Natrapharm

CLINDAMYCIN phosphate

Peldacyn®

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

℞

FORMULATION
Each 2mL ampoule contains:
Clindamycin (as phosphate).....300 mg
Each 4mL ampoule contains:
Clindamycin (as phosphate).....600 mg

Clindamycin is active against most gram-positive bacteria and gram-negative bacteria *like Bacteroides, Fusobacterium* Species. Especially it is highly active against *Staphylococcus aureus*. Clindamycin is better absorbed into gastrointestinal tract, and has stronger antibacterial action and has less side effect than lincomycin, and shows better therapeutical profile.

Clindamycin Injection is active against penicillin resistant microorganism, hence it has been effectively used as replacement of penicillin preparations if applicable.

Appearance: Amber glass ampoule with colorless and transparent liquid.

INDICATIONS
1. Susceptible strains
Bacteroides species, Fusobacterium species, Propionibacterium, Eubacterium, actinomyces species, Peptococcus species, Peptostreptococcus species. Staphylococci, Streptococci (except Streptococcus faecalis), Pneumococci.
2. Indications
Pneumonia, lung abscess, otitis media, pharyngitis, tonsillitis, bronchitis, sinusitis, scarlet fever, cellulites, peritonitis, intra-abdominal abscess, endometritis, nongonococcal tuboovarian abscess, pelvic cellulites, postsurgical vaginal cuff infection, septicemia, furuncle, skin abscess, impetigo, acne pustule, cellulitis, infection of wound.

PHARMACODYNAMICS

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

Mechanism of resistance
Resistance to clindamycin usually occurs via macrolide-lincosamide-streptogramin B (MLSB) type of resistance, which may be constitutive or inducible. 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 ribosome binding site, chromosomal mutation of the ribosomal protein and in a few staphylococcal isolates emzymatic inactivation by a
plasmid-mediated adenyltransferase.

PHARMACOKINETICS
General characteristics of active substance
Absorption
Following parenteral administration, the biologically inactive clindamycin phosphate is hydrolysed to clindamycin. When the equivalent of 300mg of clindamycin is injected intramuscularly, a mean peak plasma concentration of 6 microgram/ml is achieved within three hours; 600mg 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.

Distribution
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. The half-life is 2 to 3 hours, although this may be prolonged in pre-term neonates and patients with severe renal impairment.

Elimination
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.

DOSAGE AND ADMINISTRATION
1. Adult
Serious infection: 600—1200 mg/day as Clindamycin phosphate divided in 2 to 4 equal doses. **More severe infection:** 1200-2700 mg/day as Clindamycin phosphate divided in 2 to 4 equal doses. Clindamycin should not be injected intravenously undiluted as a bolus, but should be infused over at least 10-60 minutes as indicated below. Drug may be administered in the form of a single rapid infusion of the first dose followed by continuous I.V. infusion as follows, for maintaining serum clindamycin level.

To maintain serum Clindamycin	Rapid Infusion rate	Maintenance Infusion rate
Above 4 mcg/mL	10 mg/min. for 30 min.	0.75 mg/min.
Above 5 mcg/mL	15 mg/min. for 30 min.	1.00 mg/min.
Above 6 mcg/mL	20 mg/min. for 30 min.	1.25 mg/min.

2. Children (over 1month of age)
Serious infection: 15~25 mg/kg/day in 3 to 4 equal doses.
More severe infection : 25~40 mg/kg/day in 3 to 4 equal doses.

3. Neonates (less than 1 month)
15 to 20 mg/kg/day in 3 to 4 equal doses. The lower dosage may be adequate for small premature infants. If it improves the condition as I.V. administration, it may be changed to oral dosing (capsules, syrups) by physician's opinion. In cases of ß-hemolytic Streptococcal infections, treatment should continue for at least 10 days.

DILUTION AND INFUSION RATES
Clindamycin phosphate 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 30mg per minute. The usual infusion dilutions and rates are as follows.

Dose	Diluent	Infusion 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.

Dilution and Compatibility
Physical and biological compatibility studies monitored for 24 hours at room temperature have demonstrated no inactivation or incompatibility with the use of clindamycin phosphate in I.V. solutions containing sodium chloride, glucose, calcium, potassium, and solutions containing Vitamin B complex in concentrations usually used clinically. No incompatibility has been demonstrated with the antibiotics cephalothin, kanamycin, gentamycin, penicillin or carbenicillin.

The following drugs are physically incompatible with clindamycin phosphate: ampicillin, phenytoin, barbiturates, aminophylline, calcium gluconates and magnesium sulfate.

PRECAUTIONS
1. Warnings
a) Clindamycin may be associated with severe colitis which may end fatally. Therefore, it should be reserved for serious infections where other antimicrobial agents are inappropriate. It should not be used in patients with nonbacterial upper respiratory infections, or mild bacterial infections. The colitis is usually characterized by severe, persistent diarrhea and severe abdominal pain and may be associated with the passage of blood and mucus. Endoscopic examination may reveal pseudomembranous colitis. When significant diarrhea occurs, the drug should be discontinued or, if necessary, continued only with close observation of the patient. Large bowel endoscopy has been recommended. Diarrhea, colitis and pseudomembranous colitis has been observed after several weeks following cessation of therapy with clindamycin.
b) This drug should not be used in the treatment of meningitis, since it does not penetrate into the cerebrospinal fluid.
c) Clindamycin should not be used in the treatment of nonbacterial upper respiratory tract infection or patients with mild bacterial infections.
"Read the instructions carefully before use, if necessary, consult your physician for further
information". "This drug is used under physician's prescription only"

2. Contraindication
a) Patients with a history of hypersensitivity to clindamycin or lincomycin.

3. Precautions during use
a) The aged, neonate, foetus immaturus
b) Patients with a history of colitis
c) Patients with a history or renal disease or hepatic disease
d) Atopic individuals
e) Patients with dysphagia
f) Patients with a history of hypersensitivity to drugs or allergic antigen.

4. Adverse Reactions
1) **Local Reactions:** Pain, insensibility and sterile abscess have been reported after intramuscular injection and thrombophlebitis after intravenous injection. Reactions can be minimized or avoided by giving deep intramuscular injections and avoiding prolonged use of indwelling intravenous catheters.
2) **Gastrointestinal:** Pseudomembranous colitis, diarrhea, nausea, vomiting, anorexia, glossitis,
stomatitis, abdominal pain and esophagitis may occur.
3) **Shock:** Patients should be closely observed during therapy because shock may occur infrequently.
Medication should be discontinued when cyanosis, dyspnea, shortness of breath, hypotension occurs.
4) **Hypersensitivity:** Maculopapular rash, urticaria and edema may occur during drug therapy.
If a hypersensitivity reaction occurs, the drug should be discontinued and in serious cases the usual
emergency treatment agents (epinephrine, corticosteroids, antihistamines) should be available.
5) **Skin:** Patients should be closely observed since Stevens-Johnson Syndrome, Lyell's Syndrome, exfoliative
dermatitis, erythema multiforme may occur and medication should be discontinued when these occur.
6) **Liver:** Jaundice and rise in S-GOT, S-GPT may occur.
7) **Kidney:** Renal dysfunction as azotomia, oliguria, proteinuria has been observed.
8) **Musculoskeletal:** Instances of polyarthritis have rarely been reported.
9) **Cardiovascular:** Rare instances of cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration.
10) **Hematopoietic:** Neutropenia, leukopenia, agranulocytosis, thrombocytopenic purpura, aplastic
ane-ma may occur.
11) **Nervous system:** Tinnitus, dizziness may occur during drug therapy.
12) **Others:** Facial flush, bitter taste, fever, headache, fatigue may occur.
INFORM YOUR DOCTOR OF ANY ADVERSE EFFECT SUFFERED FROM USING THIS DRUG.

5. General Precautions
1) In order to prevent appearance of resistant strains, susceptibility should be tested prior to treatment and should be used as short as therapeutic period needed.
2) Mild colitis could be covered by drug discontinuance. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated. Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolonged and or worsen the condition.
3) Vancomycin has been found to be effective in the treatment of pseudomembranous colitis associated with antibiotics produced by *Clostridium difficile*. The usual adult dosage is 500 mg to 2g of Vancomycin orally per day in three to four divided does administered for 7 to 10 days.
4) The use of clindamycin occasionally results in overgrowth of nonsusceptible organisms, particularly yeast.

6. Interaction
1) Clindamycin may enhance the action of peripheral muscle relaxant, such as suxametonium chloride, tubocurarine chloride, therefore, it should be used with caution in patients receiving such agents.
2) Antagonism has been demonstrated between clindamycin and erythromycin in vitro, therefore, the two drugs should not be administered concurrently.

7. Use in Pregnancy: Safety for use in pregnancy has not been established. Since clindamycin has been reported to appear in breast milk in ranges of 0.7 to 3.8 mcg/mL, it should not be used during lactation.

8. Use in Nursing mother: Clindamycin is excreted in 0.7-3.8 ug/mL in human milk. So, it should not be used in lactation.

9. Use in Newborn and Infants
When clindamycin is administered to newborns or infants, appropriate monitoring of organ system is advised.

10. Precautions during application
1) After solution, it should be used as soon as possible, store at room temperature, and should be used within 48 hours.
2) Pain, hardness at injected site may occur.
3) It should not be injected direct-intravenously, because cardiac arrest may occur after directly rapid intravenous administration.

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

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

AVAILABILITY:
USP Type 1 Amber Glass Ampoule by 2mL (Box of 10's and I's)
USP Type 1 Amber Glass Ampoule by 4mL (Box of 10's and I's)

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