PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]M-CLINDAMYCIN

Clindamycin Hydrochloride Capsules

Capsules, 150 mg and 300 mg clindamycin, Oral

USP

Antibiotic

Mantra Pharma Inc.
9150 Leduc Blvd., Suite 201
Brossard, Quebec
J4Y 0E3

Date of Initial Authorization:
AUG 08, 2018

Date of Revision:
NOV 17, 2022

Submission Control Number: 268960

RECENT MAJOR LABEL CHANGES

4 DOSAGE AND ADMINISTRATION, 4.2 Recommended Dose and Dosage Adjustment	11/2022
7 WARNING AND PRECAUTIONS, Renal	11/2022

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

M-CLINDAMYCIN (Clindamycin Hydrochloride Capsules) is indicated in the treatment of serious infections due to sensitive anaerobic bacteria, such as *Bacteroides* species, *Peptostreptococcus*, anaerobic streptococci, *Clostridium* species and microaerophilic streptococci.

M-CLINDAMYCIN is also indicated in serious infections due to sensitive gram-positive aerobic organisms (staphylococci, including penicillinase-producing staphylococci, streptococci and pneumococci) when the patient is intolerant of, or the organism is resistant to other appropriate antibiotics.

M-CLINDAMYCIN is indicated for the treatment of the *Pneumocystis jiroveci* pneumonia in patients with AIDS. Clindamycin in combination with primaquine may be used in patients who are intolerant to, or fail to respond to conventional therapy.

M-CLINDAMYCIN is indicated for prophylaxis against alpha-hemolytic (viridans group) streptococci before dental, oral and upper respiratory tract surgery.

a) The prophylaxis of bacterial endocarditis in patients allergic to penicillin with any of the following conditions: congenital cardiac malformations, rheumatic and other acquired valvular dysfunction, prosthetic heart valves, previous history of bacterial endocarditis, hypertrophic cardiomyopathy, surgically constructed systemic-pulmonary shunts, mitral valve prolapse with valvular regurgitation or mitral valve prolapse without regurgitation but associated with thickening and/or redundancy of the valve leaflets.

b) Patients taking oral penicillin for prevention or recurrence of rheumatic fever should be given another agent such as clindamycin, for prevention of bacterial endocarditis.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of M-CLINDAMYCIN and other antibacterial drugs, M-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.

1.1 Pediatrics

Pediatrics (over one month of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Clindamycin Hydrochloride Capsules in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. It is not known if use of clindamycin in pediatric patients is associated with differences in safety or effectiveness compared with adult patients.

1.2 Geriatrics

Geriatrics (> 65 years of age): Insufficient data are available to Health Canada. Clinical studies of clindamycin did not include sufficient numbers of patients age 65 and over to determine whether they respond differently from younger patients.

2 CONTRAINDICATIONS

M-CLINDAMYCIN is contraindicated in patients with a known hypersensitivity to clindamycin or lincomycin or to any ingredient in the formulation or component of the container.

Until further clinical experience is obtained M-CLINDAMYCIN is not indicated in the newborn (infant below 30 days of age). For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

M-CLINDAMYCIN dose modification may not be necessary in patients with renal disease. M-CLINDAMYCIN dosage modification is not necessary in patients with hepatic insufficiency. Dosage adjustments are not necessary in the elderly with normal hepatic function and normal (age-adjusted) renal function.

4.2 Recommended Dose and Dosage Adjustment

Adults:	
Mild infections:	150 mg every 6 hours.
Moderately severe infections:	300 mg every 6 hours.
Severe infections:	450 mg every 6 hours.

Children (over one month of age and able to swallow capsules):
M-CLINDAMYCIN should be dosed based on total body weight regardless of obesity.

One of the following two dosage ranges should be selected depending on the severity of the infection:

1. 8-16 mg/kg/day (4-8 mg/lb/day) divided into 3 or 4 equal doses.
2. 16-20 mg/kg/day (8-10 mg/lb/day) divided into 3 or 4 equal doses.

M-CLINDAMYCIN capsules are not suitable for children who are unable to swallow them whole. The capsules do not provide exact mg/kg doses therefore it may be necessary to use the clindamycin granules for oral solution in some cases.

***Pneumocystis jiroveci* pneumonia in patients with AIDS**

M-CLINDAMYCIN 300-450 mg may be given orally every 6 hours in combination with 15-30 mg of primaquine for 21 days. Alternatively, DALACIN C PHOSPHATE (clindamycin phosphate) 600-900 mg (IV) may be given every 6 hours or 900 mg (IV) every 8 hours in combination with oral daily dose of 15-30 mg of primaquine. If patients should develop serious hematologic adverse effects, reducing the dosage regimen of primaquine and/or M-CLINDAMYCIN capsule should be considered.

For prevention of endocarditis

Adults:	300 mg orally 1 hour before procedure; then 150 mg 6 hours after initial dose.
Children:	10 mg/kg (not to exceed adult dose) orally 1 hour before procedure; then 5 mg/kg 6 hours after initial dose.

Note: With β-hemolytic streptococcal infections, treatment should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

4.4 Administration

Absorption of M-CLINDAMYCIN is not appreciably modified by ingestion of food and the capsules may be taken with meals.

To avoid the possibility of esophageal irritation, M-CLINDAMYCIN capsules should be taken with a full glass of water.

4.5 Missed Dose

If a dose is missed, it should be taken as soon as remembered unless it is almost time for the next dose. The dose should not be doubled to make up for a missed dose.

5 OVERDOSAGE

Activated charcoal may be administered to aid in the removal of unabsorbed drug. General supportive measures are recommended.

No cases of overdosage have been reported. It would be expected however, that should overdosage occur, gastrointestinal side effects including abdominal pain, nausea, vomiting and diarrhea might be seen. During clinical trials one 3-year old child was given 100 mg/kg of Clindamycin Hydrochloride Capsules for five days and showed mild abdominal pain and diarrhea. One 13-year old patient was given 75 mg/kg for five days with no side effects. In both cases laboratory values remained normal.

Hemodialysis and peritoneal dialysis are not effective means of removing the compound from the blood. No specific antidote is known.

The average biological half-life of clindamycin is 2.4 hours.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/ Composition	Non-medicinal Ingredients
oral	capsule 150mg, 300mg clindamycin	Ammonium hydroxide, corn starch, gelatin, iron oxide black, lactose, magnesium stearate, propylene glycol, shellac, talc, titanium dioxide

150 mg: Each hard gelatin white-white opaque capsule, size 1, imprinted with “CLIN 150” contains white to off-white crystalline powder. Clindamycin HCl is equivalent to 150 mg of clindamycin base. Available in bottles of 100 capsules.

300 mg: Each hard gelatin white-white opaque capsule, size 0el imprinted with “CLIN 300” contains

white to off-white crystalline powder. Clindamycin HCl is equivalent to 300 mg of clindamycin base. Available in bottles of 100 capsules.

7 WARNINGS AND PRECAUTIONS

General

M-CLINDAMYCIN does not diffuse adequately into cerebrospinal fluid and thus should not be used in the treatment of meningitis.

The use of antibiotics occasionally results in overgrowth of non-susceptible organisms particularly yeasts. Should super-infections occur, appropriate measures should be taken as dictated by the clinical situation.

Care should be exercised when treating patients with multiple medications (see 9 DRUG INTERACTIONS).

Gastrointestinal

M-CLINDAMYCIN should be prescribed with caution in patients with a history of gastrointestinal disease, particularly colitis, inflammatory bowel disease (including regional enteritis and ulcerative colitis), or a history of antibiotic-associated colitis (including pseudomembranous colitis).

Clostridium difficile-associated disease (CDAD)

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including Clindamycin Hydrochloride Capsules. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *C. difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated; as surgical intervention may be required in certain severe cases (see 8 ADVERSE REACTIONS).

Hematologic

In patients with G-6-PD deficiency, the combination of clindamycin with primaquine may cause hemolytic reactions. Routine blood examinations should be done during therapy with primaquine to monitor potential hematologic toxicities. Reference should also be made to the primaquine product monograph for other possible risk groups for other hematologic reactions (see 8 ADVERSE REACTIONS).

If patients should develop serious hematologic adverse effects, reducing the dosage regimen of primaquine and/or M-CLINDAMYCIN capsule should be considered (see 4 DOSAGE AND ADMINSTRATION).

Hepatic/Biliary/Pancreatic

In patients with moderate to severe liver disease, prolongation of the half-life of clindamycin has been found. However, it was postulated from studies that when given every eight hours, accumulation of clindamycin should rarely occur. Therefore, dosage reduction in liver disease is not generally considered necessary. Periodic liver enzyme determinations should be made when treating patients with severe liver disease.

Immune

M-CLINDAMYCIN should be prescribed with caution in atopic individuals. Serious hypersensitivity reactions, including anaphylactoid reactions, severe skin reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS), and dermatological reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and acute generalized exanthematous pustulosis (AGEP) have been reported in patients on clindamycin therapy. If a hypersensitivity reaction occurs clindamycin should be discontinued and appropriate therapy should be initiated (see 2 CONTRAINDICATIONS, 8 ADVERSE REACTIONS).

Monitoring and Laboratory Tests

Routine blood examinations should be done during concomitant therapy with primaquine to monitor potential hematologic toxicities.

Periodic liver and kidney function tests and blood counts should be performed during prolonged therapy when treating patients with severe liver disease.

As with all antibiotics, perform culture and sensitivity studies in conjunction with drug therapy.

Renal

M-CLINDAMYCIN dose modification may not be necessary in patients with renal disease. The serum half-life of clindamycin is increased slightly in patients with markedly reduced renal function.

Clindamycin is potentially nephrotoxic. Acute kidney injury including acute renal failure has been reported. Therefore, monitoring of renal function should be considered during therapy of patients with pre-existing renal dysfunction or taking concomitant nephrotoxic drugs and monitoring of renal function should be performed if therapy is prolonged.

Sensitivity /Resistance

Development of drug-resistant bacteria:

Prescribing M-CLINDAMYCIN in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

7.1 Special Populations

7.1.1 Pregnant Women

There are no adequate and well-controlled studies in pregnant women. Safety for use in pregnancy has not been established.

Clindamycin should not be used in pregnancy unless clearly needed and unless the expected benefits to the mother outweigh any potential risks to the fetus.

Clindamycin crosses the placenta in humans. After multiple doses, amniotic fluid concentrations were approximately 30% of maternal blood concentrations. Clindamycin was widely distributed in fetal tissues with the highest concentration found in liver.

Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin ranging from 20 to 600 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to clindamycin except at doses that caused maternal toxicity. In one mouse strain, cleft palates were observed in treated fetuses; this response was not produced in other mouse strains or in other species, and therefore may be a strain specific effect. Oral and subcutaneous reproductive toxicity studies in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus due to clindamycin, except at doses that caused maternal toxicity. Animal reproduction studies are not always predictive of human response.

7.1.2 Breast-feeding

Clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8 mcg/mL.

Clindamycin has the potential to cause adverse effects on the breastfed infant's gastrointestinal flora such as diarrhea or blood in the stool, or rash. Because of the potential for serious adverse reactions in nursing infants, if clindamycin is required by a nursing mother, it is not a reason to discontinue breastfeeding, but an alternate drug may be preferred. If M-CLINDAMYCIN is used by a nursing mother, monitor the infant for possible adverse effects on the gastrointestinal flora, such as diarrhea, candidiasis (thrush, diaper rash) or blood in the stool indicating possible antibiotic-associated colitis.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for M-CLINDAMYCIN and any potential adverse effects on the breastfed child from M-CLINDAMYCIN or from the underlying maternal condition.

7.1.3 Geriatrics

Geriatrics (> 60 years of age): Experience has demonstrated that antibiotic-associated colitis may occur more frequently and with increased severity among elderly and debilitated patients. These patients should be carefully monitored for the development of diarrhea.

8 ADVERSE REACTIONS

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in

the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Adverse drug reaction frequencies for the three clindamycin formulations (clindamycin capsules, clindamycin granules for oral solution and clindamycin injection) are based on the clinical data sources from the original drug submission and on the total number of patients enrolled in the clinical trials (N=1787).

Adverse drug reactions that were considered causally related to clindamycin and observed in ≥1% of patients are presented below in Table 2. They are listed according to MedDRA system organ class.

Table 2. Adverse Drug Reactions Occurring in ≥ 1% of Patients treated with clindamycin within the Original Clinical Trials

Adverse Reaction **System Organ Class /** Preferred Term	clindamycin Total N=1787[1] n (%)
Gastrointestinal disorders	
Diarrhea	26 (1.45)
Investigations	
Liver function test abnormal	66 (3.7)
Skin and subcutaneous tissue disorders	
Rash maculopapular	21 (1.18)

[1] clindamycin hydrochloride capsules N=851; clindamycin granules for oral solution N=340; clindamycin phosphate injection N=596

8.3 Less Common Clinical Trial Adverse Reactions

Less common adverse drug reactions that were considered causally related to clindamycin and observed in < 1% of patients are listed below

Blood and lymphatic system disorders: Eosinophilia

Gastrointestinal disorders: Nausea, abdominal pain and vomiting.

General disorders and administration site conditions: Local irritation, pain, abscess formation have been seen with IM injection.

Nervous system disorders: Dysgeusia

Skin and subcutaneous tissue disorders: Urticaria, erythema multiforme and pruritus.

8.5 Post-Market Adverse Reactions

Additional adverse events which have been reported in temporal association with clindamycin formulations (clindamycin capsules, clindamycin granules for oral solution and clindamycin injection) since market introduction are listed below. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be established.

Blood and lymphatic system disorders: Agranulocytosis, leucopenia, neutropenia and thrombocytopenia. In clindamycin/primaquine combination studies, serious hematologic toxicities (grade III, grade IV neutropenia or anemia, platelet counts < 50 x 10^9/L, or methemoglobin levels of 15% or greater) have been observed.

Cardiac disorders: Cardio-respiratory arrest and hypotension have been seen with rapid intravenous administration.

Gastrointestinal disorders: Colitis and pseudomembranous colitis. *Clostridium difficile*- associated disease (CDAD) has been observed and may manifest as a range of symptoms varying from watery diarrhea to fatal colitis, the onset of which may occur during or after antibacterial treatment (see 7 WARNINGS AND PRECAUTIONS). Esophagitis and esophageal ulcer have been reported with the oral formulations.

General disorders and administration site conditions: Injection site irritation and thrombophlebitis. These reactions can be minimized by deep IM injection and avoidance of indwelling intravenous catheters.

Hepatobiliary disorders: Jaundice.

Immune system disorders: Generalized mild to moderate morbilliform-like skin rashes, anaphylactic shock, anaphylactoid reactions, anaphylactic reactions, hypersensitivity, and drug reaction with eosinophilia and systemic symptoms (DRESS).

Infections and infestations: *Clostridium difficile* colitis.

Musculoskeletal: Polyarthritis.

Renal and urinary disorders: Renal dysfunction as evidenced by azotemia, oliguria and/or proteinuria. Acute kidney injury including acute renal failure has been reported (see 7 WARNINGS AND PRECAUTIONS).

Skin and subcutaneous tissue disorders: Toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), erythema multiforme, dermatitis exfoliative, dermatitis bullous, dermatitis vesiculobullous, rash morbilliform, vaginal infection, vaginitis, acute generalized exanthematous pustulosis (AGEP), angioedema.

Vascular disorders: Thrombophlebitis has been seen with rapid intravenous administration.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Clindamycin is metabolized predominantly by CYP3A4, and to a lesser extent CYP3A5, to the major metabolite clindamycin sulfoxide and minor metabolite, N-desmethylclindamycin. Therefore, inhibitors of CYP3A4 and CYP3A5 may reduce clindamycin clearance and inducers of these isoenzymes may increase clindamycin clearance. In the presence of strong CYP3A4 inducers such as rifampin, monitor for loss of effectiveness.

In vitro studies indicate that clindamycin does not inhibit CYP1A2, CYP2C9, CYP2C19, CYP2E1, or CYP2D6 and only moderately inhibits CYP3A4. Therefore, clinically important interactions between clindamycin and coadministered drugs metabolized by these CYP enzymes are unlikely.

Clindamycin has been shown to have neuromuscular blocking properties and potential antagonism with erythromycin and aminoglycosides (see Table 3).

In a clindamycin/primaquine combination study, serious hematologic toxicities have been observed, but the contribution of clindamycin, if any, is unknown (see 8 ADVERSE REACTIONS).

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction.

Table 3 - Established or Potential Drug-Drug Interactions

Proper name	Ref	Effect	Clinical comment
Neuromuscular blocking agents Examples include: atracurium, doxacurium, pancuronium, vecuronium	CS	Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents	Use with caution in patients receiving these agents concurrently.
aminoglycosides	T	Clindamycin is reported to antagonize bactericidal activity of aminoglycosides in vitro. In vivo antagonism has not been demonstrated.	
erythromycin	T	Antagonism has been demonstrated between clindamycin and erythromycin in vitro. Clindamycin and erythromycin may compete for the same protein binding site in bacteria.	Due to possible clinical significance the two drugs should not be administered concurrently.
Inhibitors of CYP3A4, CYP3A5	T	Clearance of clindamycin may be reduced.	
Inducers of CYP3A4, CYP3A5	T	Clearance of clindamycin may be increased.	Monitor for loss of effectiveness.
Strong inducers of CYP3A4 such as rifampin	CS and CT	Rifampin appears to dramatically decrease the serum clindamycin concentration.	Serum clindamycin levels and effectiveness should be carefully monitored. A clinically relevant effect of clindamycin on rifampin concentrations is not expected.

Legend: CS = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Efficacy of clindamycin should be closely monitored in patients using concomitant St. John's wort, a CYP3A4 inducer.

9.7 Drug-Laboratory test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Clindamycin is a lincosamide antibiotic that inhibits bacterial protein synthesis. It binds to the 50S ribosomal subunit and affects both ribosome assembly and the translation process. At usual doses, clindamycin exhibits bacteriostatic activity *in vitro*.

The mechanism of action of clindamycin in combination with primaquine on *Pneumocystis jiroveci* is not known.

10.2 Pharmacodynamics

(see 15 MICROBIOLOGY)

10.3 Pharmacokinetics

Absorption:

Clindamycin is rapidly and almost completely (90%) absorbed from the gastrointestinal tract in man and peak serum levels are seen in about 45 minutes. The average peak serum level following a single 150 mg dose in adults is 2.74 mcg/mL. Therapeutically effective average levels of 0.73 mcg/mL are found at 6 hours after a 150 mg dose.

The absorption of clindamycin is not appreciably affected by food intake. Peak serum levels following a single 250 mg oral dose of clindamycin with the patient in the fasting state were 3.1 mcg/mL at 45 minutes whereas the same dose administered with food gave a peak level of 2.4 mcg/mL. A 250 mg dose administered one hour after food gave a peak level of 2.8 mcg/mL but this peak did not occur until two hours after administration of the medication. A 250 mg dose with the patient in a fasting state and with food administered one hour after the medication resulted in peak levels of 3.1 mcg/mL at 12 hours.

Distribution:

Clindamycin binds primarily to alpha-1-acid glycoprotein. Protein binding is concentration dependent, ranging from 60% to 94% at therapeutic serum concentrations.

In three patients following the administration of 150 mg of clindamycin serum levels reached 2.25 mcg/mL in 2 hours and declined to 1.5 mcg/mL at 4 hours. During this period antibiotic synovial fluid levels were 1 mcg/mL at 2 hours and remained unchanged for the next and last 2 hours of observation.

Clindamycin is widely distributed in body fluids and tissues. Serum levels are rapidly attained as noted above. Tissue levels of clindamycin have been determined in various tissues in adult

patients undergoing surgical procedures as noted in Table 4.

Clindamycin does not cross the blood-brain-barrier even in the presence of inflamed meninges.

TABLE 4

Specimen	No. of Specimens	Average Serum Level	Average Fluid Level mcg/mL	Tissue Level mcg/gm
Pancreatic fluid (C6-264)	4	1.15	45.1	
Bile (C6-264)	19	3.35	52.45	
Gall Bladder (C6-24)	16	0.81		4.33
Liver (C6-265)	1	42.35		3.8
Kidney (C6-265)	1	1.5		9.07
Bone (C4-390)	2	2.44		9.91

Metabolism:

In vitro studies in human liver and intestinal microsomes indicated clindamycin is predominantly oxidized by CYP3A4, with minor contribution from CYP3A5, to form clindamycin sulfoxide and a minor metabolite, N-desmethylclindamycin.

Elimination:

The average elimination half-life is 2.4 hours. After oral administration of clindamycin hydrochloride, elimination half-life is increased to approximately 4 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 48 hour urinary excretion of clindamycin in adults following a single dose of 150 mg represented 10.9% of the administered dose (range 4.8% to 12.8%). These measurements were made by bio-assay and both the percent recovered and the urinary concentration are quite variable. The urinary concentration following a single 50 mg dose of clindamycin in the first 24 hours ranged from 8 to 25 mcg/mL of urine.

Fecal excretion of clindamycin has also been determined. Patients on a three week study when administered 1 gram of clindamycin per day had an average of 283 mcg/gm of stool. Patients on lincomycin 2 grams per day under the same conditions showed 3980 mcg/gm of stool. In single dose studies following administration of 250 mg of clindamycin, only 2.7% of the dose was excreted in the feces in 48-96 hours.

Special Populations and Conditions

Geriatrics: 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.

Obese Pediatric Patients Aged 2 to Less than 18 Years and Obese Adults Aged 18 to 20 Years: An analysis of pharmacokinetic data in obese pediatric patients aged 2 to less than 18 years and obese adults aged 18 to 20 years demonstrated that clindamycin clearance and volume of distribution normalized by total body weight are comparable regardless of obesity.

11 STORAGE, STABILITY AND DISPOSAL

Temperature:

M-CLINDAMYCIN should be stored at controlled room temperature (15-30°C) in tightly closed container. Protect from moisture.

Other:

Keep in a safe place out of the reach and sight of children.

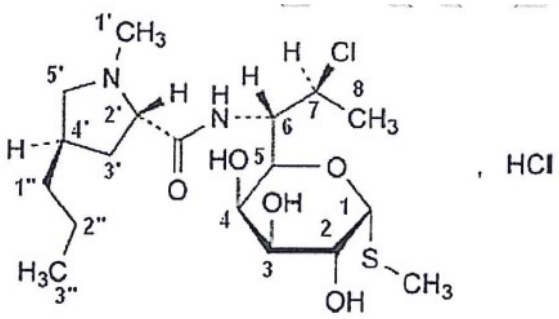
12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	clindamycin hydrochloride
Chemical name:	1. (2S-*trans*)-methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2- pyrrolidinyl)carbonyl]amino]-1-thio-L-*threo*-α-D-*galacto*-octopynranoside monohydrochloride 2. methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2 pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside monohydrochloride
Molecular formula:	$C_{18}H_{33}ClN_2O_5S.HCl$ (anhydrous)
Molecular mass:	461.44 (anhydrous), 479.46 (monohydrate)
Structural formula:	
Physicochemical properties:	Clindamycin hydrochloride is the hydrochloride salt form of clindamycin, a substance produced by the chlorination of lincomycin and is a yellow, amorphous solid. It is soluble in water, pyridine, ethanol and DMF (N,N-dimethlyformamide). Clindamycin hydrochloride has a pH of 4.4, a pKa of 7.6, a partition coefficient of 185 and a melting point of 141-143°C.

14 CLINICAL TRIALS

The authorized indications were based on safety and efficacy clinical trials which were conducted with Clindamycin Hydrochloride Capsules.

14.3 Comparative bioavailability studies

A randomized, blinded, two-way crossover, comparative bioavailability study of M-CLINDAMYCIN 300 mg capsules (Mantra Pharma Inc.) and DALACIN™ C 300 mg capsules (Pfizer Canada Inc.), administered as a 1 x 300 mg dose, was conducted in 16 healthy, adult, male and female subjects under fasting conditions. A summary of the bioavailability data is presented in the following table.

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

Clindamycin (1 x 300 mg) Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test[1]	Reference[2]	% Ratio of Geometric Means	90% Confidence Interval
AUC_T (ng h/mL)	12162.80 13205.46 (37.00)	13066.73 14203.64 (36.54)	93.1	83.6 – 103.7
AUC_I (ng h/mL)	13114.49 14293.95 (40.27)	14007.17 15225.50 (37.70)	93.6	82.8 – 105.8
C_{max} (ng/mL)	4030.80 4155.04 (24.76)	3944.90 4153.28 (32.44)	102.2	92.5 – 112.8
T_{max}[3] (h)	0.67 (0.50 – 2.00)	0.92 (0.67 - 1.67)		
$T_{½}$[4] (h)	2.94 (49.06)	2.71 (38.17)		

[1] M-CLINDAMYCIN (clindamycin as clindamycin hydrochloride) 300 mg capsules (Mantra Pharma Inc., Canada)
[2] DALACIN™ C (clindamycin as clindamycin hydrochloride) 300 mg capsules (Pfizer Canada Inc., Canada)
[3] Expressed as the median (range) only.
[4] Expressed as arithmetic mean (CV%) only.

15 MICROBIOLOGY

Efficacy is related to the time period over which the agent level is above the minimum inhibitory concentration (MIC) of the pathogen (%T/MIC).

Resistance

Resistance to clindamycin is most often due to mutations at the rRNA antibiotic binding site or methylation of specific nucleotides in the 23S RNA of the 50S ribosomal subunit. These alterations can determine *in vitro* cross resistance to macrolides and streptogramins B (MLS_B phenotype). Resistance is occasionally due to alterations in ribosomal proteins. Resistance to clindamycin may be inducible by macrolides in macrolide-resistant bacterial isolates. Inducible resistance can be demonstrated with a disk test (D-zone test) or in broth. Less frequently encountered resistance mechanisms involve modification of the antibiotic and active efflux. There is complete cross resistance between clindamycin and lincomycin. As with many antibiotics, the incidence of resistance varies with the bacterial species and the geographical area. The incidence of resistance to clindamycin is higher among methicillin-resistant staphylococcal isolates and penicillin-resistant pneumococcal isolates than among organisms susceptible to these agents.

Breakpoints

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Particularly in severe infections or therapy failure microbiological diagnosis with verification of the pathogen and its susceptibility to clindamycin is recommended.

Resistance is usually defined by susceptibility interpretive criteria (breakpoints) established by Clinical and Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST) for systemically administered antibiotics.

In order to assess the significance of *in vitro* antibiotic activity against bacterial species, it is necessary to compare the organism's minimum inhibitory concentration (MIC) to the defined susceptibility interpretive breakpoints for the antibiotic. Table 5 identifies the currently-accepted MIC interpretative breakpoints for clindamycin.

The *in vitro* activity of clindamycin in combination with primaquine has not been determined.

Clinical and Laboratory Standards Institute (CLSI) breakpoints for relevant organisms are listed below.

Table 5. CLSI Susceptibility Interpretive Criteria for Clindamycin

Pathogen	Minimal Inhibitory Concentrations (MIC in mcg/mL)			Disk Diffusion (Zone Diameters in mm)[a]		
	S	**I**	**R**	**S**	**I**	**R**
Staphylococcus spp.	≤ 0.5	1–2	≥4	≥21	15–20	≤14
Streptococcus pneumoniae	≤0.25	0.5	≥1	≥19	16–18	≤15

and other *Streptococcus* spp.						
Anaerobic Bacteria[b]	≤2	4	≥8	NA	NA	NA

NA = not applicable
[a]Disk content 2 micrograms of clindamycin
[b]MIC ranges for anaerobes are based on agar dilution methodology.

A report of "Susceptible" (S) 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" (I) 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" (R) indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the usually achievable concentrations; other therapy should be selected.

The reported clindamycin MIC_{90} value (i.e., the concentration of clindamycin that inhibits 90% of test isolates) was utilized as the most descriptive measure of clindamycin activity. Where the data from more than one study are summarized, the weighted average MIC_{90} value was calculated to account for differences in the number of strains in each study.

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. Standard clindamycin powder should provide the MIC ranges in Table 6 For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 6 should be achieved.

Table 6. CLSI Acceptable Quality Control (QC) Ranges for Clindamycin to be Used in Validation of Susceptibility Test Results

QC Strain	Minimum Inhibitory Concentration Range (mcg/mL)	Disk Diffusion Range (Zone Diameters in mm)
Staphylococcus aureus ATCC 29213	0.06–0.25	NA
Staphylococcus aureus ATCC 25923	NA	24–30
Streptococcus pneumoniae ATCC 49619	0.03–0.12	19–25
Bacteroides fragilis ATCC 25285	0.5–2[a]	NA
Bacteroides thetaiotaomicron ATCC 29741	2–8[a]	NA
Eggerthella lenta ATCC 43055	0.06–0.25[a]	NA

NA=Not applicable.
ATCC® is a registered trademark of the American Type Culture Collection
[a]MIC ranges for anaerobes are based on agar dilution methodology.

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints are presented below.

Table 7. EUCAST Susceptibility Interpretive Criteria for Clindamycin

	MIC breakpoints (mg/L)		Zone diameter breakpoints (mm)[a]	
Organism	**S ≤**	**R >**	**S ≥**	**R <**
Staphylococcus spp.	0.25	0.5	22	19
Streptococcus Groups A, B, C and G	0.5	0.5	17	17
Streptococcus pneumoniae	0.5	0.5	19	19
Viridans group streptococci	0.5	0.5	19	19
Gram-positive anaerobes	4	4	NA	NA
Gram-negative anaerobes	4	4	NA	NA
Corynebacterium spp.	0.5	0.5	20	20

[a]Disk content 2 mcg of clindamycin

NA=not applicable; S=susceptible; R=resistant

EUCAST QC ranges for MIC and disk zone determinations are in the table below.

Table 8. EUCAST Acceptable Quality Control (QC) Ranges for Clindamycin to be Used in Validation of Susceptibility Test Results

QC Strain	Minimum Inhibitory Concentration Range (mcg/mL)	Disk Diffusion Range (Zone Diameters in mm)
Staphylococcus aureus ATCC 29213	0.06–0.25	23-29
Streptococcus pneumoniae ATCC 49619	0.03–0.125	22-28

ATCC® is a registered trademark of the American Type Culture Collection

The *in vitro* susceptibility of clinical isolates to clindamycin is presented in Table 9 (gram- positive aerobic bacteria), Table 10 (gram-negative aerobic bacteria), Table 11 (gram-positive anaerobic bacteria), Table 12 (gram-negative anaerobic bacteria) and Table 13 (*Chlamydia* spp and *Mycoplasma* spp).

Table 9: *In vitro* activity of clindamycin against gram-positive aerobic bacteria[a]			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Bacillus cereus	46	1	1
Corynebacterium diphtheriae	192	0.1	0.1
Listeria monocytogenes	218	1-8	2.22
Staphylococcus aureus (methicillin-susceptible)	286	0.12-2	0.5
Staphylococcus saprophyticus	57	0.12-0.25	0.16
Streptococcus agalactia	59	≤ 0.06-0.5	0.15

Table 9: *In vitro* activity of clindamycin against gram-positive aerobic bacteria[a]			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Streptococcus bovis	22	0.04	0.04
Streptococcus pneumonia (penicillin-susceptible)	660	0.03-0.25	0.23
Streptococcus pyogenes	141	0.13-0.25	0.08
Streptococcus spp, Group B	38	≤ 0.12-0.25	0.15
Streptococcus spp, Group C	30	≤ 0.12-0.5	0.22
Streptococcus spp, Group G	34	0.06-0.5	0.31
Streptococcus spp, viridans Group (penicillin-susceptible)	67	≤ 0.06-1.6	0.53

[a] clinical efficacy has not been established for some of these species

[b] N, total number of isolates

[c] Range of reported MIC_{90} values

[d] MIC_{90} for single study or weighted average MIC_{90} for two or more studies

Table 10: *In vitro* activity of clindamycin against gram-negative aerobic bacteria[a]			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Campylobacter jejuni	449	0.39-8	1.7
Campylobacter fetus	41	1-1.6	1.2
Campylobacter coli	31	0.5	0.5
Gardnerella vaginalis	156	≤ 0.06-0.39	0.3
Helicobacter pylori	47	2-3.1	2.6
Neisseria gonorrhoeae (β-lactamase-negative)	77	4	4
Neisseria gonorrhoeae (β-lactamase-positive)	54	2	2

[a] clinical efficacy has not been established for some of these species

[b] N, total number of isolates

[c] Range of reported MIC_{90} values

[d] MIC_{90} for single study or weighted average MIC_{90} for two or more studies

Table 11: *In vitro activity of clindamycin against gram-positive anaerobic bacteria[a]*			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Actinomyces israelii	46	0.12	0.12
Actinomyces spp	38	0.5-1	0.8
Clostridium botulinum	224	4	4
Clostridium difficile	191	4->256	57.7
Clostridium novyi	18	2	2
Clostridium perfringens	386	0.25-8	3.4
Clostridium ramosum	98	4-12.5	8.3
Eubacterium spp	45	0.4-2	1.1
Lactobacillus spp	88	0.5-1	0.8
Peptostreptococcus anaerobes	283	0.25-0.5	0.4
Peptostreptococcus asaccharolyticus	268	0.25-2	1.5
Peptostreptococcus magnus	90	2	2
Peptostreptococcus prevotii	87	0.12-4	2.9

Table 11: *In vitro activity of clindamycin against gram-positive anaerobic bacteria*[a]			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Peptostreptococcus tetradius	28	0.5	0.5
Anaerobic gram-positive cocci	247	0.5-1	0.9
Propionibacterium acnes	267	0.1-0.25	0.2
Propionibacterium spp	71	0.12-0.2	0.16

[a] clinical efficacy has not been established for some of these species
[b] N, total number of isolates
[c] Range of reported MIC_{90} values
[d] MIC_{90} for single study or weighted average MIC_{90} for two or more studies

Table 12: *In vitro activity of clindamycin against gram-negative anaerobic*			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Bacteroides fragilis group	4,284	0.5-8	2.45
Bacteroides fragilis	2,002	≤ 0.2-4	2.22
Bacteroides melaninogenicus	224	≤ 0.03-0.5	0.07
Bacteroides spp	141	≤ 0.06-0.5	0.31
Bacteroides bivius	155	≤ 0.03-≤ 0.05	≤ 0.11
Bacteroides disiens	33	≤ 0.03-≤ 0.06	≤ 0.05
Fusobacterium spp	330	≤ 0.1-2	0.85
Mobiluncus mulieris	10	0.06	0.06
Mobiluncus curtisii	12	0.12	0.12
Veillonella spp	38	0.06-0.25	0.2

[a] clinical efficacy has not been established for some of these species
[b] N, total number of isolates
[c] Range of reported MIC_{90} values
[d] MIC_{90} for single study or weighted average MIC_{90} for two or more studies

Clindamycin has demonstrated *in vitro* activity against *Chlamydia trachomatis* and *Mycoplasma* spp (see Table 13). For *Chlamydia trachomatis*, the MIC_{90} for clindamycin is reached at 2.3 mcg/mL; *in vitro* synergism with gentamicin has also been demonstrated.

Table 13: ***In vitro*** **activity of clindamycin against *Chlamydia* spp and *Mycoplasma* spp[a]**			
Organism	**N[b]**	**MIC_{90} Range[c]**	**MIC_{90}[d]**
Chlamydia trachomatis	84	0.5-5.9	2.3
Mycoplasma hominis	106	0.25-0.8	0.58
Mycoplasma pneumoniae	9	4	4

[a] clinical efficacy has not been established for some of these species
[b] N, total number of isolates
[c] Range of reported MIC_{90} values
[d] MIC_{90} for single study or weighted average MIC_{90} for two or more studies

Development of resistance to clindamycin by staphylococci is slow and stepwise rather than rapid and streptomycin-like. Clindamycin, like lincomycin, participates in the dissociated cross-resistance phenomenon with erythromycin. Clindamycin is not cross-resistant with penicillin,

ampicillin, tetracycline or streptomycin. It is, however, cross-resistant with lincomycin.

Resistance to clindamycin may occur by one of several mechanisms. Resistance does not appear to be caused by reduced drug uptake but rather is generally due to alterations in the bacterial target site (50S ribosomal subunit). Resistance can result from either changes in a ribosomal protein at the receptor site or a change in the 23S ribosomal RNA by methylation of adenine. Rare isolates of staphylococci and some veterinary isolates of streptococci may enzymatically inactivate clindamycin by adenylation. Plasmid-mediated transferable resistance to clindamycin (and erythromycin) in *B. fragilis* was reported in 1979. Despite the existence of multiple resistance mechanisms, the reported incidence of clindamycin resistance in the *B.fragilis* group has remained relatively low (averaging 5.3% from 1970-1987 in over 7,600 isolates). Susceptibility of isolates to clindamycin should be assessed by individual MIC determinations.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

Animal

The results of acute toxicity studies are shown in Table 14:

TABLE 14

Animal LD_{50} Results		
Species	**Route**	LD_{50} (mg/kg)
Adult mouse	IP	262
Adult mouse	IV	143
Adult rat	Oral	2714
Adult rat	SC	2618
Newborn rat	SC	245

The following subacute and chronic animal toxicology was performed:

5 Day Oral Tolerance Study in Rats

500 mg/kg was administered to rats with no drug related toxicity noted except that all rats developed diarrhea at this dose level.

5 Day Oral Tolerance Study in the Dog

Doses of 113 mg/kg and 500 mg/kg were administered. The higher dose was vomited 1-2 hours after administration but otherwise no abnormalities of a drug related nature were noted.

6 Month Subacute Oral Toxicity in the Rat

Clindamycin, at doses of 30, 100 and 300 mg/kg, was given to groups of 20 rats daily for 6 months. Data obtained after one month were normal. Similarly, data at the end of 6 months showed no drug related effects. A fourth group of 20 rats received a dose of 600 mg/kg for 3 months and also showed the drug to be well tolerated by male and female rats without any drug related effects.

1 Month Subacute Oral Toxicity in the Dog

Clindamycin, at doses of 30, 100 and 300 mg/kg, was given to 3 groups of 6 dogs with a comparable group of 6 dogs as a control. All dogs were healthy and all dose levels well tolerated.

Fluctuations in the serum glutamic pyruvic transaminase values were seen in the 300 mg/kg group after 2 weeks therapy. Less fluctuation was seen in the SGOT levels and other tests of hepatic function did not reflect the adaptive metabolic change which these elevated transaminase values are believed to show. Two dogs in each group were sacrificed and no drug related lesions were found upon complete necropsy and microscopic observations on these dogs.

1 Year Chronic Oral Toxicity in the Rat

Doses of 0, 30, 100 and 300 mg/kg were administered daily to rats for one year and 600 mg/kg for 6 months. As expected, mortality did occur due to coincidental disease and the group at 600 mg/kg had a higher mortality rate although no definitive drug related findings were noted.

1 Year Chronic Oral Toxicity in the Dog

Dogs were administered clindamycin at doses of 0, 30, 100 and 300 mg/kg for 1 year. Some dose related elevations of serum glutamic pyruvic transaminase values were seen during the 7th to 9th month of this study, but periodic liver biopsies examined by light and electron microscopy did not disclose any hepatic cell damage. All other data noted no drug related changes.

Carcinogenicity: Long term studies in animals have not been performed with clindamycin to evaluate carcinogenic potential.

Genotoxicity: Genotoxicity tests performed included a rat micronucleus test and an Ames Salmonella reversion test. Both tests were negative.

Reproductive and Developmental Toxicology:

Teratogenic and Reproductive Studies in the Rat and Rabbit

Teratology evaluation of 20-day rat foetuses was made and no evidence of teratogenic effect was noted. Treated rat dams gave birth to normal litters and no evidence was obtained that clindamycin affected the fecundity of the dam or the development of the offspring. Oral and subcutaneous reproductive toxicity studies in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus due to clindamycin, except at doses that caused maternal toxicity.

In oral embryo fetal development studies in rats and subcutaneous embryo fetal development studies in rats and rabbits, no developmental toxicity was observed except at doses that produced maternal toxicity.

Teratogenic and Reproductive Studies in the Mouse

Clindamycin, in doses of 20, 50 and 200 mg/kg, was administered to pregnant mice from day 6 through day 15 of gestation. At the 200 mg/kg level there was pronounced expected toxicity associated with a 40% mortality. Similarly, at this toxic level there was increased foetal loss. Litter size, litter weight and mean pup weight were significantly reduced. At the 200 mg/kg level there was an increased incidence of major malformations which is thought to be due to malnutrition of the dam as a result of this toxic dose of the drug.

17 SUPPORTING PRODUCT MONOGRAPHS

1. DALACIN® C (Capsules, 150 mg and 300 mg), submission control 255793, Product Monograph, Pfizer Canada ULC. (January 10, 2022)

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrM-CLINDAMYCIN

Clindamycin Hydrochloride Capsules USP

Read this carefully before you start taking **M-CLINDAMYCIN** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **M-CLINDAMYCIN**.

Antibacterial drugs like M-CLINDAMYCIN treat <u>only</u> bacterial infections. They do not treat viral infections such as the common cold. Although you may feel better early in treatment, M-CLINDAMYCIN should be taken exactly as directed. Misuse or overuse of M-CLINDAMYCIN could lead to the growth of bacteria that will not be killed by M-CLINDAMYCIN (resistance). This means that M-CLINDAMYCIN may not work for you in the future. Do not share your medicine.

What is M-CLINDAMYCIN used for?

- To treat serious infections caused by germs (bacteria).
- To help prevent serious infections during and after surgery.

How does M-CLINDAMYCIN work?

M-CLINDAMYCIN prevents the growth of germs (bacteria) causing your infection.

What are the ingredients in M-CLINDAMYCIN?

Medicinal ingredients: Clindamycin hydrochloride.

Non-medicinal ingredients: Ammonium hydroxide, cornstarch, gelatin, iron oxide black, lactose, magnesium stearate, propylene glycol, shellac, talc and titanium dioxide.

M-CLINDAMYCIN comes in the following dosage forms:

150 mg and 300 mg capsules

Do not use M-CLINDAMYCIN if:

- You are allergic (hypersensitive) to
    - Clindamycin
    - Lincomycin

- Other ingredients in the product (see list of non-medicinal ingredients)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take M-CLINDAMYCIN. Talk about any health conditions or problems you may have, including if you:

- have a history of intestinal disorders such as colitis (inflammation of the colon), or inflammatory bowel disease.
- have diarrhea or usually get diarrhea when you take antibiotics or have ever suffered from problems with your stomach or intestines (e.g. bowel disease, colitis).
- suffer from problems with your kidneys or liver.
- have glucose-6-phosphate dehydrogenase (G-6-PD) deficiency and taking primaquine. You need to have routine blood tests while taking M-CLINDAMYCIN with primaquine to monitor for potential blood cell changes.
- are pregnant or planning to become pregnant. Clindamycin passes to the human fetus.
- are breastfeeding or planning to breastfeed.
- have intolerance to some milk sugars. M-CLINDAMYCIN capsules contain lactose.

Other warnings you should know about:

Long term use of M-CLINDAMYCIN

If you have to take M-CLINDAMYCIN for a long time, your doctor may arrange regular liver, kidney and blood tests. Do not miss these check-ups with your doctor. Long term use can also make you more likely to get other infections that do not respond to M-CLINDAMYCIN treatment.

Taking M-CLINDAMYCIN with primaquine

Patients with G-6-PD deficiency taking the combination of clindamycin and primaquine should have routine blood examinations during therapy with primaquine to monitor for potential blood cell changes.

Breastfeeding

If you are breastfeeding or planning to breastfeed while taking M-CLINDAMYCIN, talk to your doctor. M-CLINDAMYCIN will pass through your breast milk to your baby. Your doctor will decide if you should take this medicine while breastfeeding. If your doctor has told you that you can take M-CLINDAMYCIN while breastfeeding, monitor your baby for possible side effects such as: diarrhea, mouth infection (thrush: white lesions in your baby's mouth), diaper rash or blood in their stool. If your baby shows any signs, talk to your doctor and to your baby's doctor.

REMEMBER: This medication is for YOU. Never give it to others. It may harm them even if their symptoms are the same as yours.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with M-CLINDAMYCIN:

- Erythromycin (an antibiotic)
- Rifampin (an antibiotic)
- Muscle relaxants used for operations
- Aminoglycosides (a class of antibiotics)
- Primaquine (antimalarial)
- St. John's Wort (*Hypericum perforatum*)

Tell your doctor if you are taking or being administered any other topical or oral medication, including erythromycin or neuromuscular blocking agents.

How to take M-CLINDAMYCIN:

Take your medicine (or give the medicine to your child) as your doctor has told you. If you are not sure, ask your doctor or pharmacist.

The capsules should be taken with a full glass of water to avoid throat irritation. The capsules can be taken with or without food.

Usual dose:

Treatment of infection:

Adult dose:
150 mg to 450 mg by mouth every 6 hours depending on the severity of infection.

Child dose (over 1 month of age and able to swallow capsules):
2 mg to 5 mg per kg every 6 hours depending on the severity of the infection.

Keep taking this medicine for the full time of treatment, even if you (or your child) begin to feel better after a few days.

Prevention of infection (patients undergoing surgery):

Adult dose:
300 mg by mouth at 1 hour before procedure; then 150 mg at 6 hours after the first dose.

Child dose (over 1 month of age and able to swallow capsules):
10 mg per kg by mouth at 1 hour before procedure; then 5 mg/kg at 6 hours after the first dose.

If you stop taking M-CLINDAMYCIN

If you stop taking the medicine too soon your infection may come back again or get worse. Do not stop taking M-CLINDAMYCIN unless your doctor tells you to.

If you have any further questions on how to take this product, ask your doctor or pharmacist.

Overdose:

If you think you, or a person you are caring for, have taken too much M-CLINDAMYCIN, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you missed a dose of this medication, take it as soon as you remember. This will help to keep a constant amount of medication in your blood. But, if it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Do not take two doses at the same time.

What are possible side effects from using M-CLINDAMYCIN?

These are not all the possible side effects you may have when taking M-CLINDAMYCIN. If you experience any side effects not listed here, tell your healthcare professional.

M-CLINDAMYCIN can cause side effects such as:

- skin reddening, rash, itching, hives
- feeling sick, vomiting, diarrhea, stomach pain
- sore throat, throat sores
- low red blood cells (anemia) with symptoms such as bruising, bleeding
- low white blood cells (neutropenia) which can lead to more infections
- vaginal infection or vaginitis (inflamed vagina)

Contact your doctor immediately if the following happens:

- You have a severe allergic reaction with symptoms such as:
    - sudden wheeziness
    - difficulty in breathing
    - swelling of eyelids, face or lips
    - rash or itching (especially affecting the whole body)
- Blistering and peeling of large areas of skin
- Fever
- Cough
- Feeling unwell
- Swelling of the gums, tongue or lips
- You have liver problems with symptoms such as:

- yellowing of the skin and whites of the eyes (jaundice).
- You have *Clostridium difficile colitis* (bowel inflammation) with symptoms such as:
  - severe, persistent watery or bloody diarrhea (watery or bloody) with or without
    - abdominal pain
    - nausea
    - fever
    - vomiting

This may happen months after the last dose of medication. If this occurs, stop taking the medication and contact your doctor right away.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Liver problem		✓	✓
COMMON			
Diarrhea		✓	
Rash		✓	
RARE			
Nausea		✓	
Abdominal pain		✓	
Vomiting		✓	
Acute kidney failure (severe kidney problems): confusion; tiredness; swelling; urinating less or not at all; shortness of breath; chest pain, seizures, coma.			✓
Skin reactions: itching Signs of a severe allergic reaction such as sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body)			✓
NOT KNOWN			
Clostridium difficile colitis (bowel inflammation) with symptoms such as severe or persistent diarrhea, abdominal pain, nausea and vomiting.			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Keep in a safe place out of the reach and sight of children.

Store at room temperature (15°C to 30°C) in tightly closed container, away from heat and direct light. Protect from moisture. Do not store in the fridge or freezer.

Do not store in the bathroom as moisture and heat can cause damage.

If you want more information about M-CLINDAMYCIN:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html or by contacting Mantra Pharma Inc. at medinfo@mantrapharma.ca or at 1-833-248-7326.

This leaflet was prepared by
Mantra Pharma Inc.
9150 Leduc Blvd., Suite 201
Brossard, Quebec
J4Y 0E3

Last revised: NOV 17, 2022