SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Clindamycin 300 mg hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 300 mg hard capsule contains 300 mg clindamycin (as hydrochloride)

Excipient with known effect:

Each 300 mg hard capsule contains 1.3 mg lactose monohydrate.
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Hard capsule

Hard cylindrical gelatin capsules size n°0 approximately 22 mm long with a blue cap and white body.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Clindamycin is indicated for the treatment of:
Serious infections caused by anaerobic bacteria, including intra-abdominal infections, skin and soft tissue infections. As needed, clindamycin should be administered in conjunction with another antibacterial agent that is active against gram negative aerobic bacteria.
- Tonsillitis
- Dental infection

Consideration should be given to official guidance regarding the appropriate use of antibacterial agents.

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

4.2 Posology and method of administration

Posology

Adults:

The usual dose is 150-450 mg every six hours, depending on the severity of the infection.

Elderly:

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:

The usual dose is 3 – 6 mg/kg every six hours depending on the severity of the infection (not to exceed the adult dose).

Clindamycin capsules are not suitable for children who are unable to swallow them whole. The capsules do not provide exact mg/kg doses therefore it may be necessary to use an alternative formulation in some cases.

The dosage of clindamycin in children should be adjusted according to total body weight, regardless of obesity.

Renal impairment:

No dose adjustment is necessary in patients with mild to moderate impairment of renal function. In patients with severe renal impairment or anuria, plasma concentration should be monitored. Depending on the results, this measure can make a reduction in dosage or an increase in the dose interval of 8 or even 12 hours necessary.

Hepatic impairment:

In patients with moderate to severe hepatic impairment, elimination half-life of clindamycin is prolonged. A reduction in dosage is generally not necessary if clindamycin is administered every 8 hours. However, the plasma concentration of clindamycin should be monitored in patients with severe hepatic impairment. Depending on the results, this measure can make a reduction in dosage or an increase in the dose intervals necessary.

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

Method of administration
For oral use.

Clindamycin should be taken whole, by swallowing them with a full glass of water. The capsules should be taken in an upright position (standing up or sitting down), without lying down for at least 30 minutes after administration. Absorption of clindamycin is not appreciably modified by the presence of food.

4.3 Contraindications

Clindamycin is contraindicated in patients previously found to be sensitive to clindamycin, lincomycin, any component of the formulation, or to any excipient listed in Section 6.1. (List of excipients).

4.4 Special warnings and precautions for use

Hypersensitivity
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).
The choice of clindamycin should be based on factors such as severity of the infection, the prevalence of resistance to other suitable agents and the risk of selecting clindamycin-resistant bacteria.

Care should be observed in the use of clindamycin in atopic individuals.
Antibiotic-associated colitis
Clindamycin 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.

Treatment with antibacterial agents can significantly alter 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* produces toxins A and B which contribute to the development of *Clostridium difficile* associated diarrhea (CDAD) and is a primary cause of “antibiotic-associated 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). 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*. 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.

Caution should be used when prescribing clindamycin to individuals with a history of gastrointestinal disease, especially colitis.

Long-term treatment
Clindamycin does not penetrate the blood/brain barrier in therapeutically effective quantities.

Since clindamycin does not diffuse adequately into cerebrospinal fluid, the drug should not be used in the treatment of meningitis.

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

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

Oesophageal damage
Due to the risk of oesophageal damage, it is important to comply with the conditions of administration (see sections 4.2 and 4.8).

Excipients
Clindamycin contains lactose. Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Muscle relaxants
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.

Antibacterial agents:
Antagonism has been demonstrated between clindamycin and erythromycin *in vitro*. Because of possible clinical significance the two drugs should not be administered concurrently and therefore clindamycin should not be given in combination with macrolides or streptogramin antibacterial 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.

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

The amount of clindamycin passed into breast milk is low, and ingested quantities are much lower than paediatric therapeutic doses following systemic use. Consequently, breast-feeding is possible when taking this antibiotic. However, breast-feeding should be reconsidered (or the medicinal product re-assessed) if diarrhoea, blood in stools, candidiasis or skin eruption occurs in the infant.

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*
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 of 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 overdose no specific treatment is indicated.

The serum biological half-life of clindamycin is 2.4 hours. Clindamycin cannot readily be removed from the blood by dialysis or peritoneal dialysis.

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

5.2 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinfectives for systemic use, ATC code: J01FF01
Clindamycin is an antibiotic of the lincosamide family.

Mechanism of action
Clindamycin inhibits the synthesis of bacterial proteins by binding to the 50S subunit of the bacterial ribosome.At usual doses, clindamycin exhibits bacteriostatic activity *in vitro*.

Pharmacokinetic/pharmacodynamic relationship
The percentage of time during which the concentration of the antibiotic is above the minimum inhibitory concentration (MIC) of the bacterium between two administrations (%T > MIC) is the most predictive parameter of the efficacy of clindamycin.

Resistance
Resistance to clindamycin is most often due to mutations on the site of antibiotic binding to rRNA or to the methylation of specific nucleotides of the 23S RNA of the 50S ribosomal subunit. These alterations may determine in vitro cross-resistance to macrolides and streptogramins B (MLSB phenotype).
Resistance mechanisms may be due to active efflux.
Resistance to clindamycin can be induced by macrolides in macrolide-resistant bacterial strains.
There is complete cross-resistance between clindamycin and lincomycin.
The incidence of clindamycin resistance is higher among methicillin-resistant strains of staphylococci and pneumococcal strains with decreased sensitivity to penicillin.

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

Antibacterial activity spectrum
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.

Classes
USUALLY SUSCEPTIBLE SPECIES **Gram-positive aerobic bacteria** *Bacillus cereus* *Corynebacterium diphtheriae* *Methicillin-susceptible staphylococcus* *Streptococcus agalactiae* **Gram-negative aerobic bacteria** *Campylobacter* **Anaerobic bacteria** *Actinomyces* *Capnocytophaga* *Clostridium perfringens* *Eubacterium* *Fusobacterium* *Gardnerella vaginalis* *Porphyromonas* *Prevotella* *Propionibacterium acnes* *Veillonella* **Other** *Chlamydia trachomatis* Leptospires *Mycoplasma hominis* *Mycoplasma pneumoniae*
Not consistently susceptible species **(Acquired resistance >10%)** **Gram-positive aerobic bacteria** *Enterococcus faecium* *Erysipelothrix* *Methicillin-resistant staphylococcus* *Streptococcus pneumoniae* *Streptococcus pyogenes* *Oral streptococci* **Anaerobic bacteria** *Bacteroides* *Clostridium (*other than *C. difficile* and *C. perfringens)* *Mobiluncus*

Peptococcus *Peptostreptococcus*
NATURALLY RESISTANT SPECIES **Gram-positive aerobic bacteria** *Corynebacterium jeikeium* *Enterococcus spp. (*other than *Enterococcus faecium)* *Listeria* *Nocardia asteroides* *Rhodococcus equi* **Gram-negative aerobic bacteria** Nonfermenting gram-negative bacilli (*Acinetobacter, Pseudomonas,*.) Enterobacter *Haemophilus* *Legionella* *Branhamella catarrhalis* *Neisseria* *Pasteurella* **Anaerobic bacteria** *Clostridium difficile* **Other** Mycobacteria *Ureaplasma urealyticum*

Anti-parasitic activity

Clindamycin has an *in vitro* and *in vivo* effect on *Toxoplasma gondii*.

5.2 Pharmacokinetic properties

General characteristics of active substance

About 90% of a dose of clindamycin is absorbed from the gastrointestinal 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. 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.

5.3 Preclinical safety data

None stated

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
Colloidal anhydrous silica
Lactose monohydrate
Maize starch
Magnesium stearate

Capsule shell:
Indigo carmine (E132)
Titanium dioxide (E171)
Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years
Bottles: Use within 6 months of opening.

6.4 Special precautions for storage

Do not store above 25°C.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

PVC/Aluminium foil blisters packs of 16 and 30 capsules.
PVC/Aluminium foil perforated unit dose blisters of 16 x 1 capsules.

Not all pack-sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Mylan
Potters Bar
Hertfordshire
EN6 1TL
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 04569/1753

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/04/2023

10 DATE OF REVISION OF THE TEXT

08/09/2025