PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

Pharma-Q Clindamycin Injection 600 mg/4 ml solution for injection

COMPOSITION:

Each 4 ml injection contains:

600 mg clindamycin as the phosphate and 0,9 % *v/v* benzyl alcohol as local anaesthetic.

Excipients: Disodium edetate, nitrogen, sodium hydroxide and water for injection.

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.1 Broad and medium spectrum antibiotics.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Clindamycin exhibits its action by binding to the 50S sub-unit of the bacterial ribosome thereby suppressing protein synthesis. The phosphate ester is rapidly hydrolyzed on parenteral administration to the active parent compound.

Clindamycin may have *in vitro activity* against isolates of the following organisms: (*in vitro* sensitivity does not necessarily imply *in vivo* efficacy). (See **INDICATIONS**.)

Gram positive cocci: *Staphylococcus aureus*; *Streptococcus* (anaerobic species); *Streptococcus pneumonia*.

Gram negative cocci: *Clostridium perfringens*.

Gram negative bacilli: *Campylobacter jejuni*, *Bacteroids* species*; Fusobacterium nucleatum*.

Pharmacokinetic properties:

Following intramuscular injection, peak plasma concentrations are attained after 3 hours in adults and 1 hour in children, this being 6 µg/ml with a 300 mg dose and 9 µg/ml with a 600 mg dose in adults.

Immediately after a 20 - 45 minute intravenous infusion of 600 mg, the plasma concentration is approximately 10 mcg/ml. The half-life of clindamycin is about 2,7 hours and modest accumulation is thus expected to occur if it is given every 6 hours. The half-life may be lengthened in patients with impaired renal function, and dosage in these patients should be adjusted according to plasma concentrations. Accumulation may also occur in patients with hepatic failure.

Clindamycin is widely distributed in many fluids and tissues including bone, but not in sufficient concentrations in the cerebrospinal fluid. It readily crosses the placental barrier. Clindamycin is 90 % bound to plasma protein. It accumulates in polymorphonuclear leucocytes and alveolar macrophages and is also concentrated in abscesses in experimental animals.

About 10 % of clindamycin is excreted unaltered in the urine and small quantities are found in the faeces.

INDICATIONS:

Pharma-Q Clindamycin Injection 600 mg/4 ml is used in the treatment of serious anaerobic infections such as those caused by *Bacteroides fragilis*. Also severe *staphylococcal* and *streptococcal* infections, including *staphylococcal osteomyelitis*. It is unlikely to be effective against central nervous system infections because of its poor penetration of the blood brain barrier.

Pharma-Q Clindamycin Injection 600 mg/4 ml is indicated in the treatment of infections caused by susceptible strains of:

Staphylococcus aureus: Abscesses, bacteraemia, endocarditis, pneumonia and osteomyelitis, but not in meningitis or in methicillin resistant organisms.

Streptococcus (anaerobic species): Bacteraemia, endocarditis, abscesses and upper respiratory infections (sinusitis).

Streptococcus pneumonia: Pneumonia, arthritis and upper respiratory infections.

Clostridium perfringens: Gas gangrene.

Campylobacter jejuni: Enteritis.

Bacteroides species: Oral disease, upper respiratory tract infections and lung abscess.

Fusobacterium nucleatum: Ulcerative pharyngitis, lung abscess, empyema, genital infections, gingivitis.

CONTRAINDICATIONS:

Pharma-Q Clindamycin Injection 600 mg/4 ml is contraindicated in:

- Patients with a hypersensitivity to clindamycin or lincomycin, or to any of the other ingredients of **Pharma-Q Clindamycin Injection 600 mg/4 ml**.
- Patients with gastro-intestinal disease, particularly those with a history of colitis.
- Patients who suffer from meningitis since no significant levels are attained in the cerebrospinal fluid, even in the presence of inflamed meninges.
- Patients who are pregnant or breastfeeding since safety for use in pregnancy and lactation has not been established (see **PREGNANCY AND LACTATION**).

WARNINGS and SPECIAL PRECAUTIONS:

Pharma-Q Clindamycin Injection 600 mg/4 ml:

- Should be used with caution with other medicines having a neuromuscular blocking activity since it also displays neuromuscular blocking activity.

- Should be used with caution in patients with impaired liver and renal function. Periodic tests of liver function and blood is recommended in patients receiving prolonged therapy.
- When used in infants of less than 1 month in age, appropriate monitoring of organ system functions is desirable (see **DOSAGE AND DIRECTIONS FOR USE - Neonates**).
- Should be reserved for serious infections where less toxic anti-microbial agents are inappropriate since therapy has been associated with severe colitis, which may end fatally.
- Should be used with caution in atopic patients.

Pharma-Q Clindamycin Injection 600 mg/4 ml associated colitis:

- The colitis is usually characterized by severe persistent diarrhoea and severe abdominal cramps and may be associated with the passage of blood and mucus.
- When significant diarrhoea occurs the medication should be discontinued.
- Diarrhoea, colitis and pseudomembranous colitis may occur commencing up to several weeks following cessation of therapy.
- Elderly and female patients are more likely to experience severe diarrhoea or pseudomembranous colitis.

Effects on the ability to drive and use machines:

Patients should be instructed that they should avoid potentially hazardous tasks such as driving and operating machinery until they know how **Pharma-Q Clindamycin Injection 600 mg/4 ml** affects them.

INTERACTIONS:

Pharma-Q Clindamycin Injection 600 mg/4 ml:

Activity with other antimicrobial agents:

1. Synergistic effects occur when used in combination with:
   - Ceftazidime or metronidazole and also with ciprofloxacin against some anaerobes.
   - Can be used in combination with aminoglycosides for infections resulting from fecal spillage (intra-abdominal or pelvic abscesses and peritonitis.
   - Can be used in combination with pyrimethamine and folinic acid for acute treatment of encephalitis caused by *T. gondii* in patients with AIDS (Acquired Immune Deficiency Syndrome).
   - Can be used in combination with primaquine for the treatment of mild to moderate *P. carinii* pneumonia in patients with AIDS.
2. It may diminish the activity of ampicillin *in vitro* against *Staph. aureus.*

Pharma-Q Clindamycin Injection 600 mg/4 ml:

Activity with other anti-diarrhoeal agents:

- Concomitant use with anti-diarrhoeal agents which reduce peristalsis, such as diphenoxylate, loperamide or opioids, may exacerbate the syndrome of anti-biotic associated colitis by delaying excretion of the toxin.
- When administered together with a kaolin-pectin suspension, the suspension has no effect on the extent of absorption of the injection but markedly reduces the absorption rate.

PREGNANCY AND LACTATION:

Pharma-Q Clindamycin Injection 600 mg/4 ml is contraindicated in pregnancy and lactation as safety during pregnancy and lactation has not been established (see **CONTRAINDICATIONS**).

DOSAGE AND DIRECTIONS FOR USE:

Pharma-Q Clindamycin Injection 600 mg/4 ml ampoules are not for multiple dosing and any unused portion must be discarded.

Intramuscular Injection:

Adults:

Mild to moderate infections: 600 mg/day in 2 equal doses.

Moderate to severe infections: 600 mg to 1200 mg in 2, 3 or 4 equal doses.

Severe infections: 1200 mg to 2700 mg/day in 2, 3 or 4 equal doses.

Children: over the age of 1 month

Mild to moderate infections: 10 mg to 15 mg/kg body mass daily, in 3 to 4 equal doses.

Moderate to severe infections: 15 mg to 25 mg/kg body mass daily, in 3 to 4 equal doses.

Severe infections: 25 mg to 40 mg/kg body mass daily, in 3 to 4 equal doses.

NOTE: In severe infection, give children at least 300 mg/day regardless of body mass.

Neonates:

Safety and appropriate dosages in infants less than one month old have not been established (see **WARNINGS and SPECIAL PRECAUTIONS**).

Intravenous infusion: **(use sodium chloride 0,9 % as dilution solution)**

Pharma-Q Clindamycin Injection 600 mg/4 ml may be administered in the form of a single rapid infusion of the initial dose followed by continuous intravenous infusion. This will maintain the serum levels of **Pharma-Q Clindamycin Injection 600 mg/4 ml** at the following levels:

Serum Pharma-Q Clindamycin Injection 600 mg/4 ml levels	**Rapid infusion rate**	**Maintenance infusion rate**
Above 4 µg/ml	10 mg/min for 30 minutes	0,75 mg/minute

Above 5 µg/ml	15 mg/min for 30 minutes	1,0 mg/minute
Above 6 µg/ml	20 mg/min for 30 minutes	1,25 mg/minute

Single intramuscular injections of greater than 600 mg is not recommended. **Pharma-Q Clindamycin Injection 600 mg/4 ml** must be diluted prior to intravenous administration to a dilution of 300 mg in 50 ml of diluent (6 mg/ml) or more.

Infusion rates are as follows:

DOSE	DILUENT	TIME
300 mg	50 ml	10 minutes
600 mg	100 ml	20 minutes
900 mg	150 ml	30 minutes
1200 mg	200 ml	45 minutes

Administration of more than 1 200 mg in a single 1 hour infusion is not recommended.

Pharma-Q Clindamycin Injection 600 mg/4 ml should not be injected intravenously as an undiluted bolus, but should rather be infused over at least 20 to 60 minutes.

Suitable diluents may contain sodium chloride or dextrose.

These solutions should not be used if cloudiness occurs.

Solutions containing vitamin B complex are incompatible.

It is also incompatible with aminophylline, ampicillin sodium, barbiturates, calcium gluconate, magnesium sulphate and phenytoin sodium.

In the treatment of betahaemolytic streptococcal infections a therapeutic dose must be administered for at least 10 days.

Compatibility studies monitored for 24 hours at room temperature indicated no incompatibility with the use of **Pharma-Q Clindamycin Injection 600 mg/4 ml** in an intravenous solution containing

0,9 % sodium chloride.

SIDE EFFECTS:

Blood and lymphatic system disorders:

Frequency unknown: Agranulocytosis and thrombocytopenia. Transient leucopenia and eosinophilia.

Gastro-intestinal disorders:

Frequency unknown: Diarrhoea, which can be severe and persistent, nausea, vomiting, abdominal cramps and abnormality of taste. Severe pseudo membranous colitis, which may be lethal.

Hepato-biliary disorders:

Frequency unknown: Abnormalities of liver function tests and jaundice.

Skin and subcutaneous tissue disorders:

Frequency unknown: Hypersensitivity reactions including skin rashes, erythema multiform and urticaria. Anaphylactic reactions following intravenous infusion, thrombophlebitis (following intravenous administration).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Pharma-Q Clindamycin Injection 600 mg/4 ml overdose:

- For symptoms of overdose see **SIDE EFFECTS** and **WARNINGS and SPECIAL PRECAUTIONS**.
- Treatment should be symptomatic and supportive.

IDENTIFICATION:

A clear, colourless to faint yellow solution in a 5 ml ampoule, containing 4 ml.

PRESENTATION:

10 x 5 ml clear, colourless glass, type 1 ampoule, containing 4 ml.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN.

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

PHARMA-Q HOLDINGS (PTY) LTD

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REGISTRATION NUMBER:

32/20.1.1/0502

DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Original date of registration: 17 May 2002

DATE OF REVISION OF THE TEXT

6 March 2015