CHEMIMYCIN-300
(Clindamycin Capsules BP 300 mg)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the Medicinal Product

CHEMIMYCIN-300

(Clindamycin Capsules BP 300 mg)

2. Qualitative and Quantitative Composition

Each hard gelatin capsule contains:

Clindamycin Hydrochloride BP

eq. to Clindamycin 300 mg

3. Pharmaceutical Form

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 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 Rivopharm 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

When administered systemically during general anesthesia, clindamycin phosphate 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. This is not expected to be a concern with vaginal cream or vaginal ovule treatment due to the low systemic exposure from vaginal administration. There is a remote possibility that vaginal formulations could be administered during general anesthesia.

4.4 Special warning and special precaution for use

Hypersensitivity reactions as with all agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with Clindamycin Hydrochloride must be discontinued immediately and adequate emergency measures must be initiated. Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to Clindamycin Hydrochloride, to other cephalosporins or to any other type of beta-lactam agent. Caution should be used if Clindamycin Hydrochloride is given to patients with a history of non-severe hypersensitivity to other beta-lactam agents. Severe cutaneous adverse reactions (Stevens Johnson syndrome or Lyell's syndrome/toxic epidermal necrolysis) have been reported; however, the frequency of these events is not known.

4.5 Interaction with other medicinal products and form 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 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. 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 machines

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

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

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.

5.2 Pharmacokinetic properties

Clindamycin is widely distributed in body fluids and tissues, including bone, but it does not reach the cerebrospinal fluid in significant concentrations. It diffuses across the placenta into the foetal circulation and appears 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, to the active N-demethyl and sulphoxide metabolites and also some inactive metabolites. About 10% of the drug 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.

Absorption

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.

Distribution

Clindamycin is widely distributed in body fluids and tissues including bone, but it does not reach the cerebrospinal fluid in significant concentrations. It diffuses across the placenta into the fetal circulation and appears 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.

Elimination

Clindamycin undergoes metabolism, presumably in the liver, to the active N-demethyl and sulphoxide metabolites and also some inactive metabolites. About 10% of the drug 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.

5.3 Preclinical Studies

There is evidence from animal studies that high doses of Clindamycin Hydrochloride calcium salt led to formation of concrements and precipitates in the gallbladder of dogs and monkeys, which proved to be reversible. Animal studies produced no evidence of toxicity to reproduction and genotoxicity. Carcinogenicity studies on Clindamycin Hydrochloride were not conducted.

6. PHARMACEUTICAL EXCIPIENTS

6.1 List of excipients

- Lactose Monohydrate BP
- Maize Starch BP
- Magnesium Stearate BP
- Purified Talc BP
- Empty Hard Gelatin Capsule Size “0” BP

6.2 Incompatibilities

Based on literature reports, Clindamycin Hydrochloride is not compatible with amsacrine, vancomycin, fluconazole and aminoglycosides and labetalol.

Solutions containing Clindamycin Hydrochloride should not be mixed with or added to other agents

In particular, diluents containing calcium, (e.g. Ringer's solution, Hartmann's solution) should not be used to reconstitute Clindamycin Hydrochloride vials or to further dilute a reconstituted vial for IV administration because a precipitate can form. Clindamycin Hydrochloride must not be mixed or administered simultaneously with calcium containing solutions including total parenteral nutrition.

6.3 Shelf life

36 months.

6.4 Special precaution for storage

Store at temperature below 30°C. Protect from light.

6.5 Nature contents of container

10 x 10 Capsules

6.6 Instruction for use handling and disposal

Keep out of reach of children.

7. Manufacturer name

Alpa Laboratories Limited
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8. Marketing Authority

CHEZ RESOURCES PHARMA LIMITED
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