Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dalacin C 150 mg Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains clindamycin hydrochloride equivalent to 150 mg of clindamycin base.

Excipients: Lactose monohydrate

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Capsule, hard

Product Imported from France:
Size 1, hard gelatin capsules with an opaque white body and an opaque white cap, containing a white to off-white powder. The capsule is imprinted with 'CLIN 150' and 'Pfizer'.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of serious infections due to gram-positive organism, including staphylococci (both penicillinase and non-penicillinase producing), streptococci (except *Streptococcus faecalis*) and pneumococci. It is also indicated in serious infections caused by susceptible anaerobic pathogens.

Clindamycin does not penetrate the blood/brain barrier in therapeutically effective quantities.

4.2 Posology and method of administration

To be taken orally. Dalacin C Capsules should always be taken with a glass of water.

Absorption of Dalacin C is not appreciably modified by the presence of food.

Adults (including the elderly):
Moderately severe infection: 150 − 300 mg every six hours

Children (over 1 month of age):
The usual daily dosage is 12 - 24 mg/kg in 4 divided doses.

In children under one year of age or weighing 10 kg or less, the minimum recommended dosage is 37.5 mg every eight hours.

Dosage in Elderly
The dosage of clindamycin may require reduction in patients with renal impairment due to prolongation of the serum half-life of this drug. This is particularly important with parenteral dosage.

Dosage in Renal Impairment
Clindamycin dosage modification is not necessary in patients with renal insufficiency.

Note: In cases of beta-haemolytic streptococcal infection, treatment with Dalacin C should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

4.3 Contraindications

Dalacin C is contraindicated in patients previously found to be hypersensitive to this antibiotic. Although cross-sensitisation to lincomycin has not been demonstrated, it is recommended that Dalacin C is not used in patients who have demonstrated lincomycin sensitivity.

Dalacin C should not be prescribed concurrently with erythromycin.

Dalacin C should not be used in patients with diarrhoea or intestinal inflammatory disease.

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

4.4 Special warnings and precautions for use

Dalacin C should only be used in the treatment of serious infections. In considering the use of this product the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea that may develop, since cases of colitis have been reported. The appearance of marked diarrhoea should be regarded as an indication that the drug should be discontinued immediately, since it may progress to pseudomembranous colitis.

Studies indicate a toxin(s) produced by clostridia (especially *Clostridium difficile*) is the principal cause of antibiotic−associated colitis. These studies also indicate that this toxigenic clostridium is usually sensitive *in vitro* to vancomycin. When 125−500 mg of vancomycin are administered orally four times a day, there is a rapid observed disappearance of the toxin from faecal samples and a coincident recovery from the diarrhoea.

Clostridium difficile associated diarrhoea (CDAD) has been reported with the 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.

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

Care should be observed in the use of Dalacin C in atopic individuals e.g. asthma and allergy.

Periodic liver function tests and blood counts should be carried out during prolonged therapy. Such monitoring is also recommended in neonates and infants. Safety and appropriate dosage in infants less than one month old have not been established.

Prolonged administration of an anti-infective may result in super-infection due to organisms resistant to the anti-infective.

4.5 Interaction with other medicinal products and other forms of interaction

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. It should, therefore, be used with caution in patients receiving such agents.

Antibiotics can reduce the efficacy of the oral contraceptive pill. Additional contraceptive precautions should be taken during treatment.

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

As safety for use in pregnancy or lacatation has not been established, Dalacin C should be used only if considered essential by the physician. Dalacin C crosses the placenta in humans. After multiple doses, amniotic fluid concentrations were approximately 30% of maternal blood concentrations.

Caution should be exercised when Dalacin C is administered to a nursing mother. Dalacin C has been reported to appear in human breast milk in ranges from 0.7 to 3.8 µg/mL. It is unlikely that a nursing infant can absorb a significant amount of Dalacin C from its gastro-intestinal tract.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

System Organ Class	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 < 1/10000	Not Known (cannot be estimated from available data)
Blood and Lymphatic System Disorders						Agranulocytosis Eosinophilia Thrombocytopenia Transient neutropenia (leukopenia)
Immune System Disorders						Anaphylactoid reactions
Nervous System Disorders						Dysgeusia
Gastrointestinal Disorders		Abdominal pain Diarrhoea	Nausea Vomiting			Esophageal ulcer Esophagitis
Hepatobiliary Disorders		Abnormalities in LFTs				Jaundice
Skin and Subcutaneous Tissue Disorders			Maculo-papular rash Urticaria			Steven Johnson syndrome Toxic epidermal necrolysis Erythema multiforme Exfoliative dermatitis Morbilliform-like skin rashes Pruritus

						Vaginitis Vesiculobullous dermatitis

4.9 Overdose

In cases of overdosage no specific treatment is indicated.
The serum biological half-life of Dalacin C is 2.4 hours. Dalacin C cannot readily be removed from the blood by haemodialysis or peritoneal dialysis.

If an allergic adverse reaction occurs, therapy should be with the usual emergency treatments, including corticosteroids, adrenaline and antihistamines.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dalacin C is a lincosamide antibiotic with a primarily bacteriostatic action against Gram - positive aerobes and a wide range of anaerobic bacteria. Lincosamides such as Dalacin C bind to the 50S subunit of the bacterial ribosome similarly to macrolides such as erythromycin and inhibit the early stages of protein synthesis. The action of Dalacin C is predominantly bacteriostatic although high concentrations may be slowly bactericidal against sensitive strains.

Dalacin C has been shown to have in vitro activity against isolates of the following organisms:
Aerobic gram-positive cocci, including:
Staphylococcus aureus:
Staphylococcus epidermidis (penicillinase and nonpenicillinase producing strains):
When tested by in vitro methods some staphylococcal strains originally resistant to erythromycin rapidly develop resistance of Dalacin C phosphate:
Streptococci (except *Streptococcus faecalis*):
Pnenmococci.
Anaerobic gram-negative bacilli, including:
Bacteroids species (including Bacteroids fragilis group and Bacteroides melaninogenicus group):
Fusobacterium species.
Anaerobic gram-positive non-sporeforming bacilli, including:
Propionibacterium
Eubacterium
Actinomyces species:
Anaerobic and microaerophilic gram-positive cocci, including:
Peptococcus species:
Peptostreptococcus species:
Microaerophilic streptococci.

Clostridia: clostridia are more resistant than most anaerobes to Dalacin C. Most Clostridium perfringens are susceptible, but other species e.g., Clostridium sporogenes and Clostridium tertium are frequently resistant to Dalacin C.

Most gram-negative aerobic bacteria, including the enterobacteriaceae, are resistant to Dalacin C. Dalacin C demonstrates cross-resistance with lincomycin. When tested by *in vitro* methods, some staphylococcal strains originally resistant to erythromycin rapidly developed resistance to Dalacin C. the mechanisms for resistance are the same as for erythromycin, namely methylation of the ribosomal binding site, chromosomal mutation of the ribosomal protein and in a few staphylococcal isolates enzymic inactivation by a plasmid-mediated adenyltransferase.

5.2 Pharmacokinetic properties

Serum level studies with a 150mg oral dose of Dalacin C in 24 normal adult volunteers showed that Dalacin C was

rapidly absorbed after oral administration. An average peak serum level of 2.5 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 levels studies following multiple dose of Dalacin C for up to 14 days show no evidence of accumulation or altered metabolism of drug.

Serum half-life of Dalacin C is increased slightly in patients with markedly reduced renal function.

Haemodialysis and peritoneal dialysis are not effective in removing Dalacin C from the serum. Concentrations of Dalacin C in the serum increased linearly with increased dose. Serum levels exceed the MIC (minimum inhibitory concentrations) for most indicated organisms for at least six hours following administration of the usually recommended doses. Dalacin is widely distributed in body fluids and tissues (including bones). The average biological half-life is 2.4 hours. Approximately 10% of the bioactivity is excreted in the urine and 3.6% in the faeces; the remainder is excreted as bioinactive metabolites. Doses of up to 2 grams of Dalacin C per day for 14 days have been well tolerated by healthy volunteers, except that the incidence of gastrointestinal side effects is greater with the higher doses. No significant levels of Dalacin C are attained in the cerebrospinal fluid, even in the presence of inflamed meninges.

Pharmacokinetic studies in elderly volunteers (61-79 years) and younger adults (18-39 years) indicate that age alone does not alter Dalacin C pharmakinetics (clearance, elimination half-life, volume of distribution, and area under the serum concentrations time curve) after IV administration of Dalacin C phosphate. After oral administration of Dalacin C, elimination half-life is increased to approximately 4.0hours (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.

5.3 Preclinical safety data

There is no evidence of teratogenic effect in animals nor to date in man.

Carcinogenesis: long term studies in animals have not been performed with Dalacin C to evaluate carcinogenic potential.

Mutagenesis: Genotoxicity test performed included a rat micronucleus test and an Ames Salmonella reversion test. Both tests were negative.

Impairment of Fertility: Fertility studies in rats treated orally with up to 300 mg/kg/day (approximately 1.1 times the highest recommended adult human dose based on mg/m^2) revealed no effects on fertility or mating ability.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Talc
Magnesium stearate

Capsules:
Gelatin
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on the container and outer carton of the product as marketed in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Dalacin C 150mg Hard Capsules are available in blister packs (aluminium foil/PVC) of 12 capsules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

B & S Healthcare
Unit 4, Bradfield Road
Ruislip
Middlesex HA4 0NU
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1328/132/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th January 2010

10 DATE OF REVISION OF THE TEXT

August 2014