NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Clindamycin-hameln, 150mg/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL of solution contains 178.22 mg/mL clindamycin phosphate equivalent to 150 mg clindamycin.

Each ampoule with 2 mL of solution contains clindamycin phosphate equivalent to 300 mg of clindamycin.

Each ampoule with 4 mL of solution contains clindamycin phosphate equivalent to 600 mg of clindamycin.

Excipients with known effect:
Each mL of solution contains 9 mg of benzyl alcohol – see section 4.4.
Each mL of solution contains up to 8.6 mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, sterile solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clindamycin phosphate 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).

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*, monotherapy 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. Toxoplasmic encephalitis in patients with AIDS. In patients who are intolerant to conventional treatment, clindamycin in combination with pyrimethamine has been shown to be efficacious.

10. *Pneumocystis jirovecii* pneumonia in patients with AIDS. In patients who are intolerant to or do not respond to conventional treatment, clindamycin in combination with primaquine has been shown to be efficacious.

4.2 Dose and method of administration

Dose

Clindamycin-hameln IM administration should be used undiluted.

Clindamycin-hameln IV administration should be diluted (see Dilution for IV use and IV infusionrates below).

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

Adults: Serious Infections: 150 mg – 300 mg every six hours.

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

Children: Clindamycin should be dosed based on total body weight regardless of obesity. The maximum daily dose in obese children should not exceed the adult dose.

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.

For the treatment of Pelvic Inflammatory Disease - Inpatient treatment

Clindamycin phosphate 900 mg (IV) q8h daily plus an antibiotic with an appropriate Gram-negative aerobic spectrum administered IV; e.g. gentamicin in patients with normal renal function. Continue (IV) drugs for at least 4 days and at least 48 hours after the patientimproves. Then continue oral clindamycin hydrochloride 450 mg q6h daily to complete 10-14 days total therapy.

For the treatment of Cervicitis due to *Chlamydia trachomatis*:

Clindamycin hydrochloride by mouth 450 mg 4 times daily for 10-14 days.

For the treatment of β-haemolytic Streptococcal infections

In cases of β-haemolytic Streptococcal infections, treatment should continue for at least ten

days.

For the treatment of Toxoplasmic encephalitis in patients with AIDS

Clindamycin phosphate IV or clindamycin hydrochloride by mouth 600-1200 mg every 6 hours for two weeks followed by 300-600 mg by mouth every 6 hours. The usual total duration of therapy is 8 to 10 weeks. The dose of pyrimethamine is 25-75 mg by mouth daily for 8-10 weeks. Folinic acid 10-20 mg/day should be given with higher doses of pyrimethamine.

For the treatment of *Pneumocystis jirovecii* pneumonia in patients with AIDS

Clindamycin phosphate IV 600-900 mg every 6 hours or 900 mg IV every 8 hours or clindamycin hydrochloride 300-450 mg by mouth every 6 hours for 21 days. Primaquine 15- 30 mg dose by mouth once daily for 21 days.

Method of administration

Dilution for IV Use and IV Infusion Rates

Clindamycin must be diluted prior to IV administration. The concentration of clindamycin in diluent for infusion should not exceed 18 mg per mL AND INFUSED AT A RATE OF NOT MORE THAN 30 MG PER MINUTE AS INDICATED BELOW:

Table 1. Dilution and Infusion Rates in Relation to Total Infusion Dose

Dose	Diluent	Minimum Time
300 mg	50 mL	10 min
600 mg	50 mL	20 min
900 mg	50-100 mL	30 min
1200 mg	100 mL	40 min

Administration of more than 1200 mg in a single 1-hour infusion is not recommended.

Directions for use

The neck of the ampoule is pre-scored at the point of constriction. No ampoule file is needed to open the ampoules. A coloured dot on the ampoule head helps to orientate the ampoule. Take the ampoule and face the coloured dot. The ampoule opens easily by placing the thumb on the coloured dot and gently pressing downwards.

4.3 Contraindications

This medicine is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin, lincomycin or any of the ingredients listed under section 6.1.

4.4 Special warnings and precautions for use

SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH ADRENALINE. OXYGEN, COLLOID INFUSION, ANTIHISTAMINES AND INTRAVENOUS CORTICOSTEROIDS SHOULD ALSO BE ADMINISTERED AS INDICATED.

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. If a hypersensitivity or severe skin reaction occurs, clindamycin should be discontinued and appropriate therapy should be initiated (see section 4.3 and section 4.8).

This product contains benzyl alcohol which is associated with severe adverse effects, including fatal "gasping syndrome", in paediatric patients. The minimum amount of benzyl alcohol at which toxicity may occur is unknown. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low birth weight infants may be more likely to develop toxicity.

The use of clindamycin can lead to the development of severe colitis. Fatalities have been reported. Therefore, clindamycin should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in section 4.1. It should not be used in patients with non-bacterial infections such as most upper respiratory tract infections.

A toxin produced by *Clostridioides difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with the use of antibiotics, including parenteral clindamycin. Symptoms may occur up to several weeks after cessation of antibiotic therapy. 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, leukocytosis, fever, 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 of pseudomembranous colitis usually respond to drug discontinuation alone, however in moderate to severe cases appropriate therapy with suitable oral antibacterial agents effective against *C. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

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.

Vancomycin has been found to be effective in the treatment of antibiotic associated pseudomembranous colitis produced by *C. 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.

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.

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.

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.

C. 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.

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

Clindamycin should be prescribed with caution in atopic individuals.

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

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.

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.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy. The use of Clindamycin may result in overgrowth of non-susceptible organisms – particularly yeasts. Should superinfections occur, appropriate measures should be taken as indicated by theclinical situation.

Clindamycin should <u>not</u> be injected intravenously undiluted as a bolus, but should be infused over at least 10-60 minutes as directed in the DOSAGE AND ADMINISTRATION section.

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

Clindamycin should be used with caution in patients with a history of regional enteritis, ulcerative colitis or antibiotic associated colitis.

Stool culture for *C. difficile* and stool assay for *C. difficile* toxin maybe helpful diagnostically.

Rare instances of cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration (see section 4.2).

Local irritation, pain, induration and sterile abscess have been reported after intramuscular injection and thrombophlebitis after intravenous infusion (see section 4.8). Reactions can be

minimised by giving deep intramuscular injections and avoiding prolonged use of indwelling intravenous catheters.

Usage in the newborn and infants

When clindamycin is administered to newborns and infants, appropriate monitoring of organ system functions is desirable.

Usage in meningitis

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

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-desmethyl clindamycin. 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 fluidconcentrations were approximately 30% of maternal concentrations. Clindamycin should be used in pregnancy only if clearly needed.

Benzyl alcohol can cross the placenta (see section 4.4).

Breast-feeding

Clindamycin has been reported to appear in human breast milk in ranges from <0.5 to 3.8 micrograms/mL. Clindamycin has the potential to cause adverse effects on the breastfed infant's gastrointestinal flora such as diarrhoea or blood in the stool, or rash. Therefore, clindamycin is not recommended for nursing mothers.

If clindamycin is required by a nursing mother, it is not a reason to discontinue breastfeeding, but an alternate drug may be preferred. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for clindamycin and any potential adverse effects on the breastfed child from clindamycin or from the underlying maternal condition.

Fertility
No data available.

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 reaction
Nervous system disorders		Dysgeusia		
Cardiac disorders		Cardio-respiratory arrest§†		
Vascular disorders	Thrombophlebitis†	Hypotension§†		
Gastrointestinal disorders	Diarrhoea, abdominal pain	Vomiting, nausea		
Hepatobiliary disorders				Jaundice
Skin and subcutaneous tissue disorders	Rash maculo-papular	Urticaria	Erythema multiforme, pruritus	Toxic epidermal necrolysis (TEN), Steven 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
General disorders and administration site conditions		Pain†, injection site abscess†		Injection site irritation†
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				

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)
(<0.01%)				

† Adverse reactions apply only to injectable formulations.

§ Rare instances have been reported following too rapid intravenous administration (see section 4.2).

Post-Marketing Experience

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

Infections and infestations

Frequency not known: *C. difficile* colitis.

Immune system disorders

Frequency not known: Anaphylactic shock, anaphylactic reaction, hypersensitivity.

Skin and subcutaneous tissue disorders

Frequency not known: Angioedema.

Renal and urinary disorders

Frequency not known: Acute kidney injury.

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

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. Rapid administration of large doses has resulted in ventricular dysrhythmias, hypotension and cardiac arrest. Dermatitis, nephrotoxicity, hepatotoxicity, and various haematological abnormalities are toxic effects that occur less frequently.

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.

Neither haemodialysis nor peritoneal dialysis appear 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 Pharmacodynamics effects

Pharmacotherapeutic group: Antibacterial agents for systemic use, lincosamides, ATC Code: J01FF01.

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

Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

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 group 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 spp.
Eggerthella (Eubacterium) spp.
Peptococcus spp.
Peptostreptococcus spp. *(Finegoldia magna, Micromonas micros)*
Clostridioides spp. (except *C. 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 severeinfections. 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 2. 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 3. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 3 should be achieved.

Table 3. 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 4. 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 5. 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

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5.2 Pharmacokinetic properties

Biologically inactive clindamycin phosphate is rapidly converted to active clindamycin.

By the end of short-term intravenous infusion, peak serum levels of active clindamycin are reached.

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-desmethyl clindamycin.

Biologically-inactive clindamycin phosphate disappears rapidly from the serum, the average disappearance half-life is 6 minutes; however, the serum disappearance half-life of active clindamycin is about 3 hours in adults and 2.5 hours in children.

After intramuscular injection of clindamycin, peak levels of active clindamycin are reached within 3 hours in adults and 1 hour in children. Serum level curves may be constructed from IV peak serum levels as given in Table 6 by application of the disappearance half-lives listed above.

Serum levels of clindamycin can be maintained above the *in vitro* minimum inhibitory concentrations for most indicated organisms by administration of clindamycin every 8-12 hours in adults and every 6-8 hours in children, or by continuous intravenous infusion.An equilibrium state is reached by the third dose.

The disappearance half-life of clindamycin is increased slightly in patients with markedly reduced renal or hepatic function; dosage schedules need not be modified in the presence of mild to moderate renal or hepatic disease. No significant levels of clindamycin are attained in the cerebrospinal fluid even in the presence of inflamed meninges.

Serum assays for active clindamycin require an inhibitor to prevent *in vitro* hydrolysis of clindamycin phosphate.

Table 6: Average Peak Serum Concentrations after Dosing with clindamycin Phosphate

Dosage Regimen	Clindamycin (micrograms/mL)	Clindamycin Phosphate (micrograms/mL)
Healthy Adult Males (Post Equilibrium)		
300 mg IV in 10 min q 8h	7	15
600 mg IV in 20 min q 8h	10	23
900 mg IV in 30 min q 12h	11	29
1200 mg IV in 45 min q 12h	14	49
300 mg IM q 8h	6	3
600 mg IM q 12h*	9	3
Children (first dose)*		
5-7 mg/kg in 1 h	10	
3-5 mg/kg IM	4	
5-7 mg/kg IM	8	

*Data in this group from patients being treated for infection

Obese paediatric patients aged 2 to less than 18 years

An analysis of pharmacokinetic data in obese paediatric patients aged 2 to less than 18 years demonstrated that clindamycin clearance and volume of distribution normalized by total body weight are comparable regardless of obesity.

5.3 Preclinical safety data

None stated.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Disodium edetate
Sodium hydroxide (for pH adjustment)
Water for Injections.

6.2 Incompatibilities

Clindamycin has been known to be physically and chemically compatible for at least 24 hours in glucose 5% water and sodium chloride injection solutions containing the following antibiotics in usually administered concentrations:
amikacin sulfate, aztreonam, cefamandole nafate, cefazolin sodium, cefotaxime sodium, cefoxitin sodium, ceftazidime sodium, ceftizoxime sodium, gentamicin sulfate, netilmicin sulfate, piperacillin and tobramycin.

Clindamycin must not be administered together with ampicillin, phenytoin sodium, barbiturates, aminophylline, calcium gluconate, ceftriaxone sodium, ciprofloxacin, diphenylhydantoin, idarubicin hydrochloride, magnesium sulphate and ranitidine hydrochloride in a mixed injection. The application of this product must be conducted separately.

Solutions of clindamycin salts have a low pH and incompatibility may reasonably be expected with alkaline preparations or with medicinal products unstable at low pH.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Unopened ampoules: 24 months

Opened ampoules: The product should be used immediately after opening the container.

Diluted solution:
Chemical and physical in-use stability after dilution with 9 mg/ml (0.9%) sodium chloride solution, 50 mg/ml (5%) glucose solution or Ringer's lactate solution has been demonstrated for 48 hours at 25°C.
From a microbiological point of view, once diluted the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25°C.

For storage conditions after first opening or dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Type I colourless neutral glass 2 ml or 5 ml ampoules containing 2 ml or 4 ml solution.

Pack sizes:
2ml: 10 ampoules
4ml: 10 ampoules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

For use via intravenous infusion, this product must be diluted with 9 mg/ml (0.9%) sodium chloride solution, 50 mg/ml (5%) glucose solution, or Ringer's lactate solution. The concentration of clindamycin should not exceed 18 mg/ml.

The solution should be visually inspected prior to use and also after dilution. Only clear solutions practically free from particles should be used.
For single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription medicine.

8. SPONSOR

Max Health Ltd
PO Box 44452
Pt Chevalier, Auckland 1246

Telephone: (09) 815 2664.

9. DATE OF FIRST APPROVAL

25 August 2022

10. DATE OF REVISION OF THE TEXT

25 August 2022

Summary table of changes

Section changed	Summary of new information