CLINDAMYCIN HYDROCHLORIDE CAPSULES USP

1. Only

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

WARNING

Pseudomembranous colitis has been reported with nearly all antibacterial agents and can rarely occur as the initial manifestation of antibiotic-associated colitis. Therefore, it is important to consider this diagnosis in patients who present with diarrhea following antibiotic therapy.

Because clindamycin is produced by a strain associated with severe colitis which may be fatal, it should be reserved for serious infections where less toxic antibiotic agents are inadequate, 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 may be treated with discontinuation of the responsible antibacterial drug and sufficient fluid and electrolyte therapy.

Serious, unusual, or large volume diarrheal disease may require treatment with fluids, electrolytes, and in some cases, of metronidazole or vancomycin.

Clostridium difficile colitis has been associated with the use of clindamycin.

CLINDAMYCIN HYDROCHLORIDE is the hydrated hydrochloride salt of clindamycin, a semisynthetic lincosamide antibiotic produced by a 7(S)-

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 anaerobic bacteria. However, some bacteria have been isolated from human pathogens that are resistant to clindamycin. Therefore, it is important to consider this diagnosis in patients who present with diarrhea following antibiotic therapy.

In clinical infections, as described in the INDICATIONS AND USAGE section.

Table 2.  Acceptable Quality Control Ranges for Clindamycin to be Used in Validation of the Proposed Method

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When Testing Aerobic Pathogens

When Testing Standard Aerobes

Bacteroides fragilis ATCC 25295

Bacteroides fragilis ATCC 29741

Enterococcus faecalis ATCC 43055

NA = not applicable

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Clindamycin hydrochloride must 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 modifications 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 capsules, USP 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 hydrochloride capsules, USP should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When clindamycin hydrochloride capsules, USP 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 decrease the effectiveness of the immediate treatment and increase the likelihood that bacteria will develop resistance and will not be treatable by clindamycin hydrochloride capsules, USP 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/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 (3.2 and 1.6 times the highest recommended adult human dose based on mg/m², respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (1.3 and 0.7 times the highest recommended human dose measured on mg/m², respectively) revealed no evidence of teratogenicity. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of the human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Clindamycin has been reported to appear in breast milk in the range of 0.7 to 3.8 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.

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 anuria 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 polyarthritides 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 2818 mg/kg. In the mice, convulsions and depression were observed.

Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

DOSE 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 - 200 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 therapy or continue treatment with clindamycin hydrochloride capsules.

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

HOW SUPPLIED

Clindamycin hydrochloride capsules, USP contain clindamycin hydrochloride equivalent to 150 mg or 300 mg of clindamycin and are available as:

150 mg: red cap/blue body, imprinted “93” – “3171” in bottles of 100.

300 mg: light blue opaque colored cap and body, imprinted “93” – “3256” in bottles of 16 and 100.

Store at 20° to 25°C (68° to 77°F) (See USP Controlled Room Temperature). Dispense in a tight container as defined in the USP/NF.

References


Manufactured By: TEVA PHARMACEUTICALS USA

Sellersville, PA 18960


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