CILICAINE SYRINGE

Procaine penicillin

1 PRODUCT NAME (strength pharmaceutical form)

CILICAINE SYRINGE procaine penicillin 1.5g

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

CILICAINE 1.5 syringe: a white suspension containing 1.5g procaine penicillin in 3.4ml sterile, buffered aqueous suspension.

Note: 1 unit = 1 microgram of pure procaine penicillin.

For the full list of excipients, see section 6.1.

Procaine penicillin is a white crystalline powder. It is slightly soluble in water (1 in 250 or 4.0-4.5mg/ml), soluble in 96% alcohol (1 in 30 or 3.33mg/ml) and chloroform (1 in 60), slightly soluble in acetone and fixed oils. A 0.33% aqueous suspension has a pH of 5.0 to 7.5.

Its chemical name is 2-diethylaminoethyl 4-aminobenzoate (6R)-(2-phenylacetamido) penicillinate monohydrate with an empirical formula of $C_{13}H_{20}N_2O_2$,$C_{16}H_{18}N_2O_4S$,H_2O and a molecular weight of 588.7.

Both products are slightly viscous white suspensions. Odour faint and characteristically of penicillin.

3 PHARMACEUTICAL FORM

Solution for Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of moderately severe infections due to penicillin sensitive organisms. Therapy should be guided by bacteriological studies, including sensitivity tests and also by clinical response.

Infections which usually respond to adequate dosage are: Group A streptococcal infections including upper respiratory tract infections, skin and skin structure infections and scarlet fever; pneumococcal infections of the respiratory tract; susceptible staphylococcal infections, most gonococcal infections, syphilis, fusospirochaetosis (Vincent's gingivitis and pharyngitis).

Procaine penicillin must be administered by the intramuscular route only (see **Dosage and method of administration**).

Actions

Benzylpenicillin is a bactericidal antibiotic producing its effect on penicillin sensitive micro-organisms during the stage of active multiplication through inhibition of biosynthesis of cell wall mucopeptides.

Procaine penicillin is effective against benzylpenicillin sensitive organisms including:

- Gram-positive cocci including Streptococci (Groups A,C,G.H.L and M), non-betalactamase producing staphylococci, pneumococci, and anaerobic streptococci.
- Gram-positive bacilli including *Corynebacterium diphtheriae, Bacillus anthracis, Clostridia sp. (Cl. Tetani, Cl. Perfrigens)*.
- Gram-negative cocci including Neisseria meningitidis, N.gonorrhoeae.
- Gram-negative bacilli are generally resistant.

Treponema pallidum and Leptospirae are sensitive to benzylpenicillin.

4.2 Dose and method of administration

For use by intramuscular injection only. Before injecting the dose, aspirate to be sure that the needle is not in a blood vessel. (CILICAINE SYRINGES are designed to facilitate easy aspiration before injection). If blood appears, withdraw and inject in another site.

Adults

A common dose of procaine penicillin is 1.5g daily for two to five days, the fourth and fifth doses being dependent on the severity of the infection.

Gonorrhoea

Uncomplicated infection with sensitive gonococci. Dosage regimens vary according to treatment plane. Doses may be 1g daily for one to two weeks, or up to 4.8g as a single session treatment usually administered with probenecid.

Syphilis

Often a 10 to 14 day course of procaine penicillin 1g/day.

Use in Children

Dose should be adjusted according to age and weight.

Newborn and Premature Infants

Crystalline penicillin given at intervals of 8 or 12 hours is more suitable for more serious infections.

Children Under 3 Years

1/4 adult dose is usually sufficient.

Children Over 3 Years

1/2 adult dose is usually sufficient.

4.3 Contraindications

Known hypersensitivity to penicillins or procaine.

4.4 Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillin. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillin, cephalosporins or other allergens. If an allergic reaction occurs, procaine penicillin should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including this medicine. A toxin produced with *Clostridium 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 antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to medicine discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered.

Fluids, electrolytes and protein replacement should be provided when indicated.

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

As with any antibiotic, overgrowth with nonsusceptible organisms may occur. If noted, appropriate measures must be taken. Streptococcal infections should be treated for a minimum of 10 days, and cultures should be taken at completion of treatment to confirm that streptococci have been eradicated.

Inadvertent intravascular administration, including inadvertent direct intra-arterial injection or injection immediately adjacent to arteries has resulted in severe neurovascular damage, including transverse myelitis with permanent paralysis, gangrene requiring amputation of digits and more proximal portions of extremities and necrosis and sloughing at and surrounding the injection site. Such severe effects

have been reported following injections into the buttock, thigh and deltoid areas. Other serious complications of suspected intravascular administration which have been reported include immediate pallor, mottling or cyanosis of the extremity both distal and proximal to the injection site followed by bleb formation; severe oedema requiring anterior and/or posterior compartment fasciotomy in the lower extremity. The above described severe effects and complications have most often occurred in infants and small children.

Quadriceps femoris fibrosis and atrophy have been reported following repeated intramuscular injections of penicillin preparations into the anterolateral thigh.

Injection into or near a nerve may result in permanent neurological damage.

In prolonged therapy with penicillin, and particularly with high dosage schedules, periodic evaluation of the renal and haematopoietic systems is recommended.

Brugada syndrome
The procaine component of Cilicaine has been associated with the unmasking of Brugada syndrome. Cilicaine should be avoided in patients with known Brugada syndrome. Care should be exercised in patients with suspected cardiac conduction abnormalities.

4.5 Interaction with other medicines and other forms of interaction

Bacteriostatic agents, such as tetracyclines may antagonise the bactericidal effect of penicillin. Concurrent use of these agents should be avoided.

Concurrent administration of probenecid and penicillin will result in increased blood concentrations by reducing tubular excretion of penicillin.

Studies using procaine penicillin, ampicillin or carbeacillin indicate that penicillins can interfere with urinary glucose determinations using cupric sulphate (e.g. Benedicts' solution, Clinitest). In high concentrations, penicillins can cause false positive results in these tests for urinary glucose. Glucose oxidase tests for urinary glucose (e.g. Clinistix, Tes-tape) are reportedly not affected by the presence of penicillins.

4.6 Fertility, pregnancy and lactation

Use in Pregnancy

Human experience with the penicillins during pregnancy has not shown any positive evidence of adverse effects on the foetus. There are, however, no adequate and well controlled studies in pregnant women showing conclusively that harmful effects of these agents on the foetus can be excluded.

Use in Lactation

The medicine is excreted in breast milk in concentrations lower than plasma levels. As safety to newborn infants has not been established, it is not recommended for breast feeding mothers unless the benefits outweigh any potential risk.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Very Common

- Gastrointestinal effects like diarrhoea, nausea and vomiting
- Skin rash
- Difficulty in breathing

Common

Hypersensitivity reactions including the following: skin eruptions (maculopapular to exfoliative dermatitis), urticaria, laryngeal oedema, fever, eosinophilia; other serum-sickness like reactions (including chills, fever, oedema, arthralgia and prostration).

Rare

Anaphylactic shock occurs rarely.

Other adverse effects have generally been associated with large intravenous doses of more than 10 million units of benzylpenicillin/day. These adverse effects include haemolytic anaemia, leucopenia, thrombocytopenia, neuropathy and nephropathy. These are rare reactions usually only occurring with large doses.

Some patients being treated for syphilis may experience a Jarisch-Herxheimer reaction shortly after starting treatment with CILICAINE.

Extreme anxiety and a sensation of impending death has been reported after intramuscular injection of aqueous procaine penicillin, but show no major abnormal physical signs. Some develop hallucinations, disorientation, tachycardia, acute depersonalisation or frank psychotic behaviour. Patients may be regarded as hysterical by anyone not aware of this clinical entity. It is thought these attacks are due to the procaine. They are usually self-limiting subsiding in 15 to 30 minutes. These ''procaine' reactions have been attributed to accidental intravascular administration. They are not allergic reactions.

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

CILICAINE has the potential to cause neuromuscular hyperirritability or convulsive seizures.

Treatment

Management of overdosage should include monitoring of electrolyte balance, cardiovascular status and renal function. Penicillins are not readily removed by dialysis.

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

5 PHARMACOLOGICAL PROPERTIES

The procaine salt has low solubility and is administered intramuscularly as a suspension of crystalline procaine penicillin. These particles dissolve slowly after administration, so that absorption from the injection site takes place over a prolonged period. Because absorption continues for up to 24 hours, injection may be given only once or twice daily, or as initial treatment. A peak serum level is reached in about 2 hours.

About 60% of benzylpenicillin is bound to serum proteins. The medicine is distributed throughout the body tissues in widely varying amounts. Highest levels are found in the kidneys with lesser amounts in the liver, skin and intestines. Benzylpenicillin penetrates into all other tissues and into the cerebro-spinal fluid to a lesser degree.

With normal kidney function the medicine is excreted rapidly by tubular excretion. In neonates and young infants and in individuals with impaired kidney function, excretion is delayed considerably.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

sodium citrate,

polysorbate 80 and

Water for Injections.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Shelf Life: 15 months, Store between 2-8°C.

CILICAINE SYRINGE 1.5g in disposable syringes (sterile buffered aqueous suspension): 5's (with 5 sterile skin swabs).

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

Pharmacy Retailing (NZ) Limited
Trading as Healthcare Logistics
58 Richard Pearce Drive
Airport Oaks
Auckland
Ph (09) 918 5100
Fax (09) 901 5101

9 DATE OF FIRST APPROVAL

3 January 2010

10 DATE OF REVISION OF THE TEXT

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SUMMARY TABLE OF CHANGES