

Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

MYCLIN (Clindamycin 150mg/ml, solution for Injection)

2. Qualitative and quantitative composition

Each ml of solution contains clindamycin phosphate equivalent to 150 mg clindamycin.

Excipients with known effects:

Each ml of solution contains Benzyl Alcohol 9.45 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for Injection.

Clear, colourless, sterile 4 ml solution.

4. Clinical particulars

4.1 Therapeutic indications

Antibacterial. Serious infections caused by susceptible Gram-positive organisms, staphylococci (both penicillinase- and non-penicillinase-producing), streptococci (except *Streptococcus faecalis*) and pneumococci. It is also indicated in serious infections caused by susceptible anaerobic pathogens such as *Bacteroides* spp, *Fusobacterium* spp, *Propionibacterium* spp, *Peptostreptococcus* spp. and microaerophilic streptococci.

Clindamycin does not penetrate the blood/brain barrier in therapeutically effective quantities.

Consideration should be given to official guidance on the appropriate use of antibacterial agents including national and local guidelines.

4.2 Posology and method of administration

Parenteral (IM or IV administration) – see Method of administration below.

Posology:

Adults:

Serious infections: 600 mg - 1.2 g/day in two, three or four equal doses.

More severe infections: 1.2 - 2.7 g/day in two, three or four equal doses.

Single IM injections of greater than 600 mg are not recommended nor is administration of more than 1.2 g in a single one-hour infusion.

For more serious infections, these doses may have to be increased. In life-threatening situations, doses as high as 4.8 g daily have been given intravenously to adults.

Alternatively, the drug may be administered in the form of a single rapid infusion of the first dose followed by continuous IV infusion.

Paediatric population (over 1 month of age)

Serious infections: 15 - 25 mg/kg bodyweight/day in three or four equal doses.

More severe infections: 25 - 40 mg/kg bodyweight/day in three or four equal doses. In severe infections it is recommended that children be given no less than 300 mg/day regardless of body weight.

Elderly patients:

The half-life, volume of distribution and clearance, and extent of absorption after administration of clindamycin phosphate 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 should not be influenced, therefore, by age alone. See section 4.4. for other factors which should be taken into consideration.

Treatment for infections caused by beta-haemolytic streptococci should be continued for at least 10 days to guard against subsequent rheumatic fever or glomerulonephritis.

Method of administration

Parenteral (intramuscular or intravenous administration).

Clindamycin injection should be used undiluted for intramuscular administration. Clindamycin injection **must** be diluted prior to intravenous administration and should be infused over at least 10 – 60 minutes.

Dilution for IV use and IV infusion rates

The concentration of clindamycin in diluent for infusion should not exceed 18 mg per mL and **infusion rates should not exceed 30mg per minute**. The usual infusion rates are as follows:

Dose	Diluent	Time
300 mg	50 mL	10 min
600 mg	50 mL	20 min
900 mg	50-100 mL	30 min
1200 mg	100 mL	40 min

4.3 Contraindications

Clindamycin Injection is contra-indicated in patients previously found to be sensitive to clindamycin, lincomycin or to any of the excipients listed in section 6.1.

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 generalized 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).

Clindamycin Injection should only be used in the treatment of serious infections. In considering the use of the product, the practitioner should bear in mind the type of infection and the potential hazard of the diarrhoea which may develop, since cases of colitis have been reported during, or even two or three weeks following, the administration of clindamycin.

Treatment with antibacterial agents alters 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 diarrhoea (CDAD) and is a primary cause of 'antibiotic-associated colitis'.

The disease is likely to follow a more severe course in older patients or patients who are debilitated. Diagnosis is usually made by the recognition of the clinical symptoms but can be substantiated by endoscopic demonstration of pseudomembranous colitis. Colitis is a disease which has a clinical spectrum from mild, watery diarrhoea to severe, persistent diarrhoea, leucocytosis, fever, severe abdominal cramps, which may be associated with the passage of blood and mucus. If allowed to progress, it may produce peritonitis, shock and toxic megacolon. This may be fatal. The presence of the disease may be further confirmed by culture of the stool for *C. difficile* on selective media and assay of the stool specimen for the toxin(s) of *C. difficile*.

It is important to consider the diagnosis of CDAD in patients who present with diarrhoea 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. When 125 mg to 500 mg of vancomycin are administered orally four times a day for 7 - 10 days, there is a rapid observed disappearance of the toxin from faecal samples and a coincident clinical recovery from the diarrhoea. Drugs inhibiting peristalsis are contraindicated in this situation.

Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful

medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Precautions

Caution should be used when prescribing Clindamycin Injection to individuals with a history of gastro-intestinal disease, especially colitis. Since clindamycin does not diffuse adequately into cerebrospinal fluid, the drug should not be used in the treatment of meningitis.

If therapy is prolonged, liver and kidney function tests should be performed. Such monitoring is also recommended in neonates and infants. Safety and appropriate dosage in infants less than one month old have not been established.

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).

The use of clindamycin phosphate may result in overgrowth of non-susceptible organisms, particularly yeasts.

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

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

Clindamycin phosphate should not be injected intravenously undiluted as a bolus but should be infused over at least 10-60 minutes as directed in section 4.2.

Information about excipients

This medicinal product contains less than 1 mmol sodium (23mg) per ampoule i.e., essentially "sodium free".

4.5 Interaction with other medicinal products and other forms of interaction

Clindamycin administered by injection 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.

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 desmethylclindamycin. 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 Fertility, 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.

Breast-feeding

Orally and parenterally administered clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8 µg/mL. Clindamycin has the potential to cause adverse effects on the breastfed infant's gastrointestinal flora such as diarrhoea or blood in the stool, or rash. If oral or intravenous clindamycin is required by a nursing mother, it is not a reason to discontinue breastfeeding, but an alternate drug may be preferred. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for clindamycin and any potential adverse effects on the breastfed child from clindamycin or from the underlying maternal condition.

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

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. The frequency grouping is defined using the following convention:

Very Common ($\geq 1/10$)

Common ($\geq 1/100$, $< 1/10$)

Uncommon ($\geq 1/1,000$, $< 1/100$)

Rare ($\geq 1/10,000$, $< 1/1,000$)

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 Class	Organ	Common $\geq 1/100$ to $< 1/10$	Uncommon $\geq 1/1\ 000$ to $< 1/100$	Rare $\geq 1/10\ 000$ to $< 1/1\ 000$	Very rare $< 1/10\ 000$	Not known (Cannot be estimated from available data)
Infections and Infestations		pseudomembranous colitis*#				vaginal infection*
Blood and Lymphatic System Disorders						agranulocytosis*, leukopenia*, neutropenia*, thrombocytopenia*, eosinophilia
Immune System Disorders						anaphylactic shock*, anaphylactoid reaction*, anaphylactic reaction*, hypersensitivity*
Nervous System Disorders			dysgeusia			
Cardiac Disorders			cardiorespiratory arrest†§,			
Vascular Disorders		thrombophlebitis†	hypotension† §			
Gastrointestinal Disorders			diarrhoea, nausea			abdominal pain, vomiting, oesophageal ulcers, oesophagitis
Hepatobiliary Disorders						jaundice*
Skin and Subcutaneous Tissue Disorders		rash maculopapular	urticaria erythema multiforme, pruritus			toxic epidermal necrolysis (TEN)*, Stevens-Johnson syndrome (SJS)*, drug reaction with eosinophilia and systemic symptom (DRESS)*, acute generalised exanthematous pustulosis

					(AGEP)*, dermatitis exfoliative*, dermatitis bullous*, rash morbilliform*,
General Disorders and Administrative Conditions		pain†, injection site abscess†			injection site irritation†*
Investigations	liver function test abnormal				
Renal and urinary disorders					Acute kidney injury#

* ADR identified post-marketing.

† ADRs apply only to injectable formulations. # See section 4.4.

§ Rare instances have been reported following too rapid intravenous administration (see section 4.2).

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions ND PQMPs to <https://pv.pharmacyboardkenya.org>

4.9 Overdose

In cases of overdosage no specific treatment is indicated.

The serum biological half-life of lincomycin 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: Lincosamides, ATC code: J01FF01

Mode 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 protein synthesis. The action of clindamycin is predominantly bacteriostatic although high concentrations may be slowly bactericidal against sensitive strains. Although clindamycin

phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

Resistance

Resistance to Clindamycin usually occurs via macrolide-lincosamide-streptograminB (MLSB) type of resistance, which may be constitutive or inducible.

Breakpoints

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

EUCAST

Staphylococci: sensitive ≤ 0.25 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

PK/PD relationship

Efficacy is related to the ratio of the area of the concentration-time curve of unbound antibiotic to the MIC for the pathogen (fAUC/MIC).

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 pneumoniae

Streptococcus pyogenes

Viridans streptococci

Susceptible Anaerobes

Bacteroides fragilis group

Prevotella formerly known as *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.

Most Gram-negative aerobic bacteria, including the Enterobacteriaceae, are resistant to clindamycin. Clindamycin demonstrates cross-resistance with lincomycin. When tested by *in vitro* methods, some staphylococcal strains originally resistant to erythromycin rapidly developed resistance to clindamycin. The mechanisms for resistance are the same as for erythromycin, namely methylation of the ribosomal binding site, chromosomal mutation of the ribosomal protein and in a few staphylococcal isolates enzymatic inactivation by a plasmid-mediated adenylyltransferase.

5.2 Pharmacokinetic properties

General characteristics of active substance

Following parenteral administration, the biologically inactive clindamycin phosphate is hydrolysed to clindamycin. When the equivalent of 300 mg of clindamycin is injected intramuscularly, a mean peak plasma concentration of 6 microgram/ml is achieved within three hours; 600 mg gives a peak concentration of 9 microgram/ml. In children, peak concentration may be reached within one hour. When the same doses are infused intravenously, peak concentrations of 7 and 10 micrograms per ml respectively are achieved by the end of infusion. 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. *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, 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.

Characteristics in patients

No special characteristics. See section 4.4 "Special warnings and precautions for use" for further information.

5.3 Preclinical safety data

Fertility: Fertility studies in rats treated orally with up to 300 mg/kg/day (2-fold the human exposure based on mg/m²) revealed no effects on fertility or mating ability.

Pregnancy: In oral embryo-fetal development studies in rats and subcutaneous embryofetal development studies in rats and rabbits, embryo-fetal toxicity was observed at doses that produced maternal toxicity. In rats, maternal death occurred with an exposure ratio of approximately 1 relative to patient exposure. In rabbits, maternal toxicity, including abortions, occurred at exposure ratio of approximately 0.1. Embryo-fetal toxicity, including post implantation loss and decreased viability, occurred in rabbits at an exposure ratio of 0.2.

Carcinogenesis: Long term studies in animals have not been performed with clindamycin to evaluate carcinogenic potential.

Mutagenesis: Genotoxicity tests performed included a rat micronucleus test and an Ames test. Both tests were negative.

6. Pharmaceutical particulars

6.1 List of excipients

Disodium edetate (EDTA)

Sodium hydroxide

Benzyl Alcohol

Water for injections

6.2 Incompatibilities

Solutions of clindamycin salts have a low pH and incompatibilities may reasonably be expected with alkaline preparations or drugs unstable at low pH. Incompatibility has been reported with: ampicillin sodium, aminophylline, barbiturates, calcium gluconate, ceftriaxone sodium, ciprofloxacin, diphenylhydantoin, idarubicin hydrochloride, magnesium sulphate, phenytoin sodium and ranitidine hydrochloride. This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Type 1 Flint glass ampoule containing 4 ml sterile solution.

Each carton contains 1 or 5 such ampoules.

5 X 4ml Flint glass Ampoule Type-I

1 X 4ml Flint glass Ampoule Type-I

6.6 Special precautions for disposal and other handling

Clindamycin Injection has been shown to be physically and chemically compatible for at least 24 hours in 5% dextrose and sodium chloride injection solutions. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally be no longer than 24 hours at 2-8°C unless dilution has taken place in controlled and validated aseptic conditions.

The product should not be admixed with other drug products which are chemically or physically unstable at low pH (see section 6.2).

The compatibility and duration of stability of drug admixtures will vary depending upon concentration and other conditions.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Simba Pharmaceuticals Ltd.,
1st Floor, Almont Park, Westlands
P.O. Box 1541-00606, Nairobi,
Kenya.

Manufacturing site address:

Samrudh Pharmaceuticals Pvt. Ltd.,
Plot No. J-174, J-168, J-168/1, MIDC,
Tarapur, Boisar, Thane 401506
Maharashtra State.
India.

8. Marketing authorization number

CTD9953

9. Date of first registration

18/04/2023

10. Date of revision of the text:

16/09/2023

11. Dosimetry:

Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals:

Not Applicable