1. Name of the Medicinal Product

1.1 Name of the Medicinal Product

CLINCAP-150 (Clindamycin Hydrochloride Capsules USP)

1.2. Strength

Clindamycin Hydrochloride USP	
Eq. to Clindamycin	150 mg
Excipients	q.s.

1.3. Pharmaceutical Dosage Form

Hard Capsule (Solid oral dosage form)

2. Qualitative And Quantitative Composition

Qualitative Declaration

The **CLINCAP-150 Capsule** contains Clindamycin Hydrochloride USP.

Quantitative Declaration

Composition:

Clindamycin Hydrochloride USP	
Eq. to Clindamycin	150 mg
Excipients	q.s.

Approved colour used in empty gelatin capsules shell

3. Pharmaceutical Form

Capsule

4. Clinical Particulars

4.1 Therapeutic Indications

CLINCAP-150 is indicated in serious infections caused by organisms susceptible to its action.

In vitro susceptibility studies should be performed. Infections due to susceptible organisms, which respond to an effective dose, include infections of the upper and lower respiratory tract (pharangitis, tonsillitis, sinusitis, otitis media, bronchitis, pneumonia). Infections of the skin and soft tissue (abscesses, cellulitis, infected wounds) and dental infections (periapical abscesses and gingivitis)

Serious infections such as acute and chronic osteomyelitis and bacteraemia, have responded to the usually recommended dose.

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 patients

Dosage requirements in elderly patients should not be influenced by age alone.

Paediatric population

Clincap-150 is 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.

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.

Method of administration

Clincap-150 is given orally. The product should always be taken with a full glass of water in an upright position.

Absorption of Clincap-150 is not appreciably modified by the presence of food.

4.3 Contraindications

Hypersensitivity to Clindamycin.

Patients with a hypersensitivity to lincomycin.

4.4 Special Warning and Precautions for Use

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.

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 pseudo membranous colitis. Which may range from mild to fatal colitis If antibiotic-associated diarrhea 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.

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.

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

If therapy is prolonged, liver and kidney function tests should be performed.

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

Care should be observed in the use of Clindamycin in atopic individuals.

Clincap-150 contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine.

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.

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

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

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.

Oral and subcutaneous reproductive toxicity studies in rats and rabbits revealed no evidence of impaired fertility or harm to the foetus due to Clindamycin

Breast-feeding

Clindamycin is excreted in breast milk. Orally and parenterally administered Clindamycin has been reported to appear in human breast milk in ranges from 0.7 to 3.8µg/ml. Because of the potential for serious adverse reactions in nursing infants Clindamycin should not be taken by nursing mothers.

Fertility

In animal studies, Clindamycin had no effect 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

Diarrhoea, nausea, vomiting, abdominal pain; erythema multiforme, contact dermatitis, exfoliative and vesiculous dermatitis, urticaria; eosinophilia; local irritation, thrombophloebitis. Potentially Fatal: Gasping syndrome (neonates); pseudomembranous colitis.

4.9 Overdose

The serum biological half-life of Clindamycin is 2.4 hours. Clindamycin 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.

5.0 Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lincosamides

ATC code: Clindamycin 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.

Mechanism of resistance

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

Breakpoints

The minimum inhibitory concentrations (MIC) breakpoints are as follows:

Eucast

Staphylococci: sensitive ≤ 0.5 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

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* *Streptococcus viridans* **Anaerobes** *Bacteriodes fragilis* group *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

Absorption

After oral administration Clindamycin is absorbed quickly and almost completely (>90%). The absorption is not affected by food. The peak plasma concentration is achieved within approximately 45 minutes after oral administration. The bioavailability is non-linear and decreases with increasing doses. Following a 600 mg dose the absolute bioavailability is 53±14%

Distribution

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 fetal 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

Biotransformation

Clindamycin undergoes metabolism, presumably in the liver, to the active *N*-demethyl and sulfoxide 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.

Elimination

Half-life is approximately two and a half hour in children and approximately 3 hours in adults. Clindamycin is excreted as biological active and biological inactive metabolites in faeces, urine and bile. Faecal excretion is predominant. About 10% of the drug is excreted in the urine as active drug and about 4% in the faeces; the remainder is excreted as inactive metabolites.

Characteristics in patients

Elderly:

The half-life, volume of distribution and clearance, and extent of absorption after administration of clindamycin phosphate are not altered by increased age.

Patients with renal impairment:

In the presence of renal impairment, elimination half-life is prolonged; however, a dosage reduction is unnecessary in the event of mild to moderate impairment of renal function.

Patients with hepatic impairment:

In patients with moderate to severe hepatic impairment the half life is prolonged, but when giving the dose every 8 hours, accumulation is rarely seen. Dose reduction is normally not necessary in patients with hepatic impairment.

5.3 Preclinical Safety Data

Preclinical data reveal no special hazard for humans based on studies of repeat dose toxicity, reproductive toxicity or genotoxicity. Carcinogenicity studies have not been conducted.

In dogs, repeated high oral doses produced ulceration of the mucosa of the stomach and gall bladder.

6.0 Pharmaceutical Particulars

6.1 List of Excipients

- Purified Talc BP
- Magnesium Stearate BP
- Colloidal Anhydrous Silica BP
- Lactose BP
- Starch BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

<36 Months>

6.4 Special Precautions for Storage

Store in a cool & dry place at a temperature not exceeding 25°C. Protect from light.

6.5 Nature and Contents of Container

1 X 10 Capsules packed in a unit carton along with patient information leaflet.

6.6 Special Precautions for Disposal and Other Handling

None stated

7. Registrant/Sole Agent

EMBASSY PHARMACEUTICAL & CHEMICAL LTD.

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8. Manufacturer

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9. Date of Revision of Text

To be given after approval of product

10. Dosimetry (If applicable)

Not applicable

11. Instructions for Preparation of Radiopharmaceuticals (If applicable)

Not applicable