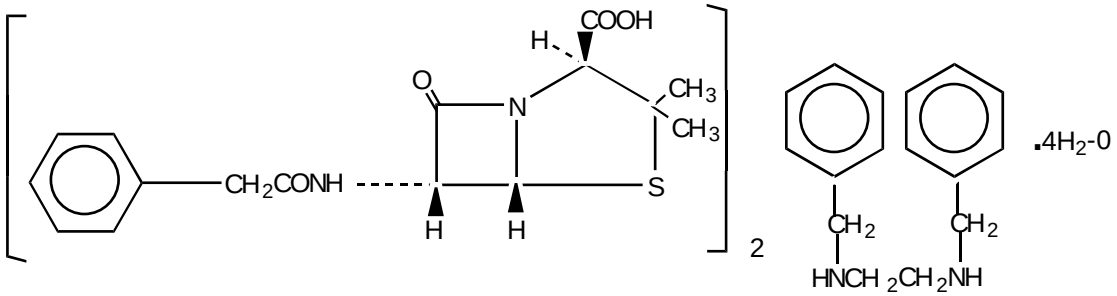
DATA SHEET

BICILLIN® L-A 2.3 mL
(Benzathine Benzylpenicillin Injection)
for deep **IM** injection only

NAME OF DRUG
BICILLIN L-A
Benzathine Benzylpenicillin 900 mg (1,200,000 Units)/2.3mL size Pre-filled syringe and Needle.

DESCRIPTION
BICILLIN L-A (sterile benzathine benzylpenicillin suspension) is chemically designated as (2S,5R,6R)-3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid compound with *N,N'*-dibenzylethylenediamine (2:1), tetrahydrate.
Its chemical structure is as follows:



BICILLIN L-A contains benzathine benzylpenicillin (the benzathine salt of benzylpenicillin) in aqueous suspension with anhydrous sodium citrate buffer; and as w/v, approximately 0.5% lecithin, 0.6% carmellose sodium, 0.6% povidone, 0.1% methyl hydroxybenzoate and 0.01% propyl hydroxybenzoate.

BICILLIN L-A suspension in the disposable pre-filled syringe formulation is viscous and opaque.

MICROBIOLOGY
Benzylpenicillin exerts a bactericidal action against penicillin-sensitive micro-organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell-wall mucopeptide. It is not active against the penicillinase-producing bacteria which include many strains of Staphylococci. The following in-vitro data are available but the clinical significance is unknown. Benzylpenicillin exerts high in vitro activity against Staphylococci (except penicillinase-producing strains), Streptococci (Groups A, C, G, H, L and M) and Pneumococci. Other organisms sensitive to benzylpenicillin are: *Neisseria gonorrhoea*, *Corynebacterium diphtheria*, *Bacillus anthracis*, Clostridia spp, *Actinomyces bovis*, *Streptobacillus moniliformis*, *Listeria monocytogenes* and Leptospira spp. *Treponema pallidum* is extremely sensitive to the bactericidal action of benzylpenicillin.

Intramuscular benzathine benzylpenicillin is absorbed very slowly into the bloodstream from the intramuscular site and converted by hydrolysis to benzylpenicillin. This combination of hydrolysis and slow absorption results in blood serum levels much lower but much more prolonged than other parenteral penicillins.

Intramuscular administration of 225 mg of benzathine benzylpenicillin in adults results in blood

levels of 22.5 to 37.5 nanogram per mL, which are maintained for 4 to 5 days. Similar blood levels may persist for 10 days following administration of 450 mg and for 14 days following administration of 900 mg. Blood concentrations of 2.25 nanogram per mL may still be detectable 4 weeks following administration of 900 mg.

Approximately 60% of benzylpenicillin is bound to serum protein. The drug 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 the spinal fluid to a lesser degree.

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

INDICATIONS

Intramuscular benzathine benzylpenicillin is indicated in the treatment of infections due to penicillin-sensitive micro-organisms that are susceptible to the low and very prolonged serum levels common to this particular dosage form. Therapy should be guided by bacteriological studies (including sensitivity tests) and by clinical response.

The following infections will usually respond to adequate dosage of intramuscular benzathine benzylpenicillin:

Streptococcal infections (Group A - without bacteraemia). Mild-to-moderate infections of the upper respiratory tract (eg., pharyngitis).

Venereal infections - Syphilis, yaws, bejel and pinta.

Medical conditions in which benzathine benzylpenicillin therapy is indicated as prophylaxis:

Rheumatic fever and/or chorea - Prophylaxis with benzathine benzylpenicillin has proven effective in preventing recurrence of these conditions. It has also been used as follow-up prophylactic therapy for rheumatic heart disease and acute glomerulonephritis.

CONTRAINDICATIONS

Previous hypersensitivity reaction to any of the penicillins.

Do not inject into or near an artery or nerve.

PRECAUTIONS

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 penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens. There have been well-documented reports of individuals with a history of penicillin hypersensitivity reactions who have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins and other allergens. If an allergic reaction occurs, the drug should be discontinued and the patient treated with the usual agents, e.g., pressor amines, antihistamines and corticosteroids. Severe anaphylactoid reactions require emergency treatment with adrenaline. Oxygen and intravenous corticosteroids and airway management, including intubation, should

also be administered as indicated.

Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma. Whenever allergic reactions occur, penicillin should be withdrawn unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy.

Do not inject intravenously or admix with other intravenous solutions. There have been reports of inadvertent intravenous administration of benzathine which has been associated with cardiorespiratory arrest and death. (See **DOSAGE AND ADMINISTRATION**.)

Inadvertent intravascular administration, including inadvertent direct intra-arterial injection or injection immediately adjacent to arteries, of BICILLIN L-A and other penicillin preparations 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.

Severe effects and complications following accidental intravascular administration have most often occurred in infants and small children. Prompt consultation with an appropriate specialist is indicated if any evidence of compromise of the blood supply occurs at, proximal to, or distal to the site of injection. (See "Contraindications" and "Dosage and Administration" sections).

Injection into or near a nerve may result in permanent neurological damage. Quadriceps femoris fibrosis and atrophy have been reported following repeated intramuscular injections of penicillin preparations into the anterolateral thigh.

Antibiotic-associated pseudomembranous colitis has been reported with many antibiotics including penicillin. A toxin produced by *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 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 with atropine (Lomotil) may prolong and/or worsen the condition and should not be used.

Prolonged use of antibiotics may promote the overgrowth of non-susceptible organisms, including fungi. Should superinfection occur, appropriate measures should be taken.

Check the following before use

In streptococcal infections, therapy must be sufficient to eliminate the organism otherwise the sequelae of streptococcal disease may occur. Cultures should be taken following completion of treatment to determine whether streptococci have been eradicated.

In prolonged therapy with penicillin and particularly with high-dosage schedules, periodic

evaluation of the renal and haematopoietic systems is recommended.

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

Use in pregnancy
Category A - Drugs which have been taken by a large number of pregnant women and women of child-bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Although generally considered to be safe, BICILLIN L-A should be used during pregnancy only if clearly needed.

Use in lactation
Soluble penicillin is excreted in breast milk. The effect on the infant, if any, is not known. Caution should be used when BICILLIN L-A is administered to a nursing woman.

Interaction with other drugs
Tetracycline may antagonise the bactericidal effect of penicillin and concurrent use of these drugs should be avoided.

The rate of excretion of the penicillins is decreased by concomitant administration of probenecid which prolongs, as well as increases, blood levels of the penicillins.

Effects on laboratory tests
Penicillins can interfere with the copper sulphate reagent method of testing for glycosuria, resulting in falsely elevated or falsely decreased readings. Such interference does not occur with the glucose oxidase method.

ADVERSE REACTIONS
The following adverse reactions have been reported:

General: 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), and anaphylactic/anaphylactoid reaction (including shock).

Fever and eosinophilia may frequently be the only reaction observed.

Haematologic: Haemolytic anaemia, leucopenia, thrombocytopenia

Neurologic: Neuropathy

Urogenital: Nephropathy, acute interstitial nephritis

As with other treatments for syphilis, the Jarisch-Herxheimer reaction has been reported.

DOSAGE AND ADMINISTRATION

The stated volume of 2.3mL is a theoretical volume based on potency at the time of manufacture. Use a concentration of 442mg/mL when measuring part doses.

Streptococcal (Group A) upper respiratory infections (for example, pharyngitis)

A single injection of 900 mg (1,200,000 Units) for adults.

A single injection of 675 mg (900,000 Units) for older children.

A single injection of 225 mg to 450 mg (300,000 to 600,000 Units) for infants and for children under 27 kg.

Venereal infections
Syphilis - Primary, secondary and latent - 1.8 g ((2,400,000 Units) (1-dose). Late (tertiary including neurosyphilis) - 1.8 g at 7-day intervals for three doses.

Congenital (with normal CSF) - under 2 years of age: 37.5 mg (50,000 Units)/kg body weight; ages 2-12 years; adjust dosage based on adult dosage schedule.

Yaws, bejel and pinta - 900 mg (1,200,000 Units) (single injection).

Prophylaxis - for rheumatic fever and glomerulonephritis
Following an acute attack, benzathine benzylpenicillin (parenteral) may be given in doses of 900 mg (1,200,000 Units) once a month or 450 mg (600,000 Units) every 2 weeks.

TO ADMINISTER
Because of the high concentration of suspended material in this product, the needle may be blocked if the injection is not made at a slow, steady rate.

Administer by DEEP, INTRAMUSCULAR INJECTION in the upper, outer quadrant of the buttock. In infants and small children, the midlateral aspect of the thigh may be preferable. When doses are repeated, vary the injection site.

Method of administration is the same as with conventional syringe. Remove needle cover by grasping it securely; twist and pull. Introduce needle into patient, aspirate by pulling back slightly on the plunger, and inject.

Discard any unused portion.

OVERDOSAGE
There have been no reported overdoses with BICILLIN L-A. Penicillin in overdosage has the potential to cause neuromuscular hyperirritability and convulsive seizures. This is particularly so if the penicillin is given intravenously or to patients with renal failure.

PRESENTATION
BICILLIN L-A benzathine benzylpenicillin injection is supplied as follows:
2.3 mL size, containing 900 mg (1,200,000 Units) benzathine benzylpenicillin per pre-filled syringe. (The stated volume of 2.3mL is a theoretical volume based on potency at the time of manufacture. Use a concentration of 442mg/mL when measuring part doses.)

STORAGE
Store at 2 to 8^{o}C. Refrigerate, do not freeze.

MEDICINES CLASSIFICATION

Prescription Only Medicine.

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DATE OF PREPARATION
18 January 2012

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