CLINDAMYCIN Phosphate

CLINDAL

150 mg/mL (300 mg/2 mL, 600 mg/4 mL)
Solution for Injection (I.M./I.V.)
Antibacterial (Lincosamide)

FORMULATION:
Each mL contains:
Clindamycin (as phosphate), USP..... 150 mg

DESCRIPTION:
Clindamycin is a sterile colorless solution filled in amber glass ampoule.

PHARMACOKINETICS:
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 μg/mL is achieved within three hours; 600 mg gives a peak concentration of 9 μg/mL. In children, peak concentration may be reached within one hour. When the same doses are infused intravenously, peak concentrations of 7 and 10 μg/mL, respectively are achieved by the end of infusion.
Clindamycin is widely distributed in body fluids and tissues including the 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 remove from the blood by dialysis.

PHARMACODYNAMICS:
Clindamycin is an antibiotic, similar to and a derivative of lincomycin. Clindamycin can be used in topical or systemic treatment. It is effective as an anti-anaerobic antibiotic and antiprotozoal.

INDICATIONS:
Antibacterial, serious infections caused by susceptible gram-positive organism, stapylococci (both penicillinase and non-penicillinase producing), streptococci (except *Streptococcus faecalis*) and pneumococci. It is also indicated in serious infections caused by susceptible anaerobic pathogens.
Clindamycin does not penetrate the blood brain barrier in therapeutically effective quantities.

DOSAGE AND ADMINISTRATION:
1) 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.
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 I.V. infusion.

To maintain serum clindamycin levels	Rapid infusion rate	Maintenance infusion rate
Above 4 μg/mL	10 mg/min for 30 min	0.75 mg/min
Above 5 μg/mL	15 mg/min for 30 min	1.00 mg/min
Above 6 μg/mL	20 mg/min for 30 min	1.25 mg/min

Single I.M. injections of greater than 600 mg are not recommended.
2) Children (over 1 month of age):
Serious infections: 15-25 mg/kg/day in three or four equal doses.
More severe infections: 25-40 mg/kg/day in three or four equal doses.
Or as prescribed by the physician.
3) Treatment for infections caused by beta-haemolytic streptococci should be continued for at least 10 days to guard against subsequent rheumatic fever or glomerulonephritis.
4) Dilution and infusion rates:
Clindamycin must be diluted prior to I.V. administration. The concentration of clindamycin in diluent for infusion should not exceed 18 mg per mL. Infusion rates should not exceed 30 mg per minute. The usual infusion dilutions and rates are as follows:

Dose	Diluent	Time
300 mg	50 mL	10 min
600 mg	50 mL	20 min
900 mg	100 mL	30 min
1,200 mg	100 mL	40 min

Administration of more than 1,200 mg in a single 1 hour infusion is not recommended. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
5) Dilution and compatibility:
Physical and biological compatibility studies monitored for 24 hours at room temperature have been demonstrated no inactivitation or incompatibility with the use of clindamycin I.V. solutions containing sodium chloride, glucose, calcium or potassium, and solutions containing vitamin B complex in concentrations usually used clinically. No incompatibility has been demonstrated with the antibiotics cephalothin, kanamycin, gentamicin, penicillin, or carbenicillin.
The following drugs are physically incompatible with clindamycin phosphate: ampicillin sodium, phenytoin sodium, barbiturates, aminophylline, calcium gluconate, and magnesium sulfate.
The compatibility and duration of stability of drug admixtures will vary depending on concentration and other conditions.

CONTRAINDICATIONS:
Patient with a history of hypersensitivity to lincomycin or clindamycin.

WARNINGS:
Clindamycin 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 diarrhea which may develop, since cases of colitis have been reported during, or even two or three weeks following the administration of clindamycin.
Studies indicate a toxin(s) produced by clostridia (especially *Clostridium difficile*) is the principal direct cause of antibiotic-associated colitis. These also indicate that this toxigenic clostridium is usually sensitive in vitro to vancomycin. When 125 mg or 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 diarrhea. (When the patient is receiving cholestyramine in addition to vancomycin, consideration should be given to separating the times of administration).
Colitis is a disease which has a clinical spectrum from mild, watery diarrhea to severe, persistent diarrhea, leukocytosis, 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 appearance of marked diarrhea should be regarded as an indication that the product should be discontinued immediately. The disease is likely to follow a more severe course in older 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. The presence of the disease may be further confirmed by culture of the stool for *Clostridium difficile* on selective media and assay of the stool specimen for the toxin(s) of *C. difficile.*

OVERDOSE AND TREATMENT:
1) There is no specific antidote or treatment for overdose. The serum half-life of clindamycin is 2.4 hours. Clindamycin is not effective for hemodialysis and peritoneal dialysis to remove clindamycin in serum. If allergic reactions occur, conventional emergency treatment should be given, including corticosteroids, adrenaline, and antihistamine.
2) Significant mortality was observed when 855 mg/kg was injected intravenously in mice and about 2,618 mg/kg orally or subcutaneously in rats. Cramps and depression were observed in mice.

PRECAUTIONS:
Caution should be used when prescribing clindamycin to individuals with a history of gastrointestinal disease, especially colitis. Periodic liver and kidney function tests should be carried out during prolonged therapy. Such monitoring is also recommended in neonates and infants.
The dosage of clindamycin may require reduction in patients with renal or hepatic impairment due to prolongation of the serum half-life. Prolonged administration of clindamycin, 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 in atopic individuals.

SIDE EFFECTS:
1) Gastrointestinal tract: Nausea, vomiting, abdominal pain, and diarrhea.
2) Haematopoetic: Transient neutropenia (leucopenia), eosinophilia, agranulocytosis, and thrombocytopenia have been reported.
No direct etiologic relationship to concurrent clindamycin therapy could be made in any of the foregoing.
3) Skin and mucous membranes: Pruritus, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported.
4) Hypersensitivity reactions: Maculopapular rash and urticaria have been observed during drug therapy. Generalized mild to moderate morbilliform-like skin rashes are the most frequent reported reactions.
Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome have been associated with clindamycin.
A few cases of anaphylactic reactions have been reported.
5) Liver: Jaundice and abnormalities in liver function tests have been observed during clindamycin therapy.

DRUG 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.

PREGNANCY AND LACTATION:
Safety for use in pregnancy has not been established.
Clindamycin is excreted in human milk. Caution should be exercised when clindamycin is administered to nursing mother. It is unlikely that a nursing infant can absorb a significant amount of clindamycin from its gastrointestinal tract.

PRECAUTIONS DURING ADMINISTRATION:
Because esophagus ulcer may occur if this drug stays and disintegrates in esophagus, administer with water or milk and be careful to administer this drug right before sleep.

STORAGE:
Store at temperatures not exceeding 30°C.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription

PACKAGING:
USP Type I Amber Glass Ampoule x 2 mL and 4 mL (Box of 10's)

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction."

Registration Number: DR-XY33407
Date of Renewal of Authorization: August 2024
Date of Revision of Package Insert: November 2024

Manufactured by:
UNION KOREA PHARM. CO., LTD.
247, Munmakgongdan-gil, Munmak-eup, Wonju-si, Gangwon-do, Republic of Korea
Tel: 82-2-489-3611 Fax: 82-2-487-3611

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ONE PHARMA
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