

CLINDAMYCIN - clindamycin phosphate injection, solution
General Injectables & Vaccines, Inc

Clindamycin Injection, USP Fliptop Vial

To reduce the development of drug-resistant bacteria and maintain the effectiveness of clindamycin and other antibacterial drugs, clindamycin 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, 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, a water soluble ester of clindamycin and phosphoric acid, is a sterile solution for intramuscular or intravenous use.

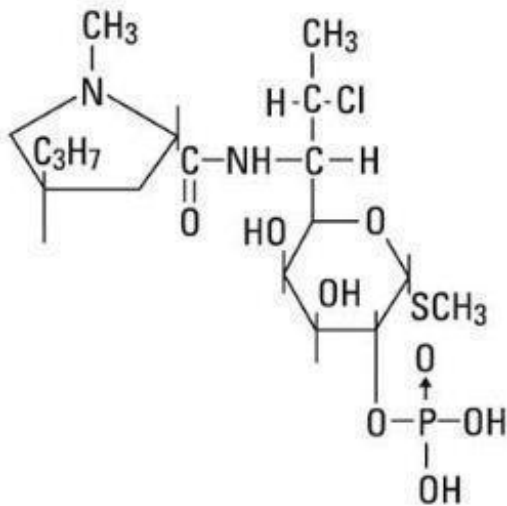
May contain sodium hydroxide and/or hydrochloric acid for pH adjustment. pH is 6.5 range 5.5 to 7.0.

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 methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-trans-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-threo- α -D-galacto-octopyranoside 2-(dihydrogen phosphate).

The molecular formula is C₁₈H₃₄ClN₂O₈PS and the molecular weight is 504.97.

The structural formula is represented below:



Each mL contains clindamycin phosphate equivalent to 150 mg clindamycin, 0.5 mg disodium edetate and 9.45 mg benzyl alcohol added as a preservative.

CLINICAL PHARMACOLOGY

Distribution

Biologically inactive clindamycin phosphate is rapidly converted to active clindamycin.

By the end of short-term intravenous infusion, peak serum levels of active clindamycin are reached. 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 2 1/2 hours in pediatric patients.

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.

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.

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 2 1/2 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 the age groups and no dosage alteration is necessary for the elderly with normal hepatic function and normal (age-adjusted) renal function¹.

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
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 q12*	9	
Pediatric Patients (first dose)*		
5-7 mg/kg IV in 1 hour	10	
5-7 mg/kg IM	8	
3-5 mg/kg IM	4	

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

Microbiology

Clindamycin inhibits bacterial protein synthesis by binding to the 50S subunit of the ribosome. It has activity against Gram-positive aerobes and anaerobes, as well as some Gram-negative anaerobes. Clindamycin is bacteriostatic. Cross-resistance between clindamycin and lincomycin is complete. Antagonism *in vitro* has been demonstrated between clindamycin and erythromycin. Clindamycin inducible resistance has been identified in macrolide-resistant staphylococci and beta-hemolytic streptococci. Macrolide-resistant isolates of these organisms should be screened for clindamycin inducible resistance using the D-zone test.

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 Aerobes:

Staphylococcus aureus (methicillin-susceptible strains)

Streptococcus pneumoniae (penicillin-susceptible strains)

Streptococcus pyogenes

Anaerobes

Prevotella melaninogenica

Fusobacterium necrophorum

Fusobacterium nucleatum

Peptostreptococcus anaerobius

Clostridium perfringens

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 trials.

Gram-positive aerobes

Staphylococcus epidermidis (methicillin-susceptible strains)

Streptococcus agalactiae

Streptococcus anginosus

Streptococcus oralis

Streptococcus mitis

Anaerobes

Prevotella intermedia

Prevotella bivia

Propionibacterium acnes

Micromonas ("Peptostreptococcus") micros

Finegoldia ("Peptostreptococcus") magna

Actinomyces israelii

Clostridium clostridioforme

Eubacterium lentum

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 the most effective antimicrobial.

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 procedure based on dilution methods (broth, agar or microdilution) 2,3 or equivalent using standardized inoculum and concentrations of clindamycin. 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 also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The standardized procedure 2,4 requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 2 mcg of clindamycin to test the susceptibility of microorganisms to clindamycin. Reports from the

laboratory providing results of the standard single-disk susceptibility test with a 2 mcg clindamycin disk should be interpreted according to the criteria in Table 2.

Table 2. Susceptibility Interpretive Criteria for Clindamycin

Pathogen	Susceptibility Interpretive Criteria					
	Minimal Inhibitory Concentrations (MIC in mcg/mL)			Disk Diffusion (Zone Diameters in mm)		
	S	I	R	S	I	R
<i>Staphylococcus</i> spp.	≤0.5	1-2	≥4	≥21	15-20	≤14
<i>Streptococcus pneumoniae</i> and other <i>Streptococcus</i> spp.	≤0.25	0.5	≥1	≥19	16-18	≤15
Anaerobic Bacteria	≤2	4	≥8	NA	NA	NA

NA=not applicable

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.

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 to be Used in Validation of Susceptibility Test Results

QC Strain	Acceptable Quality Control Ranges	
	Minimal Inhibitory Concentration Range (mcg/mL)	Disk Diffusion Range (Zone Diameters in mm)
When Testing Aerobic Pathogens		
<i>Staphylococcus aureus</i> ATCC 29213	0.06-0.25	NA
<i>Staphylococcus aureus</i> ATCC 25923	NA	24-30
<i>Streptococcus pneumoniae</i> ATCC 49619	0.03-0.12	19-25
When Testing Anaerobes		
<i>Bacteroides fragilis</i> ATCC 25285	0.5-2	NA
<i>Bacteroides thetaiotaomicron</i> ATCC 29741	2-8	NA
<i>Eubacterium lentum</i> ATCC 43055	0.06-0.25	NA

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 **WARNING** box, 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 and other antibacterial drugs, clindamycin 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 **WARNING** box.

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

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

This product contains benzyl alcohol as a preservative. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants. (See **PRECAUTIONS- Pediatric Use**).

Usage in Meningitis

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

SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. OXYGEN AND INTRAVENOUS CORTICOSTEROIDS SHOULD ALSO BE ADMINISTERED AS INDICATED.

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

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

Clindamycin phosphate should not be injected intravenously undiluted as a bolus, but should be infused over at least 10-60 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 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 should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When clindamycin 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 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/m²) revealed no effects on fertility or mating ability.

Pregnancy: Teratogenic Effects

Pregnancy Category B

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/m², 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/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 it is clearly needed.

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 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 phosphate injection 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.

The potential for the toxic effect in the pediatric population from chemicals that may leach from the single dose premixed IV preparation in plastic 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 polyarthrititis 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 (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 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 4800 mg daily have been given intravenously to adults. See **Dilution and Infusion Rates** section below.

Single IM 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	1.00 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 three to four 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/m²/day for serious infections and 450 mg/m²/day for more severe infections.

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

In cases of B-hemolytic streptococcal infections, treatment should be continued 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 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	50-100 mL	30 min
1200 mg	100 mL	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.

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 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.

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 Ringer's 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 Ringer's 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 Ringer's 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.

Caution: Do not use plastic containers 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 Injection, USP (150 mg/mL) is supplied as follows:

NDC No.	Volume	Type Container	Clindamycin base Total Content
0409-4050-01	2 mL	Single-dose fliptop vial/ 25 vials per tray	300 mg
0409-4051-01	4 mL	Single-dose fliptop vial/ 25 vials per tray	600 mg
0409-4052-01	6 mL	Single-dose fliptop vial/ 25 vials per tray	900 mg

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

Do not refrigerate.

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

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Revised: 01/2012

Hospira, Inc., Lake Forest, IL 60045 USA

SAMPLE PACKAGE LABEL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:52584-006-01	1 in 1 BAG		
1		4 mL in 1 VIAL, SINGLE-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA062800	01/03/2010	

Labeler - General Injectables & Vaccines, Inc (108250663)

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General Injectables & Vaccines, Inc