

## CLINDAMYCIN HYDROCHLORIDE - clindamycin hydrochloride capsule Stat Rx USA

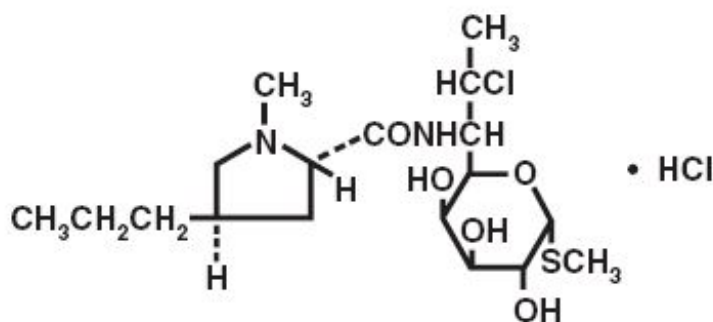
### Clindamycin Hydrochloride (clindamycin hydrochloride) Capsule

#### DESCRIPTION

Clindamycin hydrochloride is the hydrated hydrochloride salt of clindamycin. 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 for clindamycin hydrochloride is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*- $\alpha$ -D-galacto-octopyranoside monohydrochloride.

The structural formula is represented below:



$C_{18}H_{33}ClN_2O_5S \cdot HCl$  M.W. 461.45

Clindamycin hydrochloride capsules, USP for oral administration contain clindamycin hydrochloride equivalent to 150 mg or 300 mg of clindamycin.

Inactive ingredients: **150 mg** - black iron oxide, corn starch, D and C yellow #10, FD and C blue no. 1, gelatin, lactose monohydrate, magnesium stearate, talc and titanium dioxide; **300 mg** - black iron oxide, corn starch, FD and C blue no. 1, gelatin, lactose monohydrate, magnesium stearate, talc and titanium dioxide.

#### CLINICAL PHARMACOLOGY Human Pharmacology

Serum level studies with a 150 mg oral dose of clindamycin hydrochloride in 24 normal adult volunteers showed that clindamycin was rapidly absorbed after oral administration. An average peak serum level of 2.50 mcg/mL was reached in 45 minutes; serum levels averaged 1.51 mcg/mL at 3 hours and 0.70 mcg/mL at 6 hours. Absorption of an oral dose is virtually complete (90%), and the concomitant administration of food does not appreciably modify the serum concentrations; serum levels have been uniform and predictable from person to person and dose to dose. Serum level studies following multiple doses of clindamycin hydrochloride for up to 14 days show no evidence of accumulation or altered metabolism of drug.

Serum half-life of clindamycin is increased slightly in patients with markedly reduced renal function. Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

Concentrations of clindamycin in the serum increased linearly with increased dose. Serum levels exceed the MIC (minimum inhibitory concentration) for most indicated organisms for at least six hours following administration of the usually recommended doses. Clindamycin is widely distributed in body fluids and tissues (including bones). The average biological half-life is 2.4 hours. Approximately 10% of the bioactivity is excreted in the urine and 3.6% in the feces; the remainder is excreted as bioinactive

metabolites.

Doses of up to 2 grams of clindamycin per day for 14 days have been well tolerated by healthy volunteers, except that the incidence of gastrointestinal side effects is greater with the higher doses.

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.

#### 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 the 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 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*

The following *in vitro* data are available, but their clinical significance is unknown. At least 90% of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for clindamycin. However, the safety and effectiveness of clindamycin in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical 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

**NOTE:** Susceptibility testing by dilution methods requires the use of clindamycin susceptibility powder.

When available, the results of *in vitro* susceptibility tests should be provided 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. Standardized procedures are based on a dilution method (broth and agar)<sup>1,2,3</sup> or equivalent with standardized inoculum concentrations and standardized concentrations of clindamycin powder. The MIC values should be interpreted according to the criteria provided in Table 1.

### Diffusion Techniques

Quantitative methods that require the measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure<sup>2,3</sup> 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.

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 quality control microorganisms to control the technical aspects of the test procedures. **NOTE:** Quality control microorganisms are specific strains of organisms with intrinsic biological properties relating to resistance mechanisms and their genetic expression within bacteria; the specific strains used for microbiological quality control are not clinically significant.

## INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectiveness of clindamycin hydrochloride capsules and other antibacterial drugs, clindamycin hydrochloride capsules 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.

Clindamycin is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

Clindamycin 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 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).

**Anaerobes:** Serious respiratory tract infections such as empyema, anaerobic pneumonitis and lung abscess; serious skin and soft tissue infections; septicemia; intra-abdominal infections such as peritonitis and intra-abdominal abscess (typically resulting from anaerobic organisms resident in the normal gastrointestinal tract); infections of the female pelvis and genital tract such as endometritis, nongonococcal tubo-ovarian abscess, pelvic cellulitis and postsurgical vaginal cuff infection.

**Streptococci:** Serious respiratory tract infections; serious skin and soft tissue infections.

**Staphylococci:** Serious respiratory tract infections; serious skin and soft tissue infections.

**Pneumococci:** Serious respiratory tract infections.

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

## CONTRAINDICATIONS

Clindamycin hydrochloride capsules are contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

## WARNINGS

See **WARNING** box.

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.**

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

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

*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

Prescribing clindamycin hydrochloride capsules 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.

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

Clindamycin hydrochloride should be prescribed with caution in atopic individuals.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

The use of clindamycin hydrochloride occasionally results in overgrowth of nonsusceptible organisms—particularly yeasts. Should superinfections occur, appropriate measures should be taken as indicated by the clinical situation.

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.

## ADVERSE REACTIONS

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

*Gastrointestinal:* Abdominal pain, pseudomembranous colitis, esophagitis, nausea, vomiting and diarrhea (see **WARNING** box). The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment (see **WARNINGS**).

*Hypersensitivity Reactions:* Generalized mild to moderate morbilliform-like (maculopapular) skin rashes are the most frequently reported adverse reactions. Vesiculobullous rashes, as well as urticaria, have been observed during drug therapy. Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome, and a few cases of anaphylactoid reactions have also been reported.

*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.

*Musculoskeletal:* Rare instances of polyarthritis have been reported.

## 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 significant diarrhea occurs during therapy, this antibiotic should be discontinued (see **WARNING** box).

**Adults:** *Serious infections*—150 to 300 mg every 6 hours. *More severe infections*—300 to 450 mg every 6 hours. **Pediatric Patients:** *Serious infections*—8 to 16 mg/kg/day (4 to 8 mg/lb/day) divided into three or four equal doses. *More severe infections*—16 to 20 mg/kg/day (8 to 10 mg/lb/day) divided into three

or four equal doses.

To avoid the possibility of esophageal irritation, clindamycin hydrochloride capsules should be taken with a full glass of water.

Serious infections due to anaerobic bacteria are usually treated with clindamycin phosphate sterile solution. However, in clinically appropriate circumstances, the physician may elect to initiate treatment or continue treatment with clindamycin hydrochloride capsules.

In cases of  $\beta$ -hemolytic streptococcal infections, treatment should continue for at least 10 days.

#### HOW SUPPLIED

Clindamycin hydrochloride capsules are available in the following strengths, colors and sizes:

**150 mg** Turquoise blue opaque cap and light green body printed with "RX692" on cap and body in black ink.

NDC 63304-692-01 Bottles of 100

NDC 63304-692-05 Bottles of 500

NDC 63304-692-77 Blister unit-dose of 100

**300 mg** Turquoise blue opaque cap and turquoise blue opaque body printed with "RX693" on cap and body in black ink.

NDC 63304-693-16 Bottles of 16

NDC 63304-693-01 Bottles of 100

NDC 63304-693-77 Blister unit-dose of 100

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

#### Information for Patients

Patients should be counseled that antibacterial drugs including clindamycin hydrochloride capsules should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When clindamycin hydrochloride capsules are 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 hydrochloride capsules or other antibacterial drugs in the future.

#### 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, these 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 1.6 times the highest

recommended adult human dose based on mg/m<sup>2</sup>) 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 (3.2 and 1.6 times the highest recommended adult human dose based on mg/m<sup>2</sup>, respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (1.3 and 0.7 times the highest recommended adult human dose based on mg/m<sup>2</sup>, 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 mcg/mL.

### **Pediatric Use**

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

### **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.

### **WARNING**

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.**

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. Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of therapy with clindamycin.

Packaged and distributed by: **STAT R<sub>x</sub> USA** Gainesville, GA 30501

**Clindamycin**  
150mg 30 Caps

Generic For: **Cleocin**

**NDC 16590-057-30**

Prod# 057-30  
Lot# SAMPLE

Each Capsule Contains: Clindamycin Hcl. USP  
150mg

Mfg By: Ranbaxy Pharm., Inc.  
Jacksonville, FL 32257

NDC 63304-692-01

Mfg Lot: SAMPLE

Discard After: 01/12

MD 7/17/2009 9259997

**RX ONLY-KEEP OUT OF REACH OF CHILDREN**

Dosage: See package insert  
Store between 59-86 degrees F

AK8TJ

Caution: Federal law prohibits transfer of this drug to any person other than the patient for whom it was prescribed.

**IMPORTANT: Finish all this medication unless otherwise directed by prescriber.**



16590-057-30

## CLINDAMYCIN HYDROCHLORIDE

clindamycin hydrochloride capsule

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:16590-057(NDC:63304-692)
<b>Route of Administration</b>	ORAL		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
clindamycin hydrochloride (UNII: T20OQ1YN1W) (clindamycin - UNII:3U02EL437C)	clindamycin hydrochloride	150 mg

### Product Characteristics

<b>Color</b>	blue (BLUE (Turquoise blue) , GREEN (light green) )	<b>Score</b>	2 pieces
<b>Shape</b>	CAPSULE	<b>Size</b>	19mm
<b>Flavor</b>		<b>Imprint Code</b>	RX692
<b>Contains</b>			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:16590-057-20	20 in 1 BOTTLE		
2	NDC:16590-057-30	30 in 1 BOTTLE		
3	NDC:16590-057-40	40 in 1 BOTTLE		
4	NDC:16590-057-60	60 in 1 BOTTLE		

### Marketing Information



Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065061	02/02/2001	

**Labeler** - Stat Rx USA (786036330)

Revised: 10/2009

Stat Rx USA