Clindamycin in 5% Dextrose Injection
PREMIXED SINGLE-DOSE BOTTLES

**WARNING**

*Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin in 5% dextrose injection and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*

Because clindamycin in 5% dextrose injection therapy has been associated with severe colitis which may end fatally, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in the INDICATIONS AND USAGE section. It should not be used in patients with nonbacterial infections such as most upper respiratory tract infections. *C. difficile* produces toxins A and B which contribute to the development of CDAD. 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 diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile,* and surgical evaluation should be instituted as clinically indicated.

- Clindamycin in 5% Dextrose Injection is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

- Clindamycin in 5% Dextrose Injection is also indicated in the treatment of serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Its use should be reserved for penicillin-allergic patients or other patients for whom, in the judgment of the physician, a penicillin is inappropriate. Because of the risk of antibiotic-associated pseudomembranous colitis, as described in the WARNING box, before selecting clindamycin the physician should consider the nature of the infection and the suitability of less toxic alternatives (e.g., erythromycin).

- This drug is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.
### Clindamycin in 5% Dextrose Injection 300 mg/50 mL

**ACTIVE:** Clindamycin phosphate equivalent to 300 mg of clindamycin premixed with 5% dextrose as a sterile solution;

**PRESERVATIVE:** None;

**INACTIVES:** Disodium edetate has been added at a concentration of 0.04 mg/mL. The pH has been adjusted with sodium hydroxide and/or hydrochloric acid.

**STORAGE:** Store at 20° to 25°C (68° to 77°F); [see USP Controlled Room Temperature]. Avoid temperatures above 30°C.

### Clindamycin in 5% Dextrose Injection 600 mg/50 mL

**ACTIVE:** Clindamycin phosphate equivalent to 600 mg of clindamycin premixed with 5% dextrose as a sterile solution;

**PRESERVATIVE:** None;

**INACTIVES:** Disodium edetate has been added at a concentration of 0.04 mg/mL. The pH has been adjusted with sodium hydroxide and/or hydrochloric acid.

**STORAGE:** Store at 20° to 25°C (68° to 77°F); [see USP Controlled Room Temperature]. Avoid temperatures above 30°C.

### Clindamycin in 5% Dextrose Injection 900 mg/50 mL

**ACTIVE:** Clindamycin phosphate equivalent to 900 mg of clindamycin premixed with 5% dextrose as a sterile solution;

**PRESERVATIVE:** None;

**INACTIVES:** Disodium edetate has been added at a concentration of 0.04 mg/mL. The pH has been adjusted with sodium hydroxide and/or hydrochloric acid.

**STORAGE:** Store at 20° to 25°C (68° to 77°F); [see USP Controlled Room Temperature]. Avoid temperatures above 30°C.
Clindamycin in 5% Dextrose Injection

Premixed Single-dose Bottles

- Single-step premix vial
- No manual compounding necessary (may reduce compounding workload and simplify USP <797> compliance)¹
- Small vial footprint for automated dispensing machines
- 24 month shelf life
- Available in 300 mg/50 mL, 600 mg/50 mL, and 900 mg/50 mL premixed vials

Reference:

Clindamycin in 5% Dextrose Injection

<table>
<thead>
<tr>
<th>NDC #</th>
<th>STRENGTH</th>
<th>TOTAL CLINDAMYCIN PHOSPHATE/BOTTLE</th>
<th>SIZE</th>
<th>UNIT OF SALE</th>
<th>ORANGE BOOK CODE</th>
</tr>
</thead>
<tbody>
<tr>
<td>17478-120-50</td>
<td>6 mg/mL</td>
<td>300 mg/50 mL Single-dose Bottle</td>
<td>50 mL</td>
<td>1</td>
<td>AP</td>
</tr>
<tr>
<td>17478-121-50</td>
<td>12 mg/mL</td>
<td>600 mg/50 mL Single-dose Bottle</td>
<td>50 mL</td>
<td>1</td>
<td>AP</td>
</tr>
<tr>
<td>17478-122-50</td>
<td>18 mg/mL</td>
<td>900 mg/50 mL Single-dose Bottle</td>
<td>50 mL</td>
<td>1</td>
<td>AP</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NDC #</th>
<th>CARDINAL</th>
<th>AMERISOURCEBERGEN</th>
<th>MCKESSON</th>
<th>MORRIS DICKSON</th>
</tr>
</thead>
<tbody>
<tr>
<td>17478-120-50</td>
<td>4883252</td>
<td>10118105</td>
<td>1990605</td>
<td>380063</td>
</tr>
<tr>
<td>17478-121-50</td>
<td>4883302</td>
<td>10118106</td>
<td>1990597</td>
<td>380071</td>
</tr>
<tr>
<td>17478-122-50</td>
<td>4883310</td>
<td>10118107</td>
<td>1990589</td>
<td>380162</td>
</tr>
</tbody>
</table>

To order products call 800-932-5676 or fax 800-943-3694 • www.akorn.com

NOT FOR PRESCRIBING PURPOSES. PLEASE REFER TO INCLUDED PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION AND BOXED WARNING.
Clindamycin in 5% Dextrose Injection

To reduce the development of drug-resistant bacteria and maintain the effectiveness of clindamycin in 5% dextrose injection and other antibacterial drugs, clindamycin in 5% dextrose injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

For Intravenous Use only

WARNING

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

Clindamycin in 5% Dextrose Injection in bottle contains clindamycin phosphate equivalent to 300, 600 and 900 mg of clindamycin premixed with 5% dextrose as a sterile solution. Disodium edetate has been added at a concentration of 0.04 mg/mL. The pH has been adjusted with sodium hydroxide and/or hydrochloric acid.

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 L-threo-D-galacto-Octopyranoside, methyl-7-chloro-6, 7, 8-trideoxy-6-[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl] amino]-1-thio,-2-(dihydrogen phosphate), (2S-trans)-threo-

The molecular formula is C20H26ClIN6O12PS and the molecular weight is 504.96. The structural formula is represented below.

CLINICAL PHARMACOLOGY

Distribution

Biologically inactive clindamycin phosphate is converted to active clindamycin. By the end of short-term intravenous infusion, peak serum levels of active clindamycin are reached. After intramuscular injection of clindamycin phosphate, peak levels of active clindamycin are reached within 3 hours in adults and 1 hour in pediatric patients. Serum level curves may be constructed from IV peak serum levels as given in Table 1 by application of elimination half-lives (see Excretion). Serum levels of clindamycin can be maintained above the in vitro minimum inhibitory concentrations for most indicated organisms by administration of clindamycin phosphate every 8 to 12 hours in adults and every 6 to 8 hours in pediatric patients, or by continuous intravenous infusion. An equilibrium state is reached according to the criteria in Table 2.

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

Excretion

Biologically inactive clindamycin phosphate disappears rapidly from the serum; the average elimination half-life is 6 minutes; however, the serum elimination half-life of active clindamycin is about 3 hours in adults and 2½ hours in pediatric patients.

Special Populations

Renal/Hepatic Impairment

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.

Use in Elderly

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, 4.0 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.

Table 1 Average Peak and Trough Serum Concentrations of Active Clindamycin After Dosing with Clindamycin Phosphate

<table>
<thead>
<tr>
<th>Dosage Regimen</th>
<th>Peak mcg/mL</th>
<th>Trough mcg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Adult Males (Post Equilibrium)</td>
<td>10.9</td>
<td>2.0</td>
</tr>
<tr>
<td>600 mg IV in 30 min q6h</td>
<td>10.8</td>
<td>1.1</td>
</tr>
<tr>
<td>900 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>

Table 2. Susceptibility Interpretive Criteria for Clindamycin

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Minimal Inhibitory Concentrations (MIC in mcg/mL)</th>
<th>Disk Diffusion (Zone Diameters in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus spp.</td>
<td>≤0.5</td>
<td>S</td>
</tr>
<tr>
<td>Streptococcus pneumoniae and other Streptococcus spp.</td>
<td>≤0.25</td>
<td>I</td>
</tr>
<tr>
<td>Anaerobic Bacteria</td>
<td>≤2</td>
<td>NA</td>
</tr>
</tbody>
</table>

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation.

A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.
Clindamycin in 5% Dextrose Injection is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution 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.

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 test and an Ames Salmonella reversion test. Both tests were negative.

Fertility studies in rats treated orally with up to 300 mg/kg/day (approximately 1.1 times the highest recommended adult human dose based on mg/m²) revealed no effects on fertility or mating ability.

Pregnancy
Teratogenic effects
Pregnancy Category B
Reproductive studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (2.1 and 1.4 times the highest recommended adult human dose based on mg/m², respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (0.9 and 0.3 times the highest recommended adult human dose based on mg/m², respectively) 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 the human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers
Clindamycin has been reported to appear in breast milk in the range of 0.7 to 3.8 mg/mL at dosages of 150 mg orally to 600 mg intravenously. Because of the potential for adverse reactions due to clindamycin in neonates (see Pediatric Use), the decision to discontinue the drug should be made, taking into account the importance of the drug to the mother.

Pediatric Use
When Clindamycin in 5% Dextrose Injection is administered to the pediatric population (birth to 16 years) appropriate monitoring of organ system functions is desirable.

Usage in Newborns and Infants
The potential for the toxic effect in the pediatric population from chemicals that may leach from the single dose premixed IV preparation in glass has not been evaluated.
**Geriatric Use**

Clinical studies of clindamycin did not include sufficient numbers of patients age 65 and over to determine whether they respond differently from younger patients. However, other reported clinical experience indicates that antibiotic-associated colitis and diarrhea (due to *Clostridium difficile*) seen in association with most antibiotics occur more frequently in the elderly (>60 years) and may be more severe. These patients should be carefully monitored for the development of diarrhea.

Pharmacokinetic studies with clindamycin have shown no clinically important differences between young and elderly subjects with normal hepatic function and normal (age-adjusted) renal function after oral or intravenous administration.

**ADVERSE REACTIONS**

The following reactions have been reported with the use of clindamycin.

**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). An unpleasant or metallic taste occasionally has been reported after intravenous administration of the higher doses of clindamycin phosphate.

**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 associated with clindamycin. A few cases of anaphylactoid reactions have been reported. If a hypersensitivity reaction occurs, the drug should be discontinued. The usual agents (epinephrine, corticosteroids, antihistamines) should be available for emergency treatment of serious reactions.

**Skin and Mucous Membranes**

Pruritus, vaginitis, and rare instances of exfoliative dermatitis have been reported (see Hypersensitivity Reactions).

**Liver**

Jaundice and abnormalities in liver function tests have been observed during clindamycin therapy.

**Renal**

Although no direct relationship of clindamycin to renal damage has been established, renal dysfunction as evidenced by azotemia, oliguria, and/or proteinuria has been observed in rare instances.

**Hematopoietic**

Transient neutropenia (leukopenia) and eosinophilia have been reported. Reports of agranulocytosis and thrombocytopenia have been made. No direct etiologic relationship to concurrent clindamycin therapy could be made in any of the foregoing.

**Local Reactions**

Pain, induration and sterile abscess have been reported after intramuscular injection and thrombophlebitis after intravenous infusion. Reactions can be minimized or avoided by giving deep intramuscular injections and avoiding prolonged use of indwelling intravenous catheters.

**Musculoskeletal**

Rare instances of polyarthritides have been reported.

**Cardiovascular**

Rare instances of cardiopulmonary arrest 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, Peptococcus 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, Peptococcus 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 4680 mg daily have been given intravenously to adults. See Infusion Rates section 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:

<table>
<thead>
<tr>
<th>To maintain serum clindamycin levels</th>
<th>Rapid infusion rate</th>
<th>Maintenance infusion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above 4 mcg/mL</td>
<td>10 mcg/min for 30 min</td>
<td>0.75 mcg/min</td>
</tr>
<tr>
<td>Above 5 mcg/mL</td>
<td>15 mcg/min for 30 min</td>
<td>1.00 mcg/min</td>
</tr>
<tr>
<td>Above 6 mcg/mL</td>
<td>20 mcg/min for 30 min</td>
<td>1.25 mcg/min</td>
</tr>
</tbody>
</table>

**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 babies.

**Pediatric patients 1 month of age to 16 years**

Parenteral (IV) Administration: 20 to 40 mg/kg/day in 3 or 4 equal doses. The higher doses would be used for more severe infections. As an alternative to dosing on a body weight basis, pediatric patients may be dosed on the basis of square meters body surface: 350 mg/m²/day for serious infections and 450 mg/m²/day for more severe infections.

Parenteral therapy may be changed to oral clindamycin palmitate hydrochloride for oral solution or clindamycin hydrochloride capsules when the condition warrants and at the discretion of the physician.

In cases of β-hemolytic streptococcal infections, treatment should be continued for at least 10 days.

**Infusion Rates**

Infusion rates for Clindamycin in 5% Dextrose Injection should not exceed 30 mg per minute. The usual infusion rates are as follows:

<table>
<thead>
<tr>
<th>Dose</th>
<th>Strength</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg/50 mL</td>
<td>6 mg/mL</td>
<td>10 min</td>
</tr>
<tr>
<td>600 mg/50 mL</td>
<td>12 mg/mL</td>
<td>20 min</td>
</tr>
<tr>
<td>900 mg/50 mL</td>
<td>18 mg/mL</td>
<td>30 min</td>
</tr>
</tbody>
</table>

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.

**Compatibility**

Physical and biological compatibility studies monitored for 24 hours at room temperature have demonstrated no inactivation or incompatibility with the use of clindamycin in 5% dextrose injection in IV 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 carbencillin.

The following drugs are physically incompatible with clindamycin phosphate: ampicillin sodium, phenytoin sodium, barbiturates, amphotericin B, calcium gluconate, and magnesium sulfate.

**DIRECTIONS FOR USE**

Premixed Clindamycin in 5% Dextrose Injection is for intravenous administration using sterile equipment. If leaks are found, discard solution as sterility may be impaired. Do not add supplemental medication.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Do not use unless solution is clear and seal is intact.

**Caution:** Do not use in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.

**HOW SUPPLIED**

Clindamycin in 5% Dextrose Injection is a sterile solution of clindamycin phosphate with 5% dextrose. It is available in 50 mL clear molded glass bottle fitted with an injection stopper. Bottles are intended for single use only and are available as follows:

<table>
<thead>
<tr>
<th>Strength</th>
<th>Total Clindamycin Phosphate/bottle</th>
<th>NDC#</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mg/mL</td>
<td>300 mg/50 mL containers</td>
<td>17478-120-50</td>
</tr>
<tr>
<td>12 mg/mL</td>
<td>600 mg/50 mL containers</td>
<td>17478-121-50</td>
</tr>
<tr>
<td>18 mg/mL</td>
<td>900 mg/50 mL containers</td>
<td>17478-122-50</td>
</tr>
</tbody>
</table>

Exposure of pharmaceutical products to heat should be minimized.

**Storage:** Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Avoid temperatures above 30°C.

**ANIMAL TOXICOLOGY**

One year oral toxicity studies in Spartan Sprague-Dawley rats and beagle dogs at dose levels up to 300 mg/kg/day (approximately 1.1 and 3.6 times the highest recommended adult human dose based on mg/m², respectively) have shown clindamycin to be well tolerated. No appreciable difference in pathological findings has been observed between groups of animals treated with clindamycin and comparable control groups.

Rats receiving clindamycin hydrochloride at 600 mg/kg/day (approximately 2.1 times the highest recommended adult human dose based on mg/m²) for 6 months tolerated the drug well; however, dogs dosed at this level (approximately 7.2 times the highest recommended adult human dose based on mg/m²) vomited, would not eat, and lost weight.

**REFERENCES**


