New Zealand Data Sheet

1 PRODUCT NAME

CLINDAMYCIN ABM 150 mg capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Clindamycin ABM capsule contains clindamycin hydrochloride equivalent to 150 mg of clindamycin.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Clindamycin ABM capsules are hard gelatin capsules with a lavender body and maroon cap, imprinted with 'CL 150' in white.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Clindamycin hydrochloride has been shown to be effective in the treatment of the following infections when caused by susceptible anaerobic bacteria or susceptible strains of Gram-positive bacteria such as streptococci, staphylococci and pneumococci:

1. Upper respiratory infections including tonsillitis, pharyngitis, sinusitis, otitis media and scarlet fever.
2. Lower respiratory infections including bronchitis, pneumonia, empyema and lung abscess.
3. Skin and soft tissue infections including acne, furuncles, cellulitis, impetigo, abscesses, and wound infections. For specific skin and soft tissue infections like erysipelas and paronychia (panaritium), it would seem logical that these conditions would respond very well to clindamycin therapy.
4. Bone and joint infections including osteomyelitis and septic arthritis.
5. Pelvic infections including endometritis, cellulitis, vaginal cuff infection, tubo-ovarian abscesses, salpingitis and pelvic inflammatory disease when given in conjunction with an antibiotic of appropriate Gram-negative aerobic spectrum. In cases of cervicitis due to *Chlamydia trachomatis*, mono therapy with clindamycin has been shown to be effective in eradicating the organism.
6. Intra-abdominal infections including peritonitis and abdominal abscess when given in conjunction with an antibiotic of appropriate Gram-negative aerobic spectrum.
7. Septicaemia and endocarditis - the effectiveness of clindamycin in the treatment of

selected cases of endocarditis has been documented when clindamycin is determined to be bactericidal to the infecting organism by *in vitro* testing of appropriate achievable serum concentrations.
8. Dental infections such as periodontal abscess and periodontitis.
9. As an alternative therapy when used in combination with quinine for the treatment of multi-drug resistant *Plasmodium falciparum* infection.

4.2 Dose and method of administration

If significant diarrhoea occurs during therapy, this antibiotic should be discontinued (see section 4.4).

To avoid the possibility of oesophageal irritation, Clindamycin ABM capsules should be taken with a full glass of water and in an upright position.

Adults
Serious infections: 150 mg – 300 mg every six hours.
More severe infections: 300 mg – 450 mg every six hours.

Children
Serious infections: 8 – 16 mg/kg/day divided into three or four equal doses.
More severe infections: 16 – 25 mg/kg/day divided into three or four equal doses.

Clindamycin ABM capsules should only be used for children who are able to swallow capsules.

The use of capsules may not be suitable to provide the exact mg/kg doses required for the treatment of children.

For the treatment of anaerobic infections
Clindamycin phosphate solution for injection should be used initially. This may be followed by oral therapy with clindamycin capsules at the discretion of the physician.

For treatment of Pelvic Inflammatory Disease - inpatient treatment
Clindamycin phosphate 900 mg (i.v.) every 8 hours daily plus an antibiotic with an appropriate Gram-negative aerobic spectrum administered i.v.; e.g. gentamicin 2.0 mg/kg followed by 1.5 mg/kg every 8 hours daily in patients with normal renal function. Continue (i.v.) drugs for at least 4 days and at least 48 hours after the patient improves. Then continue oral clindamycin hydrochloride 450 mg every 6 hours daily to complete 10 - 14 days total therapy.

For treatment of cervicitis due to *Chlamydia trachomatis*
Clindamycin hydrochloride by mouth 450 mg 4 times daily for 10 - 14 days.

For treatment of beta-haemolytic streptococcal infections
In cases of beta-haemolytic streptococcal infections, treatment should continue for at least ten days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

For the treatment of multi-drug resistant *Plasmodium falciparum* infection

Limited data from uncontrolled studies using a variety of doses suggest that clindamycin, orally at a dose of 5 - 10 mg/kg twice daily for minimum of 5 days, is a useful alternative therapy when used in combination with quinine, for the treatment of multi-drug resistant *Plasmodium falciparum* infection.

4.3 Contraindications

Clindamycin is contraindicated in patients previously found to be sensitive to clindamycin, lincomycin or any of the excipients listed under section 6.1.

4.4 Special warnings and precautions for use

Severe hypersensitivity reactions, including severe skin reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalised exanthematous pustulosis (AGEP) have been reported in patients receiving clindamycin therapy (see section 4.3; 4.8). If a hypersensitivity or severe skin reaction occurs, Clindamycin should be discontinued and appropriate therapy should be initiated. The usual agents (adrenaline, corticosteroids, antihistamines, colloid infusion) should be available for emergency treatment of serious reactions.

Colitis and diarrhoea
As has been reported with other antibiotics, clindamycin therapy has been associated with severe colitis, which may end fatally. It should not be used in patients with non-bacterial infections. Studies indicate a toxin(s) produced by *Clostridia* is one primary cause of antibiotic associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*. The colitis is usually characterised by mild watery diarrhoea to severe, persistent diarrhoea, leucocytosis, fever, and severe abdominal cramps which may be associated with the passage of blood and mucous, and if allowed to progress may produce peritonitis, shock and toxic megacolon. Endoscopic examination may reveal pseudomembranous colitis.

Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases, appropriate therapy with a suitable oral antibacterial agent effective against *C. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis, e.g. opiates and diphenoxylate hydrochloride with atropine sulphate, may prolong and/or worsen the condition and should not be used.

Antibiotic-associated colitis and diarrhoea (due to *C. difficile*) occur more frequently and may be more severe in debilitated and/or elderly patients (> 60 years). When clindamycin is indicated in these patients, they should be carefully monitored for change in bowel frequency.

Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Stool culture for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.

When significant diarrhoea occurs, the drug should be discontinued or, if necessary, continued only with close observation of the patient. Large bowel endoscopy has been recommended.

Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen the condition. Vancomycin has been found to be effective in the treatment of antibiotic associated pseudomembranous colitis produced by *Clostridium difficile*. The usual adult dose is 500 mg to 2 g of vancomycin orally per day in three to four divided doses administered for seven to ten days.

Cholestyramine or colestipol resins bind vancomycin *in vitro*. If both a resin and vancomycin are to be administered concurrently, it may be advisable to separate the time of administration of each drug.

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

Review of experience to date suggests that a sub-group of older patients with associated severe illness may tolerate diarrhoea less well. When clindamycin is indicated in these patients, they should be carefully monitored for change in bowel frequency.

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

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

Systemic corticoids and corticoid retention enemas may help relieve the colitis. Other causes of colitis should also be considered.

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

Paediatric Use
Safety and appropriate dosage of clindamycin in infants less than one month old have not been established. When clindamycin is administered to newborns and infants, appropriate monitoring of organ system functions is desirable.

Due to the dose form, Clindamycin ABM capsules are not recommended in newborns, infants and children.

Use in meningitis
Since clindamycin does not diffuse adequately into the cerebrospinal fluid the medicine should not be used in the treatment of meningitis.

Monitoring
During prolonged therapy, periodic liver and kidney function tests and blood counts should be performed.

Renal and hepatic function
Clindamycin dosage modification is not necessary in patients with renal disease.

In patients with moderate to severe liver disease, prolongation of the half-life of clindamycin has been found, but a pharmacokinetic study has shown that, when given every eight hours, accumulation of clindamycin should rarely occur. Therefore, dosage reduction in liver disease is not considered necessary.

Patients with very severe renal disease and/or very severe hepatic disease accompanied by severe metabolic aberrations should be dosed with caution, and serum clindamycin levels monitored during high-dose therapy.

Other precautions
Certain infections may require incision and drainage or other indicated surgical procedures in addition to antibiotic therapy. The use of clindamycin occasionally results in overgrowth of non-susceptible organisms, particularly yeasts. Should superinfection occur, appropriate measures should be taken as indicated by the clinical situation.

Clindamycin should not be used in patients with non-bacterial infections.

Clindamycin ABM should be prescribed with caution in atopic individuals.

Clindamycin ABM contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Clindamycin ABM.

Use in the elderly
Refer to Colitis and diarrhoea.

4.5 Interaction with other medicines and other forms of interaction

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.

Clindamycin is metabolised predominantly by CYP3A4, and to a lesser extent by 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 rifampicin, 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 co-administered drugs metabolised by these CYP enzymes are unlikely.

4.6 Fertility, pregnancy and lactation

Pregnancy
Category A.
Clindamycin crosses the placenta in humans. After multiple doses, amniotic fluid concentrations were approximately 30% of maternal concentrations. Clindamycin should be used in pregnancy only if clearly needed.

Breastfeeding
Clindamycin has been reported to appear in breast milk in ranges of 0.7 - 3.8 microgram/mL. Therefore, it is not recommended for nursing mothers.

4.7 Effects on ability to drive and use machines

The effect of clindamycin on the ability to drive or operate machinery has not been systematically evaluated.

4.8 Undesirable effects

The adverse effects listed in the table below are presented by system organ class. Within each frequency category, the adverse effects are presented in the order of frequency and then by decreasing medical seriousness.

System Organ Class	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1000 to < 1/100)	Rare (≥ 1/10000 to < 1/1000)	Frequency not known (cannot be estimated from available data)
Infections and infestations	Pseudomembranous colitis			Vaginal infection
Blood and lymphatic system disorders	Eosinophilia			Agranulocytosis, neutropenia, thrombocytopenia, leucopenia
Immune system disorders				Anaphylactoid reactions
Nervous system disorders		Dysgeusia		
Gastrointestinal disorders	Diarrhoea, abdominal pain	Vomiting, nausea		Oesophagitis, oesphageal ulcer
Hepatobiliary disorders				Jaundice

System Organ Class	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1000 to < 1/100)	Rare (≥ 1/10000 to < 1/1000)	Frequency not known (cannot be estimated from available data)
Skin and subcutaneous tissue disorders	Rash maculopapular	Urticaria	Erythema multiforme, pruritus	Toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), dermatitis exfoliative, dermatitis bullous, rash morbilliform
Musculoskeletal and connective tissue disorders				Polyarthritis
Renal and urinary disorders				Renal dysfunction (as evidenced by azotemia, oliguria, and/or proteinuria)
Investigations	Liver function test abnormal			
CIOMS III categories: Very Common ≥ 1/10 (≥ 10%); Common ≥ 1/100 to < 1/10 (≥ 1% and < 10%); Uncommon ≥ 1/1000 to < 1/100 (≥ 0.1% and < 1%); Rare ≥ 1/10,000 to < 1/1000 (≥ 0.01% and < 0.1%); Very Rare < 1/10,000 (< 0.01%)				

Post-Marketing Experience
The following additional adverse reactions have been reported during post-marketing experience.

Infections and infestations
Not known: *Clostridium difficile* colitis.

Immune system disorders
Not known: Anaphylactic shock, anaphylactic reaction, hypersensitivity.

Skin and subcutaneous tissue disorders
Not known: Angioedema.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Symptoms

Overdosage with orally administered clindamycin has been rare. Adverse reactions similar to those seen with normal doses can be expected; however, unexpected reactions could occur (see section 4.8).

The minimal toxic or lethal dose is not well established. At therapeutic doses, the primary toxic effects may involve the gastrointestinal tract and may include severe diarrhoea and pseudomembranous colitis that may result in death. Dermatitis, nephrotoxicity, hepatotoxicity, and various haematological abnormalities are toxic effects that occur less frequently. Rapid administration of large doses intravenously has resulted in ventricular dysrhythmias, hypotension and cardiac arrest.

Treatment
No specific antidote is known. Support respiratory and cardiac function. In cases of overdose, drug levels of clindamycin are not clinically useful. However, monitoring serum concentrations in patients with markedly reduced renal and hepatic function may be indicated during high-dose therapy. Monitor full blood count in patients with significant exposure as clindamycin may produce abnormalities of the haematopoietic system. Because clindamycin may cause hepatotoxicity, monitor liver function tests in patients with significant exposure.

The serum biological half-life of clindamycin is 2.4 hours. Neither haemodialysis nor peritoneal dialysis appears to be effective in reducing clindamycin levels significantly.
Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen and intravenous corticosteroids should also be administered as indicated.

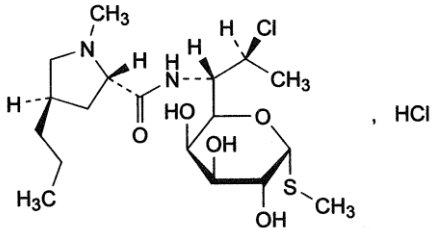
For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group
Anti-infectives for treatment of acne
Gynaecological anti-infectives and antiseptics – antibiotics
Lincosamides

Chemical structure
Clindamycin is methyl 7-chloro-6,7,8-trideoxy-6-[(2S,4R)-1-methyl-4-propylpyrrolidine-2-carboxamido]-1-thio-a-L-threo-D-galacto-octapyranoside (CAS-18323-44-9). It is a semi- synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent compound lincomycin. The structural formula of clindamycin hydrochloride is:



MW: 461.5 **CAS number:** 21462-39-5

White or almost white, crystalline powder, very soluble in water, slightly soluble in ethanol (96%).

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. Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin. At usual doses, clindamycin exhibits bacteriostatic activity *in vitro*.

Pharmacodynamic effects
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.

Antimicrobial activity
Clindamycin has been shown to have *in vitro* activity against most isolates of the following organisms:

Aerobic bacteria

Gram-positive bacteria:
Staphylococcus aureus (methicillin-susceptible isolates)
Coagulase-negative Staphylococci (methicillin-susceptible isolates)
Streptococcus pneumoniae (penicillin-susceptible isolates)
Streptococci groups A, B, C, and G

Viridans groups Streptococci
Corynebacterium spp.

Atypical bacteria:
Chlamydia trachomatis

Anaerobic bacteria

Gram-negative bacteria:
Bacteroides spp.
Fusobacterium spp.
Gardnerella vaginalis
Prevotella spp.

Gram-positive bacteria:
Propionibacterium acnes
Actinomyces (Eubacterium) spp.
Eggerthella (Eubacterium) spp.
Peptococcus spp.
Peptostreptococcus spp. *(Finegoldia magna, Micromonas micros)*
Clostridium spp. (except *Clostridium difficile)*

Fungi
Pneumocystis jirovecii

Protozoans
Toxoplasma gondii
Plasmodium falciparum

Breakpoints
Dilution or diffusion techniques – either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g.CLSI or EUCAST). Standardised susceptibility testing procedures require the use of laboratory control microorganisms to control the technical aspects of laboratory procedures.

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.

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

Table 1. CLSI Susceptibility Interpretive Criteria for Clindamycin

Pathogen	**Minimal Inhibitory Concentrations (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 spp.	≤ 0.25	0.5	≥ 1	≥ 19	16–18	≤ 15
Anaerobic bacteria[b]	≤ 2	4	≥ 8	NA	NA	NA

NA=not applicable; S=susceptible; I=intermediate; R=resistant.
[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 high dosage of drug can be used. This category also provides a buffer zone, which 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.

Standardised 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 2. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 2 should be achieved.

Table 2. 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 3. 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 µg of clindamycin
NA=not applicable; S=susceptible; R=resistant

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

Table 4. 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

5.2 Pharmacokinetic properties

Serum level studies with a 150 mg oral dose of clindamycin in 24 normal adult volunteers showed that clindamycin was rapidly absorbed after oral administration. An average peak serum level of 2.50 micrograms/mL was reached in 45 minutes; serum levels averaged 1.51 micrograms/mL at three hours and 0.70 micrograms/mL at six hours. Absorption of an oral dose is virtually complete (90%).

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. Multiple-dose studies in newborns and infants up to 6 months of age show that the drug does not accumulate in the serum and is excreted rapidly.

Serum half-life of clindamycin is increased slightly in patients with markedly reduced renal function. Haemodialysis 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. *In vitro* studies in human liver and intestinal microsomes indicated that clindamycin is predominantly oxidised by CYP3A4, with minor contribution from CYP3A5, to form clindamycin sulfoxide and a minor metabolite, N-desmethylclindamycin. The average biological half-life is 2.4 hours. Approximately 10% of the bioactivity is excreted in the urine and 3.6% in the faeces; the remainder is excreted as bioinactive metabolites. Clindamycin is mainly eliminated by hepatic metabolism and biliary excretion.

Doses of up to 2 g 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, area under the serum concentrations time curve) after i.v. administration of clindamycin phosphate. After oral administration of clindamycin, 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 function.

5.3 Preclinical safety data

There is no evidence of teratogenic effect in animals.

Fertility studies in rats treated orally with up to 300 mg/kg/day (approximately 1.1 times the highest recommended adult human dose based on mg/m2) revealed no effects on fertility or mating ability.

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Magnesium stearate
Starch – maize

Talc – purified
Gelatin
Erythrosine CI45430
Indigo carmine CI73015
Titanium dioxide
White printing ink

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

Blister packs of 16 capsules.

6.6 Special precautions for disposal

No special requirements.

7 MEDICINE SCHEDULE

Prescription medicine.

8 SPONSOR

ABM Pharma Ltd
39 Anzac Road
Browns Bay
Auckland 0753

Phone 0800 437 849

9 DATE OF FIRST APPROVAL

8 September 2011

10 DATE OF REVISION OF TEXT

29 January 2018

Summary table of changes

SECTION CHANGED	SUMMARY OF NEW INFORMATION
All sections	Update the new format and minor editorial changes.
4.2	Clarification regarding administration of capsules in children.
4.5	Deletion of antagonism of clindamycin with erythromycin paragraph. Addition of text related to metabolism of clindamycin, and interaction with CYP enzymes, including loss of effectiveness in presence of strong CYP3A4 inhibitors.
4.7	Inclusion of information about Effects on ability to drive and use machines.
5.1	Inclusion of information on mechanism of action, pharmacodynamics effects, resistance and update to the susceptible bacteria. Inclusion of information on breakpoints and susceptibility testing.
5.2	Addition of text related to the oxidation of clindamycin by CYP3A4.