SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Clindamycin ABR 300 mg capsules, hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clindamycin ABR 300 mg capsules, hard
Each hard capsule contains the active substance clindamycin hydrochloride, equivalent to 300 mg clindamycin.

Excipients with known effect: each hard capsule contains lactose monohydrate of 1.3 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules, hard

Clindamycin ABR 300 mg capsules, hard
Appearance of the capsules: hard gelatin casules with white body and blue cap.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clindamycin ABR is indicated for treatment of infections in adults and children, caused by clindamycin-susceptible microorganisms:

- Infections of the upper respiratory tract (pharyngitis, tonsillitis, otitis media).
- Infections of the lower respiratory tract (bronchitis, pneumonia, empyema, pulmonary abscess).
- Infections of the skin and soft tissues (acne, furunculosis, impetigo, cellulitis, infected wounds, abscesses).
  In erysipelas, panaritium and other similar specific infections, caused by clindamycin-susceptible pathogens, the achievement of a therapeutic effect can be expected.
- Infections of the bones and joints (osteomyelitis and septic arthritis).
- Gynaecological infections (endometritis, cellulitis, colpitis, tubo-ovarian abscesses, salpingitis, inflammatory diseases of pelvic organs).

  The product is administered in combination with an appropriate antibiotic that is active against gram-negative aerobes.

  In cervicitis, caused by *Chlamydia trachomatis*, monotherapy with clindamycin has the required therapeutic efficacy.
- Abdominal infections (peritonitis, abscesses of the abdominal cavity), in combination with antibiotics that are active against gram-negative aerobic microorganisms.
- Septicaemia and endocarditis.

In some cases of endocarditis, sufficient efficacy of clindamycin can be expected when the product has a bactericidal effect against the infection causative agent at the concentrations that are attained in the serum.

- Odontogenic infections (periodontal abscess and periodontitis).

- Encephalitis caused by Toxoplasma in patients with AIDS.
  The combination of clindamycin and pyrimethamine demonstrates therapeutic efficacy in patients intolerant to conventional therapy.

- Pneumonia caused by *Pneumosystis jiroveci* in patients with AIDS.
  For patients who do not tolerate or do not respond adequately to conventional therapy, clindamycin can be administered in combination with primaquine.

- Scarlet fever.

The use of the product should be in line with the national and local guidelines and recommendations for conducting antibacterial therapy.

4.2 Posology and method of administration

Adults and children over 14 years
Daily dose of 600 – 1,800 mg, divided in 2, 3 or 4 equal doses.

Children under 14 years
Daily dose of 8 – 25 mg/kg, divided in 3 or 4 equal doses.

In children weighing 10 kg or less, the recommended dose is 37.5 mg tid administered as age-appropriate formulation.

Elderly
No dose adjustment is required in patients with preserved hepatic and renal function (age-adjusted).

Renal impairment
Usually, no dose adjustment is required in patients with renal impairment (see section 4.4).

Hepatic impairment
Usually, no dose adjustment is required in patients with hepatic impairment (see section 4.4).

Specific indications
Infections caused by beta-haemolytic streptococci – the usual dosage regimen is applied as the duration of the treatment is not less than 10 days.

Inflammatory diseases of pelvic organs – the treatment is initiated with parenteral clindamycin in combination with an antibiotic that is active against Gram-negative aerobic bacteria.
The duration of administrations is not less than 4 days. The same should be continued for at least 48 hours after recording clinical improvement; after then, the treatment should be performed with oral clindamycin at a dose of 450 – 600 mg every 6 hours. The duration of the entire course is 10 - 14 days.

Chlamydial cervicitis – 450 – 600 mg clindamycin, 4 times daily for 10 - 14 days.

Encephalitis caused by Toxoplasma in patients with AIDS – 600 – 1200 mg every 6 hours for 14 days and then the dose should be reduced to 300 – 600 mg, four times daily. Usually, the course of therapy lasts 8 - 10 weeks. Clindamycin is co-administered with pyrimethamine at a dose of 25 – 75 mg and folic acid at a dose of 10 – 20 mg daily.

Pneumonia caused by Pneumocystis jiroveci in patients with AIDS – 300 – 450 mg clindamycin, four times daily for 21 days, is co-administered with primaquine at a dose of 15-30 mg, once daily for 21 days.

Acute streptococcal tonsillitis/pharyngitis – 300 mg twice daily for 10 days.

Method of administration

Clindamycin ABR capsules are swallowed whole with plenty of water to avoid possible oesophageal irritation.

4.3 Contraindications

- known hypersensitivity to clindamycin or to any of the excipients listed in section 6.1.
- known hypersensitivity to lincomycin.

4.4 Special warnings and precautions for use

Superinfections

During treatment with clindamycin, there is a possibility of developing superinfections (including fungal infections).
As with other antibacterial products, monitoring for symptoms of superinfections caused by non-susceptible organisms, including fungi, is recommended.

Pseudomembranous colitis of varying severity may develop. Mild clinical forms usually respond to discontinuation of the product; moderate and severe forms require treatment with electrolyte and amino acid solutions and those for parenteral nutrition, antibacterial agents with high activity against *Clostridium difficile*.

Cases of diarrhoea caused by *Clostridium difficile* (CDAD) have been reported with the use of nearly all antibacterial agents, including clindamycin, as their severity may range from mild diarrhoea to fatal colitis leading to colectomy.
CDAD should always enter into consideration in the patients, where the antibiotic treatment has been accompanied by the appearance of diarrhoea. Careful monitoring by a specialist is required, since CDAD may occur over two months after cessation of the antibiotic administration.

Renal and hepatic impairment

During long-term treatment with clindamycin (exceeding 3 weeks), regular monitoring of renal and hepatic function is required. Dose reduction is not usually required if the administration of clindamycin is over intervals of 8 or more hours.
During long-term use, monitoring of plasma concentrations in patients with renal or hepatic disorders is recommended and upon the physician's judgment, dose reduction or extension of dosing intervals should be considered, as the half-life of clindamycin is prolonged in significant renal and hepatic impairment.

Other

Clindamycin is not suitable for the treatment of meningitis, as the penetration into the cerebrospinal fluid is low and does not result in production of adequate therapeutic levels.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product because it contains lactose monohydrate as an excipient.

4.5 Interaction with other medicinal products and other forms of interaction

Erythromycin
There are data of *in vitro* antagonism between clindamycin and erythromycin. In view of possible clinical significance of this antagonism, co-administration of the two products is not recommended.

Neuromuscular blockers
Caution should be exercised upon concomitant administration of clindamycin due to the neuromuscular blocking potential of clindamycin and potentiation of neuromuscular blockers.

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 placental barrier in humans, as the estimated concentration in the amniotic fluid after repeated administration represents about 30% of the plasma levels measured in the mother.

In clinical studies in pregnant women, systemic administration of clindamycin during the second and third trimester of pregnancy did not lead to an increased incidence of congenital abnormalities. There are no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy.

Clindamycin should not to be used during pregnancy unless clearly needed.

Breast-feeding

Clindamycin is excreted in human breast milk, as the measured concentrations are in the range 0.7 – 3.8 μg/ml.
A risk for the breast-fed child cannot be excluded. The decision to continue/discontinue breast-feeding or to continue/discontinue therapy with clindamycin should be made after consideration of the benefit of clindamycin treatment for the mother and of breast-feeding for the child.

Fertility
Fertility studies conducted in rats treated with oral clindamycin showed no effects on fertility or reproduction.

4.7 Effects on ability to drive and use machines

There are no data of clindamycin effects on the ability to drive and use machines.

4.8 Undesirable effects

The following terminology has been used for the classification of undesirable effects in terms of frequency: 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 (the frequency cannot be estimated from the available data).

Blood and lymphatic system disorders	
Not known	Transient neutropenia (leukopenia), eosinophilia, agranulocytosis and thrombocytopenia
Gastrointestinal disorders	
Common	Diarrhoea, abdominal discomfort
	Pseudomembranous colitis
Uncommon	Gastritis, vomiting
Not known	Oesophageal ulcer, oesophagitis
Immune system disorders	
Not known	Anaphylactic and anaphylactoid reactions
Infections and infestations	
not known	Vaginitis, candidosis
Nervous system disorders	
Not known	Dysgeusia
Hepatobiliary disorders	
Common	Abnormal liver function tests
Not known	Jaundice
Skin and subcutaneous tissue disorders	
Uncommon	Maculopapular rash, urticaria
Not known	Stevens-Johnson syndrome, toxic dermal necrolysis, erythema multiforme, exfoliative dermatitis, morbilliform rash, pruritus, vesiculobulous dermatitis

4.9 Overdose

Clinical symptoms
The adverse events, observed at doses significantly exceeding the recommended therapeutic doses, are similar to these during the treatment with conventional therapeutic doses. The clinical manifestations of overdose with clindamycin are atypical.

Management
In the event of overdose, the administration of medicinal charcoal and general symptomatic treatment is required. Additional supportive measures, in terms of vital functions, should be also considered. Haemodialysis and peritoneal dialysis are not effective methods for eliminating clindamycin from the serum.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lincosamide antibiotics.
ATC code: J01FF01

Mechanism of action
Clindamycin is a semisynthetic antibiotic produced by substitution of the 7-(R)-hydroxyl group with 7-(S)-chlorine. It belongs to the group of lincosamides. Clindamycin inhibits bacterial protein synthesis as a result of binding the ribosomal 50s subunit and inhibiting the translocation of ribosomes.

Antibacterial spectrum
Depending on the susceptibility of the microorganism and the concentration of the antibiotic, clindamycin may act both bacteriostatically and bactericidally.

Susceptible microorganisms
Aerobic Gram(+) cocci
*Staphylococcus aureus**
Staphylococcus epidermidis (penicillinase-producing and penicillinase-non-producing strains)**
Streptococcus spp. (with the exception of *S. faecalis*)
Pneumococcus spp.

* Isolates of methicillin-susceptible *Staphylococcus aureus* are usually also sensitive to clindamycin. The antibiotic is also potentially active against many methicillin-resistant strains, but due to the isolation of a substantial number of methicillin-resistant strains, resistant to clindamycin, sensitivity testing should be conducted prior to the use of clindamycin in infections caused by these microorganisms.

** *In vitro* studies have shown rapid development of resistance to clindamycin in certain erythromycin-resistant Staphylococci.

Anaerobic Gram(-) bacteria
*Bacteroide spp. (*including *B. fragilis* and *B. melaninogenicus)*
Fusobacterium spp.

Anaerobic Gram(+) non-spore forming bacteria
Propionibacterium
Eubacterium
Actinomyces spp., including *A. israelii*

Anaerobic and microaerophilic Gram(+) cocci
Peptococcus spp.
Peptostreptococcus spp.
Microaerophilic streptococci
*Clostridia****

*** These demonstrate higher resistance to clindamycin than most of the anaerobes. Most strains of *Clostridium perfringens* are susceptible to clindamycin, but other species, e.g., *C. sporogenes* and *C. tertium*, are frequently resistant to its action. Sensitivity testing is required prior to initiating therapy with clindamycin.

Other microorganisms
Chlamydia trachomatis
Mycoplasma hominis
Mycoplasma pneumoniae
Toxoplasma gondii
Pneumocystis jiroveci
Plasmodium falciparum
Babesia microti

Commonly resistant microorganisms
Aerobic Gram(-)bacilli

Streptococcus faecalis
Nocardia species
Neisseria meningitidis
Methicillin-resistant strains of *S. aureus* and strains of *H.influenzae*

Cross-resistance between clindamycin and lincomycin has been observed under *in vitro* conditions. Antagonism between clindamycin and erythromycin and other chemical analogues of the macrolide group has been found.

5.2 Pharmacokinetic properties

Absorption
After oral administration, clindamycin is rapidly absorbed and the rate of absorption is high (≈ 90%). The bioavailability decreases with increasing the dose.

After administration of a 600 mg dose, the bioavailability approximates 53 ± 14%.

Peak plasma concentrations of about 2.5 μg/ml are attained 45 minutes, on the average, after oral administration of 150 mg clindamycin. Food does not reduce the extent of absorption of clindamycin, administered as a solid oral dosage form, but may slow it down.

Distribution
Orally administered clindamycin is extensively distributed in the body. Pharmacokinetic studies have shown that clindamycin is distributed mainly intracellularly because of its lipophylic properties – intracellular levels are 10-50 times higher than extracellular.

Plasma protein binding varies between 40% and 90%. After oral administration, no accumulation has been observed in the body. Clindamycin penetrates readily in most of the tissues and fluids. Tissue concentrations, as compared to plasma concentrations, are as follows: bone tissue 20% - 75%, human breast milk 50% - 100%, synovial fluid 50%, peritoneal fluid 50%, pleural fluid 50% - 90%, sputum 30% - 75%, foetal blood 40%, pus 30%.

Clindamycin does not penetrate through the blood-brain barrier even in cases of inflamed meninges.

Biotransformation and elimination
Clindamycin is metabolised mainly in the liver. It is excreted as a biologically active metabolite in 10% - 20% via the urine and in 4% via the faeces (N-demethyl and sulfoxide metabolites). The remainder is excreted as a metabolised, biologically inactive product via the bile and faeces.

Following administration of a single oral dose of 600 mg clindamycin, the plasma concentrations decrease polyphasically, with a mean value of the plasma half-life of ±1.5 - 3.5 hours.

In severe impairment of the renal or hepatic function, the plasma half-life is slightly prolonged.

5.3 Preclinical safety data

Preclinical data revealed no special risk for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity, reproductive toxicity and developmental toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Clindamycin ABR 300 mg capsules, hard

Silica, colloidal anhydrous
Lactose monohydrate/Maize starch (85:15)
Magnesium stearate

Hard gelatin capsule: titanium dioxide (E171), indigo carmine (E132), gelatin

6.2 Incompatibilities

Not known.

6.3 Shelf life

Three (3) years from the date of manufacture.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Clindamycin ABR 300 mg capsules, hard
8 (eight) hard gelatin capsules per PVC/AL foil blister.
2 (two) blisters with a leaflet/information for the patient per carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Antibiotic-Razgrad AD
Office 201, 68 "Aprilsko vastanie" Blvd.
7200, Razgrad, Bulgaria

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

10/2015