CLINDAMYCIN HYDROCHLORIDE - clindamycin hydrochloride capsule
Lake Erie Medical DBA Quality Care Products LLC

Clindamycin Hydrochloride 150 mg

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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 (61-79 years) and younger adults (18-39 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 3.4-5.1 h) in the elderly compared to 3.2 hours (range 2.1-4.2 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 functio

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

INDICATIONS AND USAGE

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.

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

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

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. Prescribing clindamycin hydrochloride 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.

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 injection. However, in clinically appropriate circumstances, the physician may elect to initiate treatment or continue treatment with clindamycin hydrochloride capsules.

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

HOW SUPPLIED

Clindamycin Hydrochloride Capsules USP (equivalent to 150 mg of Clindamycin) are opaque gray and opaque pink capsules imprinted **DAN 5708** supplied in bottles of 100.

Clindamycin Hydrochloride Capsules USP (equivalent to 300 mg of Clindamycin) are opaque pink capsules imprinted **DAN 3120** supplied in bottles of 16 and 100.

Information for Patients

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

WARNING

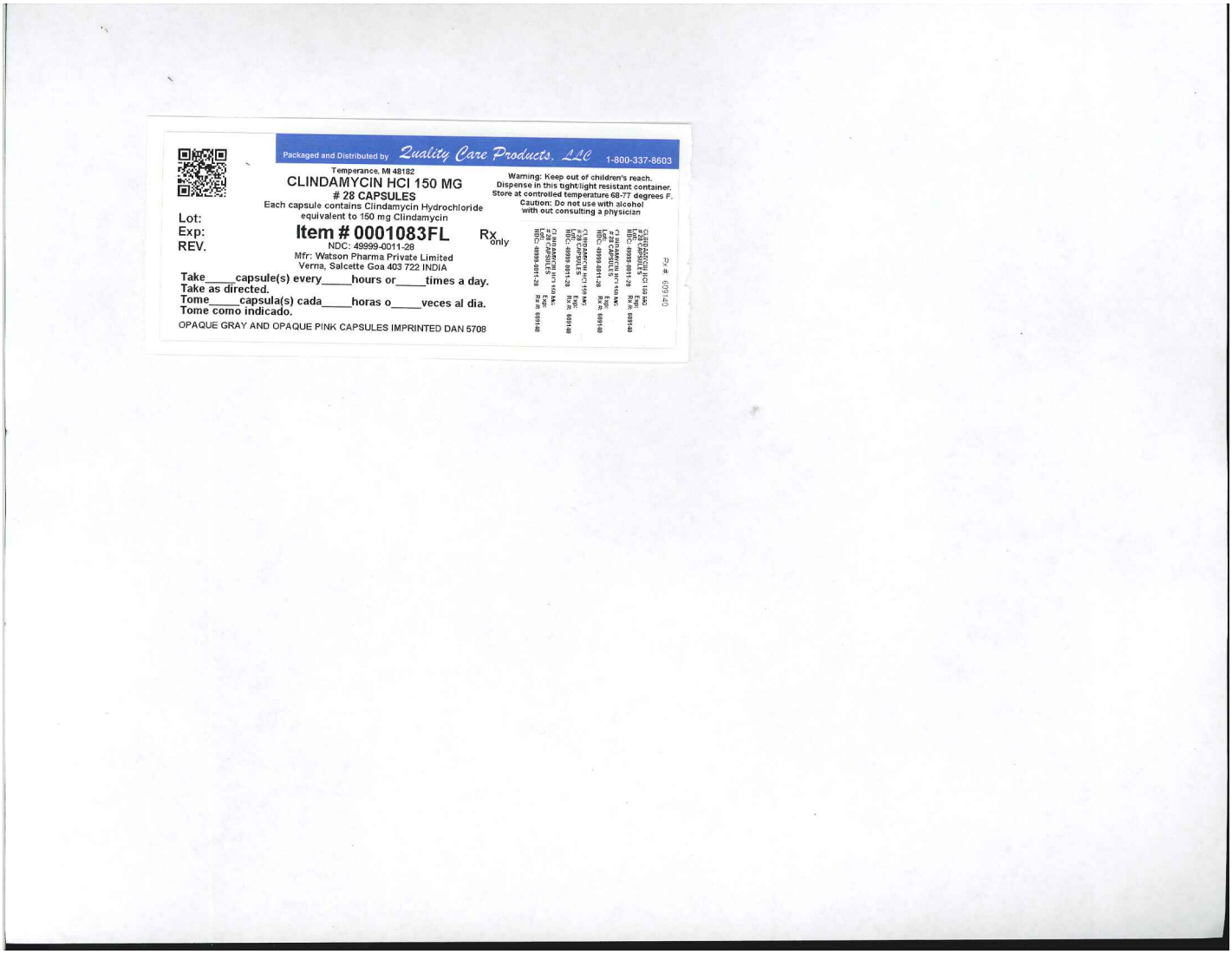
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial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

Image of label



CLINDAMYCIN HYDROCHLORIDE

clindamycin hydrochloride capsule

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:49999-011(NDC:0591-5708)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CLINDAMYCIN HYDROCHLORIDE (UNII: T20OQ1YN1W) (CLINDAMYCIN - UNII:3U02EL437C)	CLINDAMYCIN HYDROCHLORIDE	150 mg

Inactive Ingredients	
Ingredient Name	**Strength**
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
STARCH, CORN (UNII: O8232NY3SJ)	

TALC (UNII: 7SEV7J4R1U)	
D&C RED NO. 28 (UNII: 767IP0Y5NH)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
GELATIN (UNII: 2G86QN327L)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	

Product Characteristics

Color	gray (opaque gray) , pink (opaque pink)	**Score**	no score
Shape	CAPSULE	**Size**	19mm
Flavor		**Imprint Code**	DAN;5708
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:49999-011-28	10 in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA063083	11/08/2010	

Labeler - Lake Erie Medical DBA Quality Care Products LLC (831276758)

Establishment

Name	Address	ID/FEI	Business Operations
Lake Erie Medical DBA Quality Care Products LLC		831276758	repack

Establishment

Name	Address	ID/FEI	Business Operations
Watson Pharma Private Limited		677605709	manufacture

Revised: 11/2010 Lake Erie Medical DBA Quality Care Products LLC