some strains of meticillin-resistant *Staph. aureus* are also resistant to clindamycin. In some countries and institutions there is evidence of an increase in resistance amongst the *B. fragilis* group to about 25% of strains or more. Resistance to clindamycin by anaerobes has also been reported in 10 to 20% of *Clostridium* spp. Other than *C. perfringens*, 8% of peptostreptococci, 9% of *Fusobacterium* spp., and 11% of *Prevotella* strains.

DOSAGE AND ADMINISTRATION

Clindamycin is a lincosamide antibacterial that is a chlorinated derivative of lincomycin. It is a mainly bacteriostatic drug used in the treatment of serious anaerobic infections, notably due to *Bacteroides fragilis*. Clindamycin is also used for some Gram-positive infections due to pneumococci, staphylococci, and streptococci. However, because of its potential for causing pseudomembranous colitis (see Adverse Effects) it is usually used only when alternative drugs are unsuitable. Amongst the conditions that it may be used to treat are liver abscess, actinomycosis, biliary-tract infections, staphylococcal bone and joint infections, the carrier state of diphtheria, endophthalmitis, gas gangrene, various gynaecological infections including bacterial vaginosis, endometritis, and pelvic inflammatory disease (the latter two with an aminoglycoside), intra-abdominal infections including secondary peritonitis, streptococcal pharyngitis (usually to treat the carrier state), serious respiratory-tract infections including empyema and pneumonia (especially lung abscess), septicaemia, and skin and soft-tissue infections involving heavy colonisation with streptococci or anaerobes such as necrotising fasciitis. Clindamycin is also used as part of a multidrug regimen in the treatment of anthrax. It is used in the prophylaxis of endocarditis in penicillin-allergic patients, in the prevention of perinatal streptococcal infections, and with other drugs for the prophylaxis of surgical infection. It may be used as part of a multi-drug regimen for the treatment of inhalation and gastrointestinal anthrax.

Clindamycin is given **parenterally** as the phosphate by intramuscular injection or by intermittent or continuous intravenous infusion over 10 minutes to 1 hour. Doses are again expressed in terms of the base; 1.2 g of clindamycin phosphate is equivalent to about 1 g of clindamycin. For intravenous use, the concentration of clindamycin in diluent for infusion should not exceed 18 mg/mL and the rate of infusion should be not more than 30 mg/minute. Not more than 1.2 g should be given as a single one-hour infusion, and not more than 600 mg should be given as a single intramuscular injection. The usual parenteral dose is the equivalent of 0.6 to 1.2 g of clindamycin daily in divided doses; in severe infections the dose may be increased to 2.7 g daily and up to 4.8 g daily may be given intravenously in life threatening situations.

For *prophylaxis* in adult patients at risk of developing endocarditis and who cannot be given a penicillin, an oral dose of clindamycin 600 mg, given 1 hour before procedures such as dental extractions under local or no anaesthesia, has been suggested. For high-risk patients undergoing dental procedures involving general anaesthesia and who cannot be given a penicillin, clindamycin 300 mg given intravenously over at least 10 minutes, at induction or 15 minutes before the procedure, has been suggested. However, in the UK the *BNF* and NICE now suggest that such prophylaxis is unnecessary.

ADVERSE EFFECTS & TREATMENT

Clindamycin is reported to produce diarrhoea in up to 20% of patients after systemic use. In some patient's severe antibiotic-associated or pseudomembranous colitis may develop during therapy or up to several weeks after it, and has proved fatal. It has been reported to be more frequent in middle-aged and elderly women, particularly after surgery; it may also occur rarely after topical use. Clindamycin should be stopped immediately if significant diarrhoea or colitis occurs. Protein supplementation and use of an antibacterial active against *Clostridium* spp. should be considered for severe antibiotic-associated colitis.

Other gastrointestinal effects include nausea, vomiting, abdominal pain or cramps, and oesophagitis; an unpleasant or metallic taste has occasionally been reported after high intravenous doses.

Skin rashes and urticaria, the most common hypersensitivity reactions, occur in up to 10% of patients usually after 1 to 2 weeks of therapy. Erythema multiforme, Stevens-Johnson syndrome, and exfoliative and vesiculobullous dermatitis have been reported rarely, and a few cases of anaphylaxis have occurred. Other adverse effects include transient leucopenia or occasionally agranulocytosis, eosinophilia, thrombocytopenia, polyarthritis, and abnormalities of liver function tests; in some cases, overt jaundice and hepatic damage have been reported. Renal dysfunction, shown by azotaemia, oliguria, and/or proteinuria has been reported rarely.

Although local irritation is rare, intramuscular injection has led to induration and sterile abscess, and thrombophlebitis may occur after intravenous use. Too rapid intravenous infusion can result in rare instances of cardiopulmonary arrest and hypotension. Some parenteral formulations contain benzyl alcohol which may cause fatal 'gasping syndrome' in neonates Topical application may be associated with local irritation and contact dermatitis; sufficient clindamycin may be absorbed to produce systemic effects. Cervicitis, vaginitis, or vulvovaginal irritation has been reported with intravaginal use; a small amount of systemic absorption also occurs.

PRECAUTIONS

Clindamycin should not be given to patients hypersensitive to it or to the closely related drug lincomycin. It should be used with caution in patients with a history of gastrointestinal disease, particularly colitis, and stopped immediately if significant diarrhoea or colitis occurs. Middle-aged and elderly female patients may be at greater risk of severe diarrhoea or pseudomembranous colitis. Caution has also been advised in atopic patients. Periodic tests of liver and kidney function and blood counts have been recommended in patients receiving prolonged therapy, and in infants. Caution is required during parenteral use in neonates, since some parenteral formulations contain benzyl alcohol which may cause fatal 'gasping syndrome'

INTERACTIONS

Clindamycin has neuromuscular blocking activity in high doses and may enhance the effect of other drugs with this action leading to a potential danger of respiratory depression. Clindamycin may antagonise the effects of parasympathomimetic. For mention of synergistic and antagonistic antimicrobial activity with other antibacterials.

NURSING MOTHERS

Clindamycin has been reported to appear in breast milk in the range of 0.7 to 3.8 mcg/mL at dosages of 150 mg orally to 600 mg intravenously. Because of the potential for serious adverse reactions in nursing infants, clindamycin should not be taken by nursing mothers.

OVER-DOSAGE:

Significant mortality was observed in mice at an intravenous dose of 855 mg/kg and in rats at an oral or subcutaneous dose of approximately 2618 mg/kg. In the mice, convulsions and depression were observed.

Haemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

Storage: -

Store at temperature not exceeding 30°C. The Injection should not be refrigerated and it should not be allowed to freeze.

Improper Storage may be deteriorate the product

Medicine: - Keep out of reach of children.

Presentation: -Clindamycin Phosphate Injection IP 150mg/ml (2ml or 4 ml Pack) in a glass Ampoule.

Manufactured by:
AMERICAN REMEDIES ©
Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)
ICO: American Remedies LLC, DE, USA
Gala No. 105 to 111, 1st Flr., Bldg. No. E-15/A, Harihar Complex, Bhiwandi, Mumbai - 421302
At: Vill. Suraigur Nahan Road Paonta Sahib, Distt. Sirmour, Himachal Pradesh-173025
E-mail: info@americanremedies.in

Size L80 x H180 mm

For the use only of a Registered Medical Practitioner or a hospital or a laboratory

℞ Clindamycin Phosphate Injection I.P.

AMERICAN
Clindacan 300
Injection

FOR INTRAMUSCULAR OR INTRAVENOUS USE ONLY

Composition: -

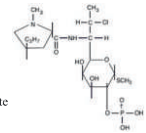
Each ml Contains: -

Clindamycin Phosphate	IP	
Eq. to anhydrous Clindamycin		150 mg
Benzyl Alcohol	IP	0.945 %v/v
(As Preservative)		
Water for Injection	IP	q.s

DESCRIPTION: -

Clindamycin Phosphate Injection IP is Sterile Solution in contains clindamycin phosphate; Clindamycin is a semisynthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent compound lincomycin.

The chemical name of clindamycin phosphate is methyl 7-chloro-6, 7, 8-trideoxy-6- [[[(2S, 4R) - 1- methyl4-propylpynolidin-2y-l] carbonyl] amino] - 1-thio-L-threo-α -D-galacto-octopyranoside-2 (dihydrogen phosphate). The molecular formula is $C_{18}H_{34}ClN_2O_8PS$ and the molecular weight is 505.0. The structural formula is represented below: -



Clindamycin Phosphate

PHARMACOLOGY

PHARMACOKINETICS

About 90% of a dose of clindamycin hydrochloride is absorbed from the gastrointestinal tract; concentrations of 2 to 3 micrograms/mL occur within 1 hour after a 150-mg oral dose, with average concentrations of about 700 nanograms/mL after 6 hours. After doses of 300 and 600 mg, peak plasma concentrations of 4 and 8 micrograms/mL, respectively, have been reported. Absorption is not significantly diminished by food in the stomach but the rate of absorption may be reduced. Clindamycin palmitate hydrochloride is rapidly hydrolysed on oral use to free clindamycin. After parenteral use, the biologically inactive clindamycin phosphate is also hydrolysed to clindamycin. When the equivalent of 300 mg of clindamycin is injected intramuscularly, a mean peak plasma concentration of 6 micrograms/mL occurs within 3 hours; 600 mg gives a peak concentration of 9 micrograms/mL. In children, peak concentrations may occur within 1 hour. When the same doses are infused intravenously, peak concentrations of 7 and 10 micrograms/mL occur by the end of infusion. Small amounts of clindamycin may be absorbed after topical application to the skin; bioavailability from topical preparations of the hydrochloride and phosphate (the former in an extemporaneous formulation) has been reported to be about 7.5% and 2% respectively. About 5% of a dose may be absorbed systemically from an intravaginal cream formulation; absorption from vaginal pessaries is reported to be about 30%. 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 preterm neonates and in patients with severe renal impairment. Clindamycin undergoes metabolism, presumably in the liver, to the active *N*-demethyl and sulfoxide metabolites, and also to 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.

ANTIMICROBIAL ACTION

Clindamycin is a lincosamide antibacterial with a primarily bacteriostatic action against Gram-positive aerobes and a wide range of anaerobic bacteria.

Mechanism of action. 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 mainly bacteriostatic, although high concentrations may be slowly bactericidal against sensitive strains. *Spectrum of activity.* Clindamycin is active against:

- most aerobic Gram-positive bacteria including streptococci, staphylococci, *Bacillus anthracis*, and *Corynebacterium diphtheriae*
- enterococci are generally resistant
- susceptible Gram-positive anaerobes include *Eubacterium*, *Propionibacterium*, *Peptococcus*, and *Peptostreptococcus* spp., and many strains of *Clostridium perfringens* and *Cl. tetani*
- Gram-negative anaerobes susceptible to clindamycin include *Fusobacterium* spp. (although *F. varium* is usually resistant), *Prevotella* spp., and *Bacteroides* spp., including the *B. fragilis* group
- several *Actinomyces* spp. and *Nocardia asteroids* are reported to be susceptible
- *Mycoplasma* spp. is generally resistant
- most Gram-negative aerobic bacteria, including the Enterobacteriaceae, are resistant to clindamycin; unlike erythromycin, *Neisseria gonorrhoeae*, *N. meningitidis*, and *Haemophilus influenzae* are generally resistant
- Fungi, yeasts, and viruses are also resistant; however, clindamycin has been reported to have some antiprotozoal activity against *Toxoplasma gondii* and *Plasmodium* spp.

Activity with other antimicrobials. Synergistic activity has been reported between clindamycin and ceftazidime or metronidazole, and also with ciprofloxacin against some anaerobes. However, there is some evidence that clindamycin inhibits the bactericidal activity of the aminoglycosides, although conflicting reports have suggested variable degrees of synergy against anaerobic organisms. Because of the adjacency of their binding sites on the ribosome, clindamycin may competitively inhibit the effects of macrolides or chloramphenicol. Clindamycin has been reported to diminish the activity of ampicillin *in vitro* against *Staph. aureus*.

It is reported to enhance the activity of primaquine against *Pneumocystis jirovecii*. Antagonism between clindamycin and erythromycin has been shown *in vitro*. *Resistance.* Most Gram-negative aerobes, such as the Enterobacteriaceae, *Pseudomonas* spp., and *Acinetobacter* spp., are intrinsically resistant to clindamycin, but acquired resistance also occurs in normally sensitive strains. The **mechanisms** of resistance are the same as those for erythromycin, namely methylation of the ribosomal binding site, chromosomal mutation of the ribosomal protein, and, in a few staphylococcal isolates, enzymic inactivation by a plasmid-mediated adenyltransferase. Methylation of the ribosome leads to cross-resistance between the lincosamides and macrolides and streptogramins (the MLSB phenotype); this type of resistance is usually plasmid-mediated and inducible.

Complete cross-resistance exists between clindamycin and lincomycin. The **incidence** of resistance varies with the organism and the geographical location; it is more frequent in organisms that are also erythromycin-resistant, and