1.3.1 Summary of Product Characteristics (SmPC)

1- Name of the Medicinal Product:

1.1 Product Name

-Generic Name or International Non-Proprietary Name (INN)

Clindamycin hydrochloride Capsules USP 300 mg

-Brand Name

PINNACLE CLINDAMYCIN

1.2 Dosage Strength

Each Hard Gelatin capsule contains:
Clindamycin Hydrochloride USP
Equivalent Clindamycin …….300 mg
Excipients…….q.s.
Approved Colour used In Capsule Shell

1.3 Dosage Form

Hard gelatin Capsule

2- Quality and Quantitative Composition:

2.1 Qualitative Declaration

Each Hard Gelatin capsule contains:
Clindamycin Hydrochloride USP
Equivalent Clindamycin …….300 mg
Excipients…….q.s.
Approved Colour used In Capsule Shell

2.2 Quantitative Declaration

Description: A light blue /dark blue colored hard gelatin Capsule size '0' containing White colour powder

Composition:

Batch Size - 1, 00,000 Tablets.

Sr. No:	Ingredients	Specification	mg/Cap	Overages %	Qty/Batch 1 lac in Kg	Function
Sifting /mixing						
1	Clindamycin Hydrochloride	USP	325.730	---	32.573	Active
2	Maize Starch	BP	150.000	---	15.000	Diluent
3	Dibasic Calcium Phosphate	BP	125.270	---	12.527	Diluent
4	Talcum	BP	8.000	---	0.800	Lubricant
5	Magnesium Stearate	BP	6.000	---	0.600	Lubricant
6	Sodium Starch Glycolate	BP	10.000	---	1.000	Disintegrants
7	Colloidal Silicon Dioxide (Light)	BP	8.000	---	0.800	Lubricant
Filling						
8	E.H.G. CAPSULES SIZE 0 LBL/DBL	IH	97.000	---	9.700	Empty Capsules Shells
Total net wt. of Content			**633 mg**	**Limit : 633 ± 7.5 %**		
Total Weight of Capsules			**730 mg**	**Limit : 730 ± 7.5 %**		

Note: Active material was calculated on assay or Potency Basis.
IHS = In-house Specification
BP = British Pharmacopoeia.
USP= United state pharmacopeia.

3- Pharmaceutical Form:

A light blue /dark blue colored hard gelatin capsule size '0' containing white colour Powder.

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 the official guidance on the appropriate use of antibacterial agents.

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

Pediatric 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.

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

Clindamycin capsules are given orally. The product should always be taken with a full glass of water in an upright position.

Absorption of Clindamycin capsules is not appreciably modified by the presence of food.

4.3 Contraindications

Hypersensitivity to the active substance, lincomycin or to any of the Excipients.

4.4 Special warning and precautions for use

Clindamycin should only be used in the treatment of serious infections and when the possible benefit of using clindamycin is considered to outweigh the risk of antibiotic-associated diarrhoea or colitis, which may progress to pseudomembraneous colitis, toxic megacolon and death. These intestinal complications are more likely to be severe and to become life-threatening in older patients or patients who are debilitated. Caution should also be used when prescribing clindamycin for individuals with a history of gastro-intestinal disease, especially colitis.

If marked diarrhoea occurs during therapy, clindamycin should be discontinued immediately and appropriate diagnostic and therapeutic measures should be instituted. It should be noted that the onset of these intestinal complications of clindamycin treatment may be delayed until several weeks following the cessation of therapy. The most commonly implicated cause is an overgrowth of toxin-producing *Clostridium difficile* as a result of disruption of the bowel flora by clindamycin.

Laboratory tests for renal and hepatic function should be carried out during prolonged therapy.

Close monitoring is also recommended in patients with renal or hepatic insufficiency and in neonates and infants, all of whom may require dose reduction and/or an extended interval between doses.

Prolonged administration of Clindamycin capsules, as with any anti-infective, may result in super – infection due to organism resistant to clindamycin.

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

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

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-resistance bacteria

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

Fertility

In animal studies, clindamycin had no effect on male or female fertility.

Pregnancy

Safety for use in pregnancy has not yet been established. In animal studies, no effect of Clindamycin on embryofoetal and postnatal development was observed (see

section 5.3). The use of Clindamycin capsules may be considered during pregnancy, if necessary.

Lactation

Clindamycin is excreted in human milk. Caution should be exercised when Clindamycin capsules are administered to a nursing mother.

4.7 Effects on ability to drive and use machine

Clindamycin is not known to interfere with the ability to drive or operate machinery.

4.8 Undesirable effects

Blood and the lymphatic system disorders

Transient neutropenia (leucopenia), eosinophilia, agranulocytosis and thrombocytopenia have been reported. No direct aetiologic relationship to concurrent clindamycin therapy could be made in any of the foregoing.

Immune system disorders

A few cases of anaphylactoid reactions have been reported.

Gastro-intestinal disorders

Oesophageal ulcers have been reported as serious adverse events: oesophagitis with oral preparations, nausea, vomiting abdominal pain and diarrhoea (see Section 4.4 *Special Warnings and Special Precautions for Use, Warning*)

Hepato-biliary disorders

Jaundice and abnormalities in liver function tests have been observed during clindamycin therapy.

Skin and subcutaneous tissue disorders

Maculopapular rash and urticaria have been observed during drug therapy. Generalised mild to moderate morbilliform-like skin rashes are the most frequently reported reactions. Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with clindamycin.

Pruritus, vaginitis and rare instances of exfoliative and vesiculobullous dermatitis have been reported. Serious cutaneous adverse reaction (SCAR) and rare cases of toxic epidermal necrolysis have been reported during post-marketing surveillance.

Nervous system disorders

Frequent cases of Dysgeusia have been observed upon systemic administration of clindamycin using injectables (IM or IV), capsules, or oral granulate solutions, which include a few (non-frequent) serious adverse events.

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 national reporting system listed in Appendix V

4.9 Overdose and treatment

In cases of overdosage 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- Pharmacological Properties:

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Lincosamides

ATC classification: J01FF

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

General characteristics of active substance

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. It diffuses across the placenta but not the healthy blood-brain barrier. 68 – 93 % of clindamycin in the circulation is bound to plasma proteins. Clindamycin is distributed very highly intracellular due to the lipophilic properties. The intracellular concentrations are 10-50 times higher than the extracellular concentrations.

Metabolism

Clindamycin undergoes metabolism, presumably in the liver, to the active N-demethyl and sulphoxide metabolites, and also some inactive metabolites and about 4% in the faeces: the remainder is excreted as inactive metabolites.

Excretion

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 hour accumulation is rarely seen. Dose reduction is normally not necessary in patients with hepatic impairment.

5.3 Preclinical safety Data

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

However preclinical data reveal no special hazard for humans based on studies of repeat dose toxicity, or effects on male and female fertility as well as embryofoetal and postnatal development, genotoxicity.

Carcinogenicity studies have not been conducted.

6- Pharmaceutical Particulars :

6.1 List of Excipients

Lactose monohydrate
Maize starch
Talc
Magnesium Stearate
Capsule shell
Gelatin
Titanium dioxide (E 171)
Printing ink
Shellac
Iron oxide black (E172)
Propylene glycol (E1520)

6.2 Incompatibilities

None known

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Store in a cool and dry place, protected from light

6.5 Nature and contents of container

10 Capsules packed in one Alu –PVC blister. Such one blisters packed in unit printed duplex board carton along with its package insert. Such cartons packed in export worthy shipper.

Note: All pack style may not be marketed

7- Marketing Authorization Holder:

- Name : GLOBELA PHARMA PVT. LTD.

- Address : Plot No. 357, G.I.D.C.,
Sachin,
Surat – 394 230,
Gujarat,
India.

- Phone : +91– 261–2398058
- Fax : +91– 261–2398058
- E-mail : info@globelapharma.com

8- Marketing Authorization Number (s) :

-Product license / registration Number (s)

9- Manufacturer Name :

- Name : GLOBELA PHARMA PVT. LTD.

- Address : Plot No. 357, G.I.D.C.,
Sachin,
Surat – 394 230,
Gujarat,
India.

- Phone : +91– 261–2398058
- Fax : +91– 261–2398058
- E-mail : info@globelapharma.com

10- Date of first authorization/renewal of the authorization:

11- Date of revision of the text:
