I-DLM-1

ALBERTA'S PRIDE

C7GQ

Clindamycin HCl

Dalamax®

℞

300 mg Capsule
ANTIBACTERIAL (LINCOSAMIDE)

FORMULATION

Each capsule contains:
Clindamycin (as Hydrochloride), BP..... 300 mg

PRODUCT DESCRIPTION

Clindamycin HCl (Dalamax) capsule is a white opaque, hard gelatin capsule with white to off white powder.

Clindamycin is a chlorine substituted derivative of lincomycin but is 20 times more potent than lincomycin against staphylococci and several streptococci organisms. It exerts bacteriostatic action against Gram-positive organisms and a wide scope of anaerobic pathogens. Clindamycin also possesses some antiprotozoal property.

When other antibiotics are inappropriate, clindamycin is used to treat anaerobic staphylococcal and streptococcal infections in endocarditis.

INDICATIONS

Clindamycin is a lincosamide bacteriostatic antibacterial which is used to treat anaerobic infections and some staphylococcal and streptococcal infections. However, because clindamycin may pose a risk of serious adverse effect, this drug is recommended only when penicillin or any alternative drug is not readily available or is inappropriate.

Clindamycin is used to treat gastrointestinal infections caused by *Bacteroides fragilis* and is an alternative drug for the treatment of infections caused by oropharyngeal strains of *B. fragilis.*

Clindamycin is also used in the treatment of respiratory tract infections and pharyngitis or tonsilitis caused by *Streptococcus pyogenes,* as well as in the treatment of other infections caused by *Fusobacterium*, anaerobic streptococci, *Clostridium perfringens* and penicillin-resistant strains of *Staphylococcus aureus.*

Other conditions where clindamycin is of benefit include liver abscess, actinomycosis, biliary tract infections, staphylococcal bone and joint infections, the carrier state of diphtheria, gas gangrene, gynecological infections such as bacterial vaginosis necrotizing fasciitis, secondary peritonitis, aspiration pneumonia, pneumonia including lung abscess, septicemia, skin disorders with heavy streptococci or anaerobe colonization.

Clindamycin is used in combination with an aminoglycoside or metronidazole to treat penetrating wounds of the abdomen and gut, infections originating in the female genital tract, endometriosis and pelvic inflammatory disease.

Clindamycin is used for endocarditis prophylaxis in patients allergic to penicillin. It is also used as a prophylaxis for surgical infection, in combination with other drugs, and prophylaxis to prevent perinatal streptococcal infections.

Clindamycin exerts some protozoal activity especially in babesiosis, malaria and toxoplasmosis. It is also used with primaquine in the management of pneumocystis pneumonia.

ACTION

Clindamycin is a lincosamide bacteriostatic antibiotic that exerts action against Gram-positive organisms and a wide scope of anaerobic pathogens. It inhibits the early stages of protein synthesis by interfering with the formation of initiation complexes and with aminoacyl translocation reactions.

SPECTRUM

Clindamycin exerts bacteriostatic action against Gram-positive organisms such as *streptococci, staphylococci, Bacillus anthracis and Corynebacterium diphtheriae.*

Among the Gram-positive anaerobes susceptible to clindamycin are *Eubacterium, Propionebacterium, Peptococcus, Peptostreptococcus, Cl. perfringens, and Cl. tetani.* Susceptible Gram negative anaerobes include *Fusobacterium spp.* (except F. varium), *Prevotella spp., and Bacteroides spp.* including the group of *B. fragilis.*

Also reported to be susceptible to clindamycin are several *Actinomyces spp.,* and *Nocardia asteroides.*

Clindamycin has been reported to be active against some protozoa such as *Toxoplasma gondii and Plasmodium.*

In high concentrations, clindamycin may become bactericidal against sensitive strains.

ANTIMICROBIAL RESISTANCE

Mycoplasma spp., enterococci, and most Gram-negative aerobes such as enterobacteriaceae are resistant to clindamycin.

Other organisms which may also be resistant to clindamycin are meticillin-resistant strains of *Staphyloccocus aureus, Neisseria gonorrhea, N. meningitides and Haemophilus influenzae.* Reports of decreased resistance among *B. fragilis* group have been received.

Clindamycin is not effective against fungi, yeasts and viruses, although it has some protozoal activity. (See indications and Spectrum)

Cross resistance due to the methylation of the ribosome exists between lincosamides and macrolides. The receptor on the 50S subunit of the bacterial ribosomes, 23S rRNA, is perhaps identical with the receptor for macrolides. Thus, these drugs may interfere with each other.

Complete cross resistance occurs when clindamycin is given with lincomycin.

EFFECT WHEN GIVEN WITH OTHER ANTIMICROBIALS

When given the ceftazidime, metronidazole or ciprofloxacin, clindamycin shows a synergistic effect against some anaerobes. Clindamycin may also competitively inhibit the effect of macrolides or chloramphenicol because their receptors on bacterial ribosomes are adjacent.

In vitro, clindamycin diminishes activity of ampicillin against *Staphylococcus aureus* and is said to enhance the activity of primaquine against *Pneumocystis jirovecii.*

PHARMACOKINETICS

Following oral administration, the bioavailability of the drug is about 90% with 150 mg dose and 23-38% with higher doses.

An hour after a single dose of 150 mg oral clindamycin, plasma concentration reaches 2-3 mcg/mL. After 6 hours, it increases to an average of 0.7mg/mL. Peak plasma concentrations are 4 mcg/mL for 300 mg dose and 8mcg/mL for 600 mg dose.

Food reduces the rate of absorption of clindamycin but does not affect the extent of absorption of the drug.

Clindamycin is about 90% protein bound. Its half life is 2-3 hours and is prolonged to 3.5 to 5 hours in patients with anuria, and to 7-14 hours in patients with liver disease. Half life is also prolonged in preterm neonates.

Clindamycin is metabolized in the liver to its active metabolites, *N-demethyl* and sulfoxide metabolites and to some inactive ones.

The volume of distribution of clindamycin is 0.66 mL/g. It is distributed in most tissues, body fluids and bone. Significant concentration of clindamycin enough to treat meningitis is not reached in the cerebrospinal fluid.

Clindamycin is eliminated in the liver and is slowly excreted as active drug and metabolites in the urine (10%) and in the feces (4%). Clindamycin cannot be removed by dialysis.

In patients with AIDS, clindamycin shows higher bioavailability. Plasma clearance and volume of distribution is lower.

DOSAGE AND ADMINISTRATION

The usual oral dose of clindamycin in adults is 150 to 300 mg every 6 hours.
For very severe infections, dose is increased to 300-450 mg every 6 hours.

Children may be given 3-6 mg per kg body weight every 6 hours. Children below 12 months or weighing $\leq$ 10 kg are given 37.5 mg every 8 hours.

Or as prescribed by the physician.

It is recommended that clindamycin capsule should be taken with a full glass of water to avoid esophageal irritation.

Dose must be reduced if clindamycin is to be given to patients with hepatic failure.

Prior to surgeries or procedures such as dental extractions with local or no anesthesia, patients who have high risk of endocarditis where penicillin is inappropriate should be given clindamycin 600 mg orally one hour before the procedure.

Patients who will undergo procedures with general anesthesia and cannot be given penicillin require administration of injectable 300 mg clindamycin 10-15 minutes before the procedure followed by oral or intravenous clindamycin 150 mg after 6 hours.

INTERACTIONS

Clindamycin, which exhibits neuromuscular blocking activity, should not be used with drugs that have similar property (i.e. tubercurarine, pancuronium and atracurium). Concomitant use of the said drugs increases the risk of respiratory depression.

There were reports that clindamycin may inhibit the activity of aminoglycosides, *in vitro*. However, *in vivo*, there was neither antagonism observed nor any apparent decrease in the activity of clindamycin when given with aminoglycoside.

Diphenoxylate, loperamide and other optate antidiarrheal drugs may exacerbate the symptoms of antibiotic-associated colitis by delaying the excretion of the toxin.

When kaolin-pectin suspension was given to patients taking clindamycin, the suspension did not affect the extent of absorption of clindamycin but it reduced its absorption rate significantly.

Concomitant use of clindamycin with parasympathomimetics such as neostigmine and pyridostigmine antagonizes the activity of the parasympathomimetics.

ADVERSE EFFECT

Adverse effects experienced with the use of clindamycin include abdominal pain or cramps, nausea, vomiting, diarrhea and loose stools sometimes with traces of blood and mucus. Use of clindamycin should be discontinued if and diarrhea develops.

Antibiotic-associated pseudomembranous colitis which may be fatal, develops during or weeks after therapy with clindamycin and is common in women and elderly. This is caused by necrotizing toxins secreted by *Clostridium spp.,* particularly *Cl. difficile*.

Cl. difficile is an organism which is singled out during administration of oral antimicrobials and grows to a high number in the sigmoid colon. This is treated promptly with oral vancomycin 125-500 mg 4-6 times per day or with metronidazole.

Allergic rashes and urticaria, Steven-Johnson- like syndrome, anaphylaxis transient leucopenia, leucopenia (with agranulocytosis), eosinophilia, thrombocytopenia, erythema multiforma, exfoliative and vesiculobullous dermatitis, polyarthritis, abnormalities of liver function tests, overt jaundice and hepatic damage have been reported with the use of clindamycin.

OVERDOSE AND TREATMENT

In cases of overdosage, no specific treatment is indicated. Clindamycin cannot be removed by hemodialysis and peritoneal dialysis from the serum.

If any adverse reaction occurs, usual emergency treatments should be given including corticosteroids, adrenaline, and antihistamines.

CONTRAINDICATION

Clindamycin hydrochloride is contraindicated in patients with hypersensitivity to clindamycin and lincomycin.

It should not be used in patients with gastrointestinal disease especially those with history of colitis. Clindamycin is also contraindicated in patients with diarrhea.

PRECAUTIONS

If diarrhea or colitis develops, treatment with clindamycin should be discontinued. Clindamycin should also be used with caution in atopic patients.

Use in patients with renal and hepatic impairment
Caution must be taken when giving clindamycin to patients with renal and hepatic impairment. Adjustment of the dosage is required.

Blood counts, renal and liver function should be monitored in patients receiving prolonged treatment of clindamycin.

Use in elderly patients
Renal and liver function should be monitored in the elderly being treated with clindamycin. Elderly patients must be monitored for any changes in the frequency of bowel movement or development of diarrhea.

Use in pregnant women
US FDA PREGNANCY CATEGORY B
(Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies which have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.)

Clindamycin is found to diffuse across the placenta and into the fetal circulation. It should therefore be used with caution in pregnant patients.

Use in lactating mothers
Clindamycin is excreted in breast milk. Breastfeeding should be avoided when taking the drug.

Use in infants and children
Blood counts, renal and liver function should be monitored in infants and children taking clindamycin.

STORAGE CONDITION

Store at temperatures not exceeding 30°C. Protect from direct light including sunlamps.

CAUTION

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY

Blister pack of 10's, Box of 100's

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph Seek medical attention immediately at the first sign of any adverse drug reaction."

REGISTRATION NUMBER: DRP-1455-02
DATE OF FIRST AUTHORIZATION: September 19, 2012
DATE OF REVISION OF PACKAGE INSERT:

Manufactured by: **Interphil Laboratories, Inc.**
Canlubang Industrial Estate, Bo. Pittland
Cabuyao, Laguna 4025 Philippines

Distributed by: **ALBERTA'S PRIDE INTERNATIONAL INDIGO, INC.**
Unit 1002, 88 Corporate Center
Sedeño cor. Valero Sts.,
Salcedo Village, Makati, Metro Manila