SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT: RONKLIND 300

Generic Name of Product : CLINDAMYCIN HYDROCHLORIDE CAPSULES USP 300 MG

Strength (formula) : Each Hard gelatin capsule contains:
Clindamycin Hydrochloride Monohydrate USP 338 mg Eq. to Clindamycin…..300 mg
Excipients……Q.S.
Approved colour used in empty gelatin capsule shells

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

2.1 Qualitative & Quantitative Composition Declaration:

For 3.84.000 Capsules

Sr. No.	Ingredients	Spec.	Qty. / Cap mg	% OA.	Qty. / Cap mg with % O.A.	Qty. Req. per batch Kg
1.	Clindamycin Hydrochloride equivalent to Clindamycin*	USP	338 mg 300 mg	1.01%	342 mg	131.44
2.	Lactose	BP	76.36 mg	--	76.36 mg	29.325
3.	Microcrystalline cellulose	BP	21.84 mg	--	21.84 mg	8.389
4.	Maize starch	BP	70.56 mg	--	70.56 mg	27.096
5.	Magnesium Stearate	BP	2.56 mg	--	2.56 mg	0.984
6.	Talcum	BP	9.947 mg	--	9.947 mg	3.820
7.	AC-DI-SOL	BP	6.40 mg	--	6.40 mg	2.461
8.	Size "0" Violet/Violet Colour hard Gelatin Capsules	IHS	1.00 Nos	--	1.00 Nos	3.84 LAC Nos

* Added to compensate loss during processing.

OA: Overage, IHS : - In-House specification, BP: - British Pharmacopoeia

3. PHARMACEUTICAL FORM:

Size "0" Violet/Violet Colour hard gelatin Capsules

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

4.2 Posology and Method of Administration:

Adults

Moderately severe infection: 150 - 300 mg every six hours

Severe infection: 1200 - 1800 mg daily in divided doses given every six to eight hours

Elderly

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.

Children: 3 - 6 mg/kg every six hours depending on the severity of the infection.

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

Oral.

Clindamycin capsules should always be swallowed whole with a full glass of water. Absorption of Clindamycin is not appreciably modified by the presence of food.

4.3 Contra – Indications:

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

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 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.

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.

Clindamycin capsules contain 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 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. There are inadequate data regarding the safety of clindamycin in pregnancy. Therefore, clindamycin should only be administered to pregnant women if the potential benefit is considered to outweigh the possible risk to the foetus. After multiple doses, amniotic fluid concentrations were approximatley 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.

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

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency.

Adverse reactions identified from post-marketing experience are included in italics. 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);
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						Vaginal infection
Blood and Lymphatic System Disorders						Agranulocytosis Leukopenia Neutropenia Thrombocytopenia

						Eosinophilia
Immune System Disorders						Anaphylactoid reaction Drug reaction with eosinophilia and systemic symptom (DRESS)
Nervous System Disorders						Dysgeusia
Gastrointestinal Disorders		Abdominal pain Diarrhoea Pseudomembranous colitis (see section 4.4)	Nausea Vomiting			Oesophageal ulcer Oesophagitis
Hepatobiliary Disorders		Liver function test abnormal				Jaundice
Skin and Subcutaneous Tissue Disorders			Rash maculopapular Urticaria			Toxic epidermal necrolysis Stevens-Johnson syndrome Acute generalised exanthematous pustulosis (AGEP) Erythema multiforme Dermatitis exfoliative Dermatitis bullous Rash morbilliform Pruritis

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: J01FF01

Mode of action

Clindamycin binds to the 50S subunit of the bacterial ribosome and inhibits protein synthesis. Clindamycin has a predominately bacteriostatic action.

Mechanism of resistance

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

PK/PD relationship

The efficacy mainly depends on the duration of time during which the agent level is above the minimum inhibitory concentration (MIC) of the pathogen.

Breakpoints

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

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. 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.

5.3 Preclinical safety data

No Clinical data

6. Pharmaceutical particulars

6.1 List of Excipients

Lactose, Microcrystalline cellulose, Maize starch, Magnesium Stearate, Talcum, AC-DI-SOL

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in dry place, below 30°C. Protect from light, heat and moisture.

6.5 Nature and contents of container

10 x 10 Capsules Alu-PVC blister

6.6 Special precautions for disposal and other handling

No special instructions needed.

7. Marketing authorization holder

(Company) Name: RONAK EXIM PRIVATE LIMITED
Address: Sant Kabir Road, Behind Gendi Gate,
Police Station, Baroda – 390 001, GUJARAT
Country: INDIA
E-mail: ahmedi@ronakoverseas.com

8. Marketing authorization number(s)

Not applicable.

9. Date of first authorization/renewal of the authorization

Not applicable.

RONAK EXIM PVT. LTD. INDIA

10. Date of revision of the text

Not applicable.