# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Dalacin C Capsules 75 mg or Clindamycin Hydrochloride Capsules 75 mg

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains clindamycin hydrochloride equivalent to 75 mg Clindamycin.

For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Capsule

Hard capsule (Green/White) with markings of 'CLIN 75 & Pfizer'on cap and body.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Antibacterial. Serious infections caused by susceptible Gram-positive organisms, 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

Posology

*Adults*

Moderately severe infection, 150 - 300 mg every six hours; severe infection, 300 - 450 mg every six hours.

*Elderly patients*

The half-life, volume of distribution and clearance, and extent of absorption after administration of clindamycin hydrochloride 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, therefore, should not be influenced by age alone.

*Paediatric population*
Clindamycin hydrochloride capsules should only be used for children who are able to swallow capsules

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

Doses of 12-25 mg/kg/day six hourly depending on the severity of the infection.

The use of whole capsules may not be suitable to provide the exact mg/kg doses required for the treatment of children.

*Dosage in renal/hepatic impairment*
Clindamycin dosage modification is not necessary in patients with renal or hepatic 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.

Method of administration
Oral. Dalacin C Capsules should always be taken with a full glass of water. Absorption of Dalacin C is not appreciably modified by the presence of food.

## 4.3 Contraindications

Dalacin C is contra-indicated in patients previously found to be sensitive to clindamycin, lincomycin or to any of the excipients listed in section 6.1.

## 4.4 Special warnings and precautions for use

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

Dalacin C should only be used in the treatment of serious infections. In considering the use of the product, the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea which may develop, since cases of colitis have been reported during, or even two or three weeks following, the administration of clindamycin.

Studies indicate a toxin(s) produced by clostridia (especially Clostridium difficile) is the principal direct cause of antibiotic associated colitis. These studies also indicate that this toxigenic clostridium is usually sensitive in vitro to vancomycin. When 125 mg to 500 mg of vancomycin are administered orally four times a day for 7 - 10 days, there is a rapid observed disappearance of the toxin from faecal samples and a coincident clinical recovery from the diarrhoea. (Where the patient is receiving cholestyramine in addition to vancomycin, consideration should be given to separating the times of administration).

Colitis is a disease which has a clinical spectrum from mild, watery diarrhoea to severe, persistent diarrhoea, leucocytosis, fever, severe abdominal cramps, which may be associated with the passage of blood and mucus. If allowed to progress, it may produce peritonitis, shock and toxic megacolon. This may be fatal.

The appearance of marked diarrhoea should be regarded as an indication that the product should be discontinued immediately. The disease is likely to follow a more severe course in older patients or patients who are debilitated. Diagnosis is usually made by the recognition of the clinical symptoms, but can be substantiated by endoscopic demonstration of pseudomembranous colitis. The presence of the disease may be further confirmed by culture of the stool for Clostridium difficile on selective media and assay of the stool specimen for the toxin(s) of C. difficile.

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

Precautions
: Caution should be used when prescribing Dalacin C to individuals with a history of gastro-intestinal disease, especially colitis.

Periodic liver and kidney function tests should be carried out during prolonged therapy. Such monitoring is also recommended in neonates and infants.

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).

Prolonged administration of Dalacin C, as with any anti infective, may result in super infection due to organisms resistant to clindamycin.

Care should be observed in the use of Dalacin C in atopic individuals.

## 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 be used with caution, therefore, in patients receiving such agents.

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.

Co-administration of clindamycin with inhibitors of CYP3A4 and CYP3A5
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 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.

## 4.6. Fertility, pregnancy and lactation

Pregnancy
There was evidence of maternal toxicity and embryofetal toxicity in animal studies (see section 5.3).
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 well-controlled studies in pregnant women during the first trimester of pregnancy. Clindamycin should be used in pregnancy only if clearly needed.

Breast-feeding
Orally and parenterally administered clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8µg/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 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. 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 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥ 1/10,000 to <1/1,000); Very Rare (< 1/10,000); and

Not known (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 | Not Known (cannot be estimated from 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 |
| **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.
‡ ADRs apply only to oral formulations.
# 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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

### 4.9. Overdose

In cases of overdosage no specific treatment is indicated.

The serum biological half-life of clindamycin is 2.4 hours. Haemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

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

Pharmacotherapeutic group: Lincocosamide antibiotics, ATC Code J01FF01.

Mode of action
Clindamycin is a lincosamide antibiotic with a primarily bacteriostatic action against gram-positive aerobes and a wide range of anaerobic bacteria. Lincosamides such as clindamycin bind to the 50S subunit of the bacterial ribosome similarly to macrolides such as erythromycin and inhibit protein synthesis. The action of clindamycin is predominantly bacteriostatic although high concentrations may be slowly bactericidal against sensitive strains. Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

Resistance
Resistance to clindamycin usually occurs via macrolide-lincosamide-streptogramin B (MLSB) type of resistance, which may be constitutive or inducible.

Breakpoints
The minimum inhibitory concentrations (MIC) breakpoints are as follows:
EUCAST
*Staphylococci*: sensitive ≤ 0.25 resistant > 0.5
*Streptococci ABCG* and *pneumoniae*: sensitive ≤ 0.5 resistant > 0.5
Gram positive anaerobes: sensitive ≤ 4 resistant > 4
Gram negative anaerobes: ≤ 4 resistant > 4

PK/PD relationship
Efficacy is related to the ratio of the area of the concentration-time curve of unbound antibiotic to the MIC for the pathogen (fAUC/MIC).

Susceptibility

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 local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

**Species**
**Susceptible**
**Gram-positive aerobes**
*Staphylococcus aureus**
*Staphylococcus epidermidis*
*Streptococcus pneumonia*
*Streptococcus pyogenes*
*Viridans streptococci*

**Anaerobes**
*Bacteriodes fragilis* group
*Prevotella formerly known as Bacteroides melaninogenicus*
*Bifidobacterium* spp.
*Clostridium perfringens*
*Eubacterium* spp.
*Fusobacterium* spp.
*Peptococcus* spp.
*Peptostreptococcus* spp.
*Propionibacterium* spp.
*Veillonella* spp.

**Resistant**
*Clostridia* spp.
*Enterococci*
*Enterobacteriaceae*

*Up to 50% of methicillin-susceptible *S. aureus* have been reported to be resistant to clindamycin in some areas. More than 90% of methicillin-resistant *S.aureus* (MRSA) are resistant to clindamycin and it should not be used while awaiting susceptibility test results if there is any suspicion of MRSA.

## 5.2 Pharmacokinetic properties

General characteristics of active substance
About 90% of a dose of clindamycin hydrochloride is absorbed from the gastro-intestinal tract; concentrations of 2 to 3 micrograms per ml occur within one hour after a 150 mg dose of clindamycin, with average concentrations of about 0.7 micrograms per ml after 6 hours. After doses of 300 and 600 mg peak plasma concentrations of 4 and 8 micrograms per ml, respectively, have been reported. Absorption is not significantly diminished by food in the stomach, but the rate of absorption may be reduced.

Clindamycin is widely distributed in body fluids and tissues including bone, but it does not reach the csf in significant concentrations. It diffuses across the placenta into the foetal circulation and has been reported to appear in breast milk. High concentrations occur in bile. It accumulates in leucocytes and macrophages. Over 90% of clindamycin in the circulation is bound to plasma proteins. *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 half-life is 2 to 3 hours, although this may be prolonged in pre-term neonates and patients with severe renal impairment.

Clindamycin undergoes metabolism, presumably in the liver, to the active *N*-demethyl and sulphoxide metabolites, and also some inactive metabolites. About 10% of a dose is excreted in the urine as active drug or metabolites and about 4% in the faeces; the remainder is excreted as inactive metabolites. Excretion is slow and takes place over several days. It is not effectively removed from the blood by dialysis.

Characteristics in patients
No special characteristics. See section 4.4 for further information.

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

None Stated

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Lactose
Maize starch
Talc
Magnesium stearate

*Capsule shell:*
Gelatin
Indigo carmine (E132)
Quinoline yellow (E104)
Titanium dioxide (E171)

*Printing ink:*
Shellac
Soya lecithin
Dimeticone (Antifoam DC 1510)
Black Iron Oxide (E172)

### 6.2 Incompatibilities

Not applicable.

### 6.3. Shelf life

Bottle: 60 months
Blister: 60 months

### 6.4 Special precautions for storage

Do not store above 25°C.

### 6.5 Nature and contents of container

Dalacin C Capsules 75 mg are available in blister packs (aluminium foil/PVC) of 24 capsules and bottle packs (high density polyethylene or amber glass) of 24, 100 or 500 capsules.
Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7 MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 00057/0958

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 February 1989
Date of latest renewal: 22 May 2001

## 10 DATE OF REVISION OF THE TEXT

28/04/2022