

Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Clindamycin Capsules BP 300mg (Miclyn)

2. Qualitative and quantitative composition

Each Hard Gelatin Capsules Contains:

Clindamycin Hydrochloride BP

Eq. Clindamycin.....300mg

Colour: Approved colours used in empty capsule shells.

3. Pharmaceutical form

Solid Oral- Hard Gelatin Capsule

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: 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: 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.

For Oral use.

Clindamycin Capsules should always be taken with a full glass of water.

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

4.3 Contraindications

Hypersensitivity to the active substances Clindamycin or to any of the excipients used in manufacturing of myclin.

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). 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 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. 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.

Precautions

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 functions test should be performed. 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). Such liver and renal monitoring is also recommended in neonates and infants.

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. Therefore, it should be used with caution 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.

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-desmethyclindamycin. 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 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.

Breastfeeding

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

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

Diarrhoea, abdominal pain, vomiting, nausea, rash maculo-papular, urticaria

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions to the National Regulatory Authorities.

4.9 Overdose

In cases of over dosage 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:

Lincosamide 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.

5.2 Pharmacokinetic properties

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 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.

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 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.

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5.3 Preclinical safety data

None Stated

6. Pharmaceutical Particulars

6.1 List of Excipients

Pregelatinized Starch

Magnesium Stearate

Purified Talc

Croscarmellose sodium

Colloidal Silicon Dioxide

6.2 Incompatibilities

None

6.3 Shelf-Life

36 months.

6.4 Special Precautions for storage

Store in a cool and dry place below 30 °C, protect from light

6.5 Nature and Content of container

10X1X10 Capsules in a monocarton with package Insert.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

Simba Pharmaceuticals Ltd, P.O. BOX 1541-00606 Nairobi

8. Marketing Authorization Number**9. Date of first authorization/renewal of the authorization****10. Date of revision of the text**