FRESENIUS KABI

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Clindamycin
Injection, USP

Rx only

For Intramuscular and 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.

WARNING

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Clindamycin Injection, USP 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 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.

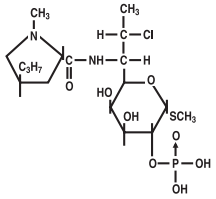
If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

DESCRIPTION:

Clindamycin Injection, USP for intramuscular and intravenous use, contains clindamycin phosphate, a water soluble ester of clindamycin and phosphoric acid. Each mL contains clindamycin phosphate equivalent to 150 mg 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 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*-α-D-*galacto*-Octopyranoside, methyl-7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl) carbonyl] amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-.

The structural formula is represented below:



$C_{18}H_{34}ClN_2O_8PS$ M.W. 504.97

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 by the third dose.

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. Dosage schedules need not be modified in the presence of mild or moderate renal or hepatic disease.

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[1].

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

Dosage Regimen	Peak mcg/mL	Trough mcg/mL
Healthy Adult Males (Post equilibrium)		
600 mg IV in 30 min q6h	10.9	2.0
600 mg IV in 30 min q8h	10.8	1.1
900 mg IV in 30 min q8h	14.1	1.7
600 mg IM q12h*	9	–
Pediatric Patients (first dose)*		
5 to 7 mg/kg IV in 1 hour	10	–
5 to 7 mg/kg IM	8	–
3 to 5 mg/kg IM	4	–

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

Microbiology

Mechanism of Action

Clindamycin inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the ribosome. Clindamycin is bacteriostatic.

Resistance

Resistance to clindamycin is most often caused by modification of specific bases of the 23S ribosomal RNA. Cross-resistance between clindamycin and lincomycin is complete. Because the binding sites for these antibacterial drugs overlap, cross-resistance is sometimes observed among lincosamides, macrolides and streptogramin B. Macrolide-inducible resistance to clindamycin occurs in some isolates of macrolide-resistant bacteria. Macrolide-resistant isolates of staphylococci and beta-hemolytic streptococci should be screened for induction of clindamycin resistance using the D-zone test.

Antimicrobial Activity

Clindamycin has been shown to be active against most of the isolates of the following microorganisms, both *in vitro* and in clinical infections, as described in the **INDICATIONS AND USAGE** section.

Gram-positive Bacteria

Staphylococcus aureus (methicillin-susceptible strains)
Streptococcus pneumoniae (penicillin-susceptible strains)
Streptococcus pyogenes

Anaerobic Bacteria

Clostridium perfringens
Fusobacterium necrophorum
Fusobacterium nucleatum
Peptostreptococcus anaerobius
Prevotella melaninogenica

At least 90% of the microorganisms listed below exhibit *in vitro* minimum inhibitory concentrations (MICs) less than or equal to the clindamycin susceptible MIC breakpoint for organisms of a similar type to those shown in Table 2. However, the efficacy of clindamycin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.

Gram-positive Bacteria

Staphylococcus epidermidis (methicillin-susceptible strains)
Streptococcus agalactiae
Streptococcus anginosus
Streptococcus mitis
Streptococcus oralis

Anaerobic Bacteria

Actinomyces israelii
Clostridium clostridioforme
Eggerthella lenta
Finegoldia (Peptostreptococcus) magna
Micromonas (Peptostreptococcus) micros
Prevotella bivia
Prevotella intermedia
Propionibacterium acnes

Susceptibility Testing Methods

When available, the clinical microbiology laboratory should provide cumulative *in vitro* susceptibility test results for antimicrobial drugs used in local hospitals and practice areas to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug for treatment.

Dilution Techniques

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method[2,3] (broth and/or agar). The MIC values should be interpreted according to the criteria provided in Table 2.

Diffusion Techniques
Quantitative methods that require the measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized method[2,5]. This procedure uses paper disks impregnated with 2 mcg of clindamycin to test the susceptibility of bacteria to clindamycin. The disk diffusion breakpoints are provided in Table 2.

Anaerobic Techniques
For anaerobic bacteria, the susceptibility to clindamycin can be determined by a standardized test method[2,4]. The MIC values obtained should be interpreted according to the criteria provided in Table 2.

Table 2. Susceptibility Test Interpretive Criteria for Clindamycin

Pathogen	Susceptibility Interpretive Criteria		
	Minimal Inhibitory Concentrations (MIC in mcg/mL)		
	S	I	R
Staphylococcus spp.	≤ 0.5	1 to 2	≥ 4
Streptococcus pneumoniae and other *Streptococcus* spp.	≤ 0.25	0.5	≥ 1
Anaerobic Bacteria	≤ 2	4	≥ 8

Pathogen	Susceptibility Interpretive Criteria		
	Disk Diffusion (Zone Diameters in mm)		
	S	I	R
Staphylococcus spp.	≥ 21	15 to 20	≤ 14
Streptococcus pneumoniae and other *Streptococcus* spp.	≥ 19	16 to 18	≤ 15
Anaerobic Bacteria	NA	NA	NA

NA=not applicable

A report of *Susceptible (S)* indicates that the antimicrobial drug is likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the site of infection. A report of *Intermediate (I)* 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 (R)* indicates that the antimicrobial drug is not likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the infection site; other therapy should be selected.

Quality Control
Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the techniques of the individuals performing the test [2,3,4,5]. Standard clindamycin powder should provide the MIC ranges in Table 3. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 2 should be achieved.

Table 3. Acceptable Quality Control Ranges for Clindamycin

QC Strain	Acceptable Quality Control Ranges
	Minimum Inhibitory Concentration Range (mcg/mL)
Enterococcus faecalis[1] ATCC 29212	4 to 16
Staphylococcus aureus ATCC 29213	0.06 to 0.25
Staphylococcus aureus ATCC 25923	NA
Streptococcus pneumoniae ATCC 49619	0.03 to 0.12
Bacteroides fragilis ATCC 25285	0.5 to 2
Bacteroides thetaiotaomicron ATCC 29741	2 to 8
Clostridium difficile[2] ATCC 700057	2 to 8
Eggerthella lenta ATCC 43055	0.06 to 0.25

Table 3. Acceptable Quality Control Ranges for Clindamycin (cont'd)

QC Strain	Acceptable Quality Control Ranges
	Disk Diffusion Range (Zone Diameters in mm)
Enterococcus faecalis[1] ATCC 29212	NA
Staphylococcus aureus ATCC 29213	NA
Staphylococcus aureus ATCC 25923	24 to 30
Streptococcus pneumoniae ATCC 49619	19 to 25
Bacteroides fragilis ATCC 25285	NA
Bacteroides thetaiotaomicron ATCC 29741	NA
Clostridium difficile[2] ATCC 700057	NA
Eggerthella lenta ATCC 43055	NA

[1] *Enterococcus faecalis* has been included in this table for quality control purposes only.
[2] Quality control for *C. difficile* is performed using the agar dilution method only, all other obligate anaerobes may be tested by either broth microdilution or agar dilution methods.
NA=Not applicable
ATCC® is a registered trademark of the American Type Culture Collection.

INDICATIONS AND USAGE:
Clindamycin Injection, USP is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

Clindamycin Injection, USP 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 **BOXED WARNING**, before selecting clindamycin the physician should consider the nature of the infection and the suitability of less toxic alternatives (e.g., erythromycin).

Bacteriologic studies should be performed to determine the causative organisms and their susceptibility to clindamycin.

Indicated surgical procedures should be performed in conjunction with antibiotic 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:

Lower respiratory tract infections including pneumonia, empyema, and lung abscess caused by anaerobes, *Streptococcus pneumoniae*, other streptococci (except *E. faecalis*), and *Staphylococcus aureus*.

Skin and skin structure infections caused by *Streptococcus pyogenes, Staphylococcus aureus,* and anaerobes.

Gynecological infections including endometritis, nongonococcal tubo-ovarian abscess, pelvic cellulitis, and postsurgical vaginal cuff infection caused by susceptible anaerobes.

Intra-abdominal infections including peritonitis and intra-abdominal abscess caused by susceptible anaerobic organisms.

Septicemia caused by *Staphylococcus aureus,* streptococci (except *Enterococcus faecalis*), and susceptible anaerobes.

Bone and joint infections including acute hematogenous osteomyelitis caused by *Staphylococcus aureus* and as adjunctive therapy in the surgical treatment of chronic bone and joint infections due to susceptible organisms.

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 susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS:
This drug is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

WARNINGS:
See **BOXED WARNING**.

Clostridium difficile-associated diarrhea
Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin 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*.

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.

Anaphylactic and Severe Hypersensitivity Reactions
Anaphylactic shock and anaphylactic reactions have been reported (see **ADVERSE REACTIONS**).

Severe hypersensitivity reactions, including severe skin reactions such as toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and Stevens-Johnson syndrome (SJS), some with fatal outcome, have been reported (see **ADVERSE REACTIONS**).

In case of such an anaphylactic or severe hypersensitivity reaction, discontinue treatment permanently and institute appropriate therapy.

A careful inquiry should be made concerning previous sensitivities to drugs and other allergens.

Benzyl Alcohol Toxicity in Pediatric Patients ("Gasping Syndrome")
This product contains benzyl alcohol as a preservative. The preservative benzyl alcohol has been associated with serious adverse events, including the "Gasping Syndrome", and death in pediatric patients. Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the "Gasping Syndrome", the minimum amount of benzyl alcohol at which toxicity may occur is not known.

The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low birth weight infants may be more likely to develop toxicity.

Usage in Meningitis – Since clindamycin does not diffuse adequately into the cerebrospinal fluid, the drug should not be used in the treatment of meningitis.

PRECAUTIONS:
General
Review of experience to date suggests that a subgroup of older patients with associated severe illness may tolerate diarrhea less well. When clindamycin is indicated in these patients, they should be carefully monitored for change in bowel frequency.

Clindamycin should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Clindamycin should be prescribed with caution in atopic individuals.

Certain infections may require incision and drainage or other indicated surgical procedures in addition to antibiotic therapy.

The use of 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 bolus, but should be infused over at least 10 to 60 minutes as directed in the **DOSAGE AND ADMINISTRATION** section.

Clindamycin dosage modification may not be necessary in patients with renal disease. In patients with moderate to severe liver disease, prolongation of clindamycin half-life has been found. However, it was postulated from studies that when given every eight hours, accumulation should rarely occur. Therefore, dosage modification in patients with liver disease may not be necessary. However, periodic liver enzyme determinations should be made when treating patients with severe liver disease.

Prescribing clindamycin injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients
Patients should be counseled that antibacterial drugs including clindamycin injection should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When clindamycin injection is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early

in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by clindamycin injection or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Laboratory Tests
During prolonged therapy periodic liver and kidney function tests and blood counts should be performed.

Drug Interactions
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/m^2) revealed no effects on fertility or mating ability.

Pregnancy
Teratogenic Effects
Pregnancy Category B
In clinical trials with pregnant women, the systemic administration of clindamycin during the second and third trimesters, has not been associated with an increased frequency of congenital abnormalities.

Clindamycin should be used during the first trimester of pregnancy only if clearly needed. There are no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy. Because animal reproduction studies are not always predictive of the human response, this drug should be used during pregnancy only if clearly needed.

Reproduction studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (2.1 and 1.1 times the highest recommended adult human dose based on mg/m^2, respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (0.9 and 0.5 times the highest recommended adult human dose based on mg/m^2, respectively) revealed no evidence of teratogenicity.

Clindamycin contains benzyl alcohol. Benzyl alcohol can cross the placenta (see **WARNINGS**).

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.

Pediatric Use
When clindamycin is administered to the pediatric population (birth to 16 years) appropriate monitoring of organ system functions is desirable.

Usage in Newborns and Infants
This product contains benzyl alcohol as a preservative. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants (see **WARNINGS**).

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.

Infections and Infestations
Clostridium difficile colitis.

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 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.

Severe skin reactions such as Toxic Epidermal Necrolysis, some with fatal outcome, have been reported (see **WARNINGS**). Cases of Acute Generalized Exanthematous Pustulosis (AGEP), erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with clindamycin. Anaphylactic shock, anaphylactic reaction and hypersensitivity have also been reported (see **WARNINGS**).

Skin and Mucous Membranes
Pruritus, vaginitis, angioedema 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.

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.

Immune System
Drug reaction with eosinophilia and systemic symptoms (DRESS) cases have been reported.

Local Reactions
Injection site irritation, 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
Polyarthritis cases have been reported.

Cardiovascular
Cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration (see **DOSAGE AND ADMINISTRATION**).

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 2,618 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 **BOXED WARNING**).

Clindamycin phosphate IM administration should be used undiluted.

Clindamycin phosphate IV administration should be diluted (see ***Dilution for IV Use and IV Infusion Rates***).

Adults
Parenteral (IM or 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 1,200 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*: 1,200 to 2,700 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 4,800 mg daily have been given intravenously to adults (see ***Dilution for IV Use and IV Infusion Rates***).

Single intramuscular injections of greater than 600 mg are not recommended.

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	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 mg/min
Above 6 mcg/mL	20 mg/min for 30 min	1.25 mg/min

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.

Pediatric Patients (1 month of age to 16 years)
Parenteral (IM or 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/m^2/day for serious infections and 450 mg/m^2/day for more severe infections.

Parenteral therapy may be changed to clindamycin palmitate hydrochloride for oral solution or clindamycin capsules (clindamycin hydrochloride) 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.

Dilution for IV Use and IV Infusion Rates
Clindamycin Injection, USP must be diluted prior to IV 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	50 to 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.

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 Injection, USP 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 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. For current information regarding compatibilities of clindamycin phosphate under specific conditions, please visit www.fresenius-kabi.us or call Fresenius Kabi USA, LLC toll-free at 1-800-551-7176.

Physico-Chemical Stability of Diluted Solutions of Clindamycin
Room Temperature: 6, 9 and 12 mg/mL (equivalent to clindamycin base) in 5% Dextrose Injection, 0.9% Sodium Chloride Injection, or Lactated Ringers Injection in glass bottles or minibags, demonstrated physical and chemical stability for at least 16 days at 25°C. Also, 18 mg/mL (equivalent to clindamycin base) in 5% Dextrose Injection, in minibags, demonstrated physical and chemical stability for at least 16 days at 25°C.

Refrigeration: 6, 9 and 12 mg/mL (equivalent to clindamycin base) in 5% Dextrose Injection, 0.9% Sodium Chloride Injection, or Lactated Ringers Injection in glass bottles or minibags, demonstrated physical and chemical stability for at least 32 days at 4°C.

IMPORTANT: This chemical stability information in no way indicates that it would be acceptable practice to use this product well after the preparation time. Good professional practice suggests that compounded admixtures should be administered as soon after preparation as is feasible.

Frozen: 6, 9 and 12 mg/mL (equivalent to clindamycin base) in 5% Dextrose Injection, 0.9% Sodium Chloride Injection, or Lactated Ringers Injection in minibags demonstrated physical and chemical stability for at least eight weeks at -10°C.

Frozen solutions should be thawed at room temperature and not refrozen.

HOW SUPPLIED:
Clindamycin Injection, USP supplied as clindamycin phosphate equivalent to clindamycin 150 mg/mL, is supplied as follows:

Product No.	NDC No.	Strength	Volume
28202	63323-282-02	300 mg per 2 mL (150 mg per mL)	2 mL fill, in a 2 mL vial.
28204	63323-282-04	600 mg per 4 mL (150 mg per mL)	4 mL fill, in a 6 mL vial.
28206	63323-282-06	900 mg per 6 mL (150 mg per mL)	6 mL fill, in a 6 mL vial.

Packaged in twenty-fives.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Do not refrigerate.

The container closure is not made with natural rubber latex.

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