**CLINDAMYCIN INJECTION, USP**

Rx only

**PHARMACY BULK PACKAGE—NOT FOR DIRECT INFUSION**

For Intravenous Use

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Clindamycin Injection, USP and other antibacterial drugs, Clindamycin Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

**DESCRIPTION:**

Clindamycin Injection, USP for intravenous use, contains clindamycin phosphate, a water soluble ester of clindamycin and phosphoric acid. Each mL contains clindamycin phosphate equivalent to 150 mcg clindamycin, 0.5 mg disodium edetate and 9.45 mg benzyl alcohol added as preservative. When necessary, pH is adjusted with sodium hydroxide and/or hydrochloric acid. Clindamycin is a semi-synthetic antibiotic produced by a 7(S)-chloro-6,7,8-trideoxy-6-[(1-methyl-4-propyl-2-threo)-d-galacto-octopyranosido, methyl 7-chloro-6,7,8-trideoxy-6-[[1-(methyl-4-propyl-2-pyrrolidinyl) carbonyl]-amino]-1-thio, 2-(dihydrogen phosphate), (2S)-].

The structural formula is represented below:

![Chemical Structure](https://via.placeholder.com/150)

**CLINDAMYCIN INJECTION, USP**

A pharmacy bulk package is a container of a sterile preparation for the manufacture of sterile products and contains many single doses. The contents are intended for use in a pharmacy admixture program utilizing a sterile transfer device and are restricted to the preparation of admixtures for intravenous infusion. FURTHER DILUTION IS REQUIRED BEFORE USE (see DOSAGE AND ADMINISTRATION).

**CLINICAL PHARMACOLOGY:**

Biologically inactive clindamycin phosphate is rapidly converted to active clindamycin.

By the end of short-term intravenous infusion, peak serum levels of active clindamycin can be reached. Biologically inactive clindamycin phosphate disappears rapidly from the serum; the average elimination half-life is 6 hours; however, the serum elimination half-life of active clindamycin is about 3 hours in adults and 2½ hours in pediatric patients.

Serum levels of clindamycin can be maintained above the in vitro minimum inhibitory concentration for most isolated organisms by administration of clindamycin phosphate every 8 to 12 hours in adults and every 8 to 12 hours in pediatric patients, or by continuous intravenous infusion. An equilibrium state is reached by the third dose.

The elimination half-life of clindamycin is increased slightly in patients with markedly reduced renal or hepatic function. Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum. Dosage schedules need not be modified in the presence of mild or moderate renal or hepatic disease.

No significant levels of clindamycin are attained in the cerebrospinal fluid even in the presence of inflamed meninges.

Pharmacokinetic studies in elderly volunteers (61 to 79 years) and younger adults (18 to 39 years) indicate that age alone does not alter clindamycin pharmacokinetics (clearance, elimination half-life, volume of distribution, and area under the serum concentration-time curve) after IV administration of clindamycin phosphate. After oral administration of clindamycin hydrochloride, elimination half-life is increased to approximately 4 hours (range 3.4 to 5.1 h) in the elderly compared to 3.2 hours (range 2.1 to 4.2 h) in younger adults. The extent of absorption, however, is not different between age groups and no dosage alteration is necessary for the elderly with normal hepatic function and normal (age-adjusted) renal function.

Serum assays for active clindamycin require an inhibitor to prevent in vitro hydrolysis of clindamycin phosphate.

**INDICATIONS AND USAGE:**

Clinical experience is limited to therapy in patients with nonbacterial infections such as: most upper respiratory tract infections, C. difficile colitis, and meningitis.

**CLINICAL PHARMACOLOGY:**

**Dosage Regimen**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Peak mcg/mL</th>
<th>Trough mcg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Adult Males (Post equilibrium)</td>
<td>600 mg IV in 30 min q8h</td>
<td>10.8</td>
</tr>
<tr>
<td>600 mg IV in 30 min q6h</td>
<td>14.1</td>
<td>1.7</td>
</tr>
<tr>
<td>Pediatric Patients (first dose)</td>
<td>5 to 7 mg/kg IV in 1 hour</td>
<td>10</td>
</tr>
</tbody>
</table>

*Data in this group from patients being treated for infection.

**Microbiology:**

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

Clindamycin has been shown to have in vivo activity against isolates of the following organisms:

- **Aerobic gram positive cocci:**
  - Staphylococcus aureus (penicillinase and non-penicillinase producing strains).
  - Staphylococcus epidermidis (penicillinase and non-penicillinase producing strains).
  - Staphylococcus epidermidis rapidly develop resistance to clindamycin.
  - Staphylococcus epidermidis (except Enterococcus faecalis).
  - Pneumococci

- **Anaerobic gram negative bacilli:**
  - Bacteroides species (including Bacteroides fragilis group and Bacteroides melaninogenicus group).
  - Fusobacterium species

- **Anaerobic gram positive nonsporeforming bacilli:**
  - Propionabacterium.
  - Eubacterium.
  - Actinomyces species

- **Anaerobic and microaerophilic gram positive cocci:**
  - Peptococcus species.
  - Peptostreptococcus species.
  - Microaerophilic streptococci

**Clostridial:** Clostridia are more resistant than most anaerobes to clindamycin. Most Clostridium perfringens are susceptible, but other species, e.g., Clostridium sporogenes and Clostridium tertium are frequently resistant to clindamycin. Susceptibility testing should be done.

**In vitro Susceptibility Testing:**

Disk diffusion technique: Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One such procedure has been recommended for use with susceptibility to clindamycin.

Reports from a laboratory using the standardized single-disk susceptibility test and a 2 mcg clindamycin disk should be interpreted according to the following criteria:

- **Susceptible organisms produce zones of 17 mm or greater,** indicating that the tested organism is likely to respond to therapy.

**Organisms of intermediate susceptibility produce zones of 5 to 16 mm,** indicating that the tested organism would be susceptible if a high dosage is used or if the infection is confined to tissues and fluids (e.g., urine), in which high antibiotic levels are attained.

- **Resistant organisms produce zones of 14 mm or less,** indicating that other therapy should be selected.

**Pharmacodynamics studies require the use of control organisms.** The 2 mcg clindamycin disk should give a zone diameter between 24 and 30 mm for S. aureus ATCC 25923.

**Dilution techniques:** A bacterial isolate may be considered susceptible if the minimum inhibitory concentration (MIC) for clindamycin is not more than 1.6 mcg/mL. Organisms are considered mod-
erately susceptible if the MIC is greater than 1.6 mcg/mL and less than or equal to 4.8 mcg/mL. Other susceptible strains of the designated organisms in the treatment of serious infections caused by susceptible strains of the designated organisms in the treatment of serious infections due to susceptible organisms.

**INDICATIONS AND USAGE:**

Topical treatment of drug-resistant bacteria and aerobic and anaerobic infections.

**Clindamycin Injection,** USP should be used only to treat or prevent infections that are known or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting an antibiotic therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Clindamycin Injection, USP is indicated in the treatment of serious infections caused by susceptible aerobic and anaerobic bacteria. Clindamycin Injection, USP is also indicated in the treatment of serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci and should be reserved for patients allergic to penicillin-allergic patients or other patients for whom, in the judgment of the physician, the potential benefits outweigh the potential risks.

**Clindamycin Injection, USP** should be strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting an antibiotic therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

**Indicated surgical procedures should be performed with appropriate antibacterial therapy. Clindamycin Injection, USP** is indicated in the treatment of serious infections caused by susceptible strains of the designated organisms in the conditions listed below:

*Streptococcus pyogenes* is considered to be an aerobic skin infection. The following reactions have been reported with the use of clindamycin.

**ADVERSE REACTIONS:**

Drug Interactions

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, concomitant administration of clindamycin in patients receiving such agents is contraindicated. The two drugs should not be administered concurrently.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term studies in animals have not been performed with clindamycin to evaluate carcinogenic potential. Genotoxicity tests performed included a rat micronucleus assay and a Salmonella mutagenesis reversion test. Both tests were negative.

**Pregnancy: Teratogenic Effects**

Reproduction studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (25 times the highest recommended adult human dose based on mg/m²) revealed no evidence of teratogenicity. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Pediatric Use**

Clindamycin has been reported to appear in breast milk in the range of 0.7 to 3.8 mcg/mL at dosages of 15 mg/kg/day or intravenously.

**Neonatal Use**

Clindamycin may result in overgrowth of nonsusceptible organisms—particularly yeasts. Should superinfections occur, appropriate measures should be taken as indicated by the clinical situation.

Clindamycin should not be injected intravenously undiluted as a single injection; it should be given at least 10 to 60 minutes as directed in the DOSAGE AND ADMINISTRATION section.

Serious anaphylactic reactions require immediate treatment with epinephrine, oxygen and intravenous fluids.

**ADVERSE REACTIONS:**

Gastrointestinal

**Antibiotic-associated colitis** (see WARNINGS), pseudomembranous colitis, abdominal pain, nausea, and vomiting. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment (see WARNINGS).

**Hypersensitivity Reactions**

**Maculopapular rash and urticaria** have been observed during drug therapy. Generalized mild to moderate morbilliform-like skin rashes are the most frequently reported of all adverse reactions. Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome, have been reported after intravenous administration of clindamycin. However, the development of antibiotic-associated colitis (Clostridium difficile) seen in association with most antibiotics occurs more frequently in the elderly (>60 years) and may be more severe. These patients should be carefully monitored for clinical evidence of pseudomembranous colitis.

Pharmacokinetic studies with clindamycin have shown impaired drug clearance in young and elderly subjects with normal hepatic function and normal (age-adjusted) renal function.

Clindamycin should not be administered concurrently with other antibiotics which usually end when the antibiotic is discontinued. If CDAD is suspected or confirmed, ongoing antibacterial therapy should be discontinued. Appropriate fluid and electrolyte management and supportive care as indicated are important. Increasing numbers of cases of Clostridium difficile colitis associated with clindamycin use, as well as with other antibiotic classes, have been reported.

**Fertility**

**Hematopoietic**

Transient neutropenia (teukopenia) and eosinophilia have been reported. Reports of agranulocytosis and thrombocytopenia have also been reported.

**Musculoskeletal**

Rare instances of polyarthralgias have been reported.

**Cardiovascular**

Rare instances of cardiomyopathy and hypotension have been reported following too rapid intravenous administration (see DOSAGE AND ADMINISTRATION section).

**OVERDOSAGE:**

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.

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

DOSAGE AND ADMINISTRATION:
If diarrhea occurs during therapy, this antibiotic should be discontinued (see WARNING box).

Adults
Parenteral IV administration
Serious infections due to aerobic gram-positive cocci and the more susceptible anaerobes (NOT generally including Bacteroides fragilis, Peptostreptococcus species and Clostridium species other than Clostridium perfringens): 600 to 1200 mg/day in 2, 3 or 4 equal doses.

More severe infections, particularly those due to proven or suspected Bacteroides fragilis, Peptostreptococcus species, or Clostridium species other than Clostridium perfringens: 1200 to 2700 mg/day in 2, 3 or 4 equal doses.

For more serious infections, these doses may have to be increased.

In life-threatening situations due to either aerobes or anaerobes these doses may be increased. Doses of as much as 4800 mg daily have been given intravenously to adults. See Dilution and Infusion Rates below.

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

To maintain serum clindamycin levels


Above 4 mcg/mL
Above 5 mcg/mL
Above 6 mcg/mL

15 to 20 mg/kg/day in 3 to 4 equal doses. The lower dosage may be adequate for small prematures.

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 prematures.

Dilution and Compatibility
Clindamycin Injection, USP must be diluted prior to IV administration. The concentration of clindamycin in the 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

300 mg
600 mg
900 mg
1200 mg

Diluent

50 mL
50 mL
50 to 100 mL
100 mL

Time

10 min
20 min
30 min
40 min

Administration of more than 1200 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.

Clindamycin Injection, USP is physically incompatible with 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.

For current information regarding compatibilities of clindamycin phosphate under specific conditions, please visit www.APPpharm.com or call our medical information and safety department toll-free at 1-800-551-7176.

REFERENCES: