SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Clindamycin 150 mg Hard Capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains clindamycin hydrochloride equivalent to 150 mg clindamycin.

Excipient(s) with known effect:

Each capsule contains 230 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, hard.

A capsule with a lavender body and maroon cap imprinted with CL 150 in white.

SUMMARY OF THE PRODUCT CHARACTERISTICS

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Antibacterial. In the treatment of serious infections due to gram-positive organisms, 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.

SUMMARY OF THE PRODUCT CHARACTERISTICS

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.

Pediatric population:

Clindamycin should be dosed based on total body weight regardless of obesity. The total daily dose should not exceed the maximum recommended daily dose for adults.

Doses of 12-25 mg/kg/day six hourly depending on the severity of the infection. Clindamycin Capsules are not suitable for children who are unable to swallow them whole. 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 Clindamycin Capsules should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

Method of administration

To be taken orally with water. Clindamycin Capsules may be taken without regard to food.

Clindamycin Capsules should always be swallowed whole and washed down with a full glass of water while in an upright position. and no less than 30 minutes before lying down to avoid possible irritation of the oesophagus.

SUMMARY OF THE PRODUCT CHARACTERISTICS

4.3 Contraindications

Hypersensitive to clindamycin, lincomycin or any of the excipients listed in section 6.1.

Diarrhoea or intestinal inflammatory disease.

SUMMARY OF THE PRODUCT CHARACTERISTICS

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 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 sections 4.3 and 4.8).

Clostridioides Difficile associated diarrhoea

Clindamycin Capsules 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 during, or even two or three weeks following, the administration of clindamycin.

Studies indicate a toxin(s) produced by clostridia (especially *Clostridioides 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 is 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 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.

Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of Clostridioides difficile. This has been reported with use of nearly all antibacterial agents, including clindamycin. Clostridioides difficile produces toxins A and B which contribute to the development of Clostridioides difficile associated diarrhoea (CDAD) and is a primary cause of “antibiotic-associated colitis”.

It is important to consider the diagnosis of CDAD in patients who present with diarrhoea 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. 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.

Due to the risk of oesophagitis and oesophageal ulcer, it is important to ensure compliance with administration guidance (see Sections 4.2 and 4.8)

Use in patients with atopic syndrome

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

Diffusion into cerebrospinal fluid

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

Liver and Kidney function tests during prolonged therapy

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

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).

Non-susceptible organisms

The use of clindamycin may result in overgrowth of non-susceptible organisms, particularly yeasts.

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

Cross Resistance

Attention should also be paid to the possibility of cross resistance to macrolides and lincosamides for some individual bacterial strains (see section 5.1).

Excipients:

This medicinal product contains lactose:

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

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 Capsules should not be prescribed concurrently with erythromycin.

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

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 well-controlled studies in pregnant women during the first trimester of pregnancy.

Clindamycin should be used in pregnancy only if clearly needed.

Breast-feeding

Clindamycin is excreted in human milk in ranges from <0.5 to 3.8µg/mL and effects (e.g. diarrhoea, blood in stool and rash) have been shown in breastfed newborns/infants of treated women.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from clindamycin therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

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.

SUMMARY OF THE PRODUCT CHARACTERISTICS

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); 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	**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 (cannot be estimated From available data)**
Infections and infestations		pseudomembranous colitis*#				*Clostridioides difficile* colitis*, Vaginal infection*
Blood and Lymphatic System						Agranulocytosis* Leukopenia*, Neutropenia* Thrombocytopenia*

Disorders						Eosinophilia
Immune System Disorders						Anaphylactic shock*, Anaphylactoid Reactions*, anaphylactic reaction*, hypersensitivity*
Nervous System Disorders						Dysgeusia
Gastrointestinal Disorders		Abdominal pain, Diarrhoea	Nausea, Vomiting			Oesophageal ulcer*‡ ≠ Oesophagitis*‡≠
Hepatobiliary Disorders						Jaundice*
Skin and Subcutaneous Tissue Disorders			Rash maculopapular, Urticaria			Toxic epidermal Necrolysis (TEN)*, Steven Johnson syndrome (SJS)*, drug reaction with eosinophilia and systemic symptoms (DRESS)*, Acute generalized exanthematous pustulosis (AGEP*), angioedema*, Erythema multiforme*, Dermatitis, exfoliative*, Dermatitis bullous*, Rash Morbilliform*, Pruritus
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.

≠ Possible occurrence of oesophagitis and oesophageal ulcer, particularly if taken in a lying position and/or with a small amount of water.

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 UK Yellow Card Scheme, Website: 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.

SUMMARY OF THE PRODUCT CHARACTERISTICS

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lincocosamide antibiotics,
ATC Code: J01FF01.

Mechanism 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 the early stages of protein synthesis. The action of clindamycin is predominantly bacteriostatic although high concentrations may be slowly bactericidal against sensitive strains.

Although Clindamcyin is inactive in vitro, rapid in vivo hydrolysis converts this compound to the antibacterially active clindamycin. At usual doses, clindamycin exhibits bacteriostatic activity in vitro.

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.

Clostridioides 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.

SUMMARY OF THE PRODUCT CHARACTERISTICS

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 18 years and obese young adults aged 18 to 20 years:

An analysis of pharmacokinetic data in paediatric patients (2 to 18 years) and young adults (18 to 20 years) demonstrated that the clearance and volume of distribution of clindamycin, when normalized to total body weight, are comparable between obese and non-obese patients.

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 clindamycin to evaluate carcinogenic potential.

Mutagenesis:

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

Reproductive toxicity:

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/m2) revealed no effects on fertility or mating ability.

In oral embryo foetal development studies in rats and subcutaneous embryo foetal 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

Capsule Contents

Lactose Monohydrate
MaizeStarch
Magnesium Stearate
Purified Talc

Capsule Body

Gelatin

Erythrosin (E127)

Indigo carmine FD&C Blue (E132)

Capsule Cap

Gelatin

Erythrosin (E127)

Indigo carmine FD&C Blue (E132)

Titanium dioxide (E171)

Printing ink

Shellac

propylene Glycol (E1520)

titanium dioxide (E171)

ethanol

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister packs composed of PVC / PE /PVdCaluminium foil; pack sizes: 4, 8, 16, 20, 24, 30, 32, 40 and 100. Polypropylene containers with polyethylene tamper evident lids; pack size: 100.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Chanelle Medical Unlimited Company, Loughrea, Co. Galway, Ireland

8. MARKETING AUTHORISATION NUMBER

PL 13931/0061

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

21/08/2009

10 DATE OF REVISION OF THE TEXT

25/03/2026