoplasmic encephalitis in patients with AIDS. In patients who are intolerant to conventional treatment, clindamycin can be used in combination with pyrimethamine.
10. *Pneumocystis jiroveci* (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 has been shown to be effective in combination with primaquine.
11. Malaria, including multi-resistant *Plasmodium falciparum* in combination with quinine.
12. Prophylaxis of endocarditis in patients hypersensitive/allergic to penicillin.
13. Perioperative prophylaxis 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

Dosages and the method of administration should be chosen according to the severity of infection, the patient's condition and the susceptibility of the micro-organisms.

Posology

*Adults*
The usual dosage is 150-450 mg every 6 hours four times a day.

*Children and adolescents*

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

For children who are able to swallow the capsules:
the usual dosage *in children over 1 month of age* is 8-25 mg/kg bw/day in 3 or 4 equal doses.

In some cases it may be necessary to use other product forms. Clindamycin capsules are not suitable for children who are not able to swallow the capsules as a whole. The capsules do not provide exact mg/kg doses.

Dosage in Elderly
Pharmacokinetic studies 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 of clindamycin. Therefore, dosage adjustments are not necessary in the elderly with normal hepatic function and normal (age-adjusted) renal function (see section 5.2).

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

Treatment of beta-haemolysing streptococcal infections should be continued for at least 10 days in the above mentioned dosages recommended for the various age groups.

Treatment of pelvic inflammatory disease and cervicitis due to *Chlamydia trachomatis* infection
For the treatment of pelvic inflammatory disease the dosage is 900 mg (IV) every 8 hours daily in combination with an antibiotic with appropriate Gram negative aerobic spectrum administered IV, e.g., gentamicin 2.0 mg/kg bw followed by 1.5 mg/kg bw 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 mg/6 h daily to complete 10-14 days total therapy.
For the treatment of cervicitis due to *Chlamydia trachomatis*: 450-600 mg orally, for 10-14 days.

Treatment of Acute Streptococcal Tonsillitis/Pharyngitis
Clindamycin hydrochloride capsules 300 mg orally twice daily for 10 days.

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 supplementary clindamycin treatment 300-600 mg orally every 6 hours. The usual total duration of therapy is 8 to 10 weeks.
If clindamycin is given in combination with pyrimethamine, the latter should be administered orally 25-75 mg/day for 8-10 weeks. Folinic acid 10-20 mg/day should be given with higher doses of pyrimethamine.

Treatment of *Pneumocystis jiroveci* (previously classified as *Pneumocystis carinii*) Pneumonia in Patients with AIDS
Clindamycin orally 300-450 mg every 6 hours for 21 days and primaquine 15 mg orally once daily for 21 days.

Prophylaxis of Endocarditis in Patients Sensitive to Penicillin (oral administration – capsules or syrup)
Adults: 600 mg 1 hour before procedure; children: 20 mg/kg bw 1 hour before procedure.

Treatment of Malaria (oral administration – capsules or syrup)

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 *intravenously* 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 intravenously followed by 5 mg base/kg intraveously every 8 hours. Avoid rapid intravenous 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 intravenously followed by 5 mg base/kg intravenously every 8 hours. Avoid rapid intracenous administration. Switch to oral clindamycin (oral dose as above) as soon as patient can take oral medication. Treatment course = 7 days.

Method of administration

For oral use.

In order to avoid the irritation of the oesophagus, it is advisable to take the capsule with a big glass of water.

**4.3 Contraindications**

Clindamycin is contraindicated in patients previously found to be hypersensitive to clindamycin, lincomycin, or to any of the excipients listed in section 6.1.

**4.4 Special warnings and precautions for use**

Severe hypersensitivity reactions, including severe skin reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens–Johnson-syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP) have been reported in patients receiving clindamycin therapy. If a hypersensitivity or severe skin reaction occurs, clindamycin should be discontinued and appropriate therapy should be initiated (see Section 4.3 Contraindications and Section 4.8 Undesirable effects).

Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *Clostridium difficile*. This has been reported with use of nearly all antibacterial agents, including clindamycin.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, and may range is severity from mild diarrhea to fatal colitis. It is important to consider the diagnosis of CDAD in patients who present with diarrhea subsequent to 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. Treatment with antibacterial agents may alters the normal flora of the colon and may permit owergrowth of C. difficile. 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. Drugs inhibiting peristalsis are contraindicated in this situation.

C. difficile produces toxins A and B which contribute to the development of CDAD and the primary reason of antibiotics-related 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.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 2 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 and kidney function tests should be performed.

Acute kidney injury, including acute renal failure, has been reported infrequently. In patients 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 may result in overgrowth of non-susceptible microorganisms, particularly yeasts.

Excipients

*Dalacin 150 mg hard capsules*
Dalacin 150 mg hard capsules contain 209.485 mg lactose-monohydrate per capsule.

*Dalacin 300 mg hard capsules*
Dalacin 300 mg hard capsules contain 253.97 mg lactose-monohydrate per capsule.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

Neuromuscular blocking agents
Clindamycin administered by injection 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-desmethyilclindamycin. Therefore inhibitors of CYP3A4 and CYP3A5 may reduce clindamycin clearance and inducers of these isoenzymes may increase clindamycin clearance. Co-administration with strong CYP3A4 inducers such as rifampicin, patients should be monitored 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
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 controlled studies in pregnant women during the first trimester of pregnancy.

Clindamycin should be used in pregnancy only if clearly needed.

Breast-feeding
Orally administered 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 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.

Fertility
Fertility studies in rats treated orally with clindamycin revealed no effects on fertility or mating ability.

### 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. The frequency grouping is defined using the following convention:
Very common (≥1/10);
Common (≥ 1/100 to <1/10);
Uncommon (≥1/1,000 to <1/100);
Rare (≥ 1/10,000 to <1/1,000);
Very Rare (< 1/10,000);
Not known (frequency cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

| **System Organ Class** | **Common** (≥ 1/100 to < 1/10) | **Uncommon** (≥ 1/1 000 to <1/100) | **Rare** (≥ 1/10 000 to <1/1 000) | **Frequency Not Known** (cannot be estimated from the available data) |
|---|---|---|---|---|
| **Infections and infestations** | pseudomembranous colitis*[#] | | | *Clostridium difficile* colitis*, vaginal infection* |
| **Blood and Lymphatic System Disorders** | | | | agranulocytosis*, neutropenia* thrombocytopenia*, leukopenia*, eosinophilia |
| **Immune System Disorders** | | | | anaphylactic shock*, anaphylactoid reaction*, anaphylactic reaction*, hypersensitivity* |
| **Nervous System Disorders** | | | | dysgeusia |

| System Organ Class | Common (≥ 1/100 to < 1/10) | Uncommon (≥ 1/1 000 to <1/100) | Rare (≥ 1/10 000 to <1/1 000) | Frequency Not Known (cannot be estimated from the available data) |
|---|---|---|---|---|
| **Gastrointestinal Disorders** | diarrhoea, abdominal pain | vomiting, nausea | | oesophageal ulcer*, oesophagitis* |
| **Hepatobiliary Disorders** | | | | jaundice* |
| **Skin and Subcutaneous Tissue Disorders** | | rash maculo-papular,,urticaria | | 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*, erythema multiforme, pruritus, rash morbilliform* |
| **Renal and urinary disorders** | | | | acute kidney injury[#] |
| **Investigations** | liver function test abnormal | | | |

*ADR identified post-marketing,
[#]See section 4.4.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after 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 via the national reporting system listed in Appendix V.

### 4.9 Overdose

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

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: macrolides, lincosamides, and streptogramins.
ATC code: J01F F01.

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

Pharmacodynamic effects

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

Resistance

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

Antimicrobial activity

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

*Aerobic bacteria*

*Gram-positive bacteria*

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

*Gram-negative bacteria*

- *Chlamydia trachomatis*

*Anaerobic bacteria*

*Gram-positive bacteria*

- *Actinomyces* spp.
- *Clostridium* spp. (except *Clostridium 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 European Committee on Antimicrobial Susceptibility Testing (EUCAST) for systemically administered antibiotics.

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

**Table 1. 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 |

[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 2. 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* | 0.06–0.25 | 23-29 |

| Table 2. 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)** |
| *Streptococcus pneumoniae* | 0.03–0.125 | 22-28 |

## 5.2 Pharmacokinetic properties

Absorption

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.

Distribution

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, however 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.

Pharmacokinetics in special patient groups

*Elderly*

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.

*Renal impairment*

Serum half-life of clindamycin is increased slightly in patients with major renal impairment. 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.

### 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 bw/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

Magnesium-stearate
Talc
Maize starch
Lactose-monohydrate

Capsule shell:
Titanium dioxide (E 171)
Gelatine.

Printing ink:
Black iron oxide (E172)

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

5 years

### 6.4 Special precautions for storage

Store below 25 °C.

### 6.5 Nature and contents of container

Dalacin 150 mg hard capsules
16 capsules or 100 hard gelatine capsules, in colourless, transparent PVC//Al foil blister and folding carton.

Dalacin 300 mg hard capsules
16 hard gelatine capsules, in colourless, transparent PVC//A1 foil blister and folding carton.

**6.6 Special precaution for disposal and other handling**

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

**Note✠✠** (double cross)
Prescription status: **Group II.**
Medicinal product subject to medicinal prescription (V).

**7. MARKETING AUTHORISATION HOLDER**

Pfizer H. C. P. Corporation, 235 East 42nd Street, 10017 New York, USA

**8.**

**9. DATE OF FIRSTAUTHORISATION/ RENEWAL OF THE AUTHORISATION**

Dalacin 150 mg hard capsules
Date of first authorisation: 17 February 1997

Date of latest renewal: 14 April 2014

Dalacin 300 mg hard capsules
Date of first authorisation: 17 February 1997

Date of latest renewal: 14 April 2014

**10. DATE OF REVISION OF THE TEXT:**

6 December 2021