

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

**PrBICILLIN® L-A**

Penicillin G benzathine

1,200,000 IU per 2 mL suspension for injection, for intramuscular injection only

Antibiotic

Pfizer Canada ULC  
17300 Trans-Canada Highway  
Kirkland, Quebec  
H9J 2M5

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® King Pharmaceuticals Research and Development, Inc.  
Pfizer Canada ULC, Licensee

## RECENT MAJOR LABEL CHANGES

3 Serious Warnings and Precautions Box
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04/2023
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## PART I: HEALTH PROFESSIONAL INFORMATION

### 1 INDICATIONS

Bicillin® L-A (intramuscular penicillin G benzathine) is indicated in the treatment of infections due to penicillin-G-sensitive microorganisms 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 penicillin G benzathine.

- **Streptococcal infections** (Group A without bacteremia): Mild-to-moderate infections of the upper respiratory tract (e.g., pharyngitis).
- **Venereal infections:** Syphilis, yaws, bejel, and pinta.
- **Medical conditions in which penicillin G benzathine therapy is indicated as prophylaxis:** Rheumatic fever and/or Sydenham chorea (strep A related chorea) - Prophylaxis with penicillin G benzathine 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 post-streptococcal glomerulonephritis.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Bicillin® L-A and other antibacterial drugs, Bicillin® L-A should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

#### 1.1 Pediatrics

Pediatrics (< 18 years of age): see [4 DOSAGE AND ADMINISTRATION](#) and [7.1.3 Pediatrics](#).

#### 1.2 Geriatrics

Geriatrics (> 65 years of age): Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Use in the geriatric population may be associated with differences in safety or effectiveness (see [7.1.4 Geriatrics](#)).

### 2 CONTRAINDICATIONS

Bicillin® L-A is contraindicated in patients who are hypersensitive to this drug, have a history of a previous hypersensitivity reaction to any of the penicillins, or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see [6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING](#).

### 3 SERIOUS WARNINGS AND PRECAUTIONS BOX

#### Serious Warnings and Precautions

- Bicillin® L-A is for intramuscular injection only. Do not inject into or near an artery or nerve, or intravenously, or admix with other intravenous solutions. There have been reports of inadvertent intravenous administration of penicillin G benzathine associated with cardiorespiratory arrest and death. Injection into or near a nerve may result in permanent neurological damage. Prior to administration of this drug, carefully read the [4 DOSAGE AND ADMINISTRATION](#), [7 WARNINGS AND PRECAUTIONS](#), and [8 ADVERSE REACTIONS](#) sections of this monograph.
- Serious and occasionally fatal hypersensitivity (anaphylactic) and severe cutaneous adverse reactions (SCAR) have been reported in patients receiving beta-lactam antibacterials, including penicillin (see [2 CONTRAINDICATIONS](#) and [7 WARNINGS AND PRECAUTIONS](#)).

Serious anaphylactic reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids and airway management, including intubation should also be administered as indicated.

### 4 DOSAGE AND ADMINISTRATION

#### 4.1 Dosing Considerations

- BICILLIN® L-A is intended for intramuscular injection only (see [3 SERIOUS WARNINGS AND PRECAUTIONS BOX](#), [4.4 Administration](#) and [7 WARNINGS AND PRECAUTIONS, General](#)).
- The risk of toxic reactions to this drug may be greater in patients with impaired renal function and elderly patients. Employ caution when dosing and monitor renal function (see [7.1.4 Geriatrics](#) and [10.3 Pharmacokinetics](#)).

#### 4.2 Recommended Dose and Dosage Adjustment

The following dosages are recommended:

- **Streptococcal Group A:** upper respiratory infections (e.g., pharyngitis):

Adults: A single dose of 1.2 million I.U.

Older children: A single dose of 900,000 I.U.

Children and infants under 27 kg (60 lbs): A single dose of 300,000 to 600,000 I.U.

- **Venereal infections:**

##### **Syphilis:**

Primary, secondary, and early latent: 2.4 million I.U. (1 dose).

Late latent and tertiary (not involving the central nervous system): 2.4 million I.U. at 7-day intervals for three doses.

Congenital: Under 2 years of age: 50,000 I.U./kg/body weight; Ages 2-12 years: Adjust dosage based on adult dosage schedule.

Persons co-infected with HIV may require a longer course of treatment, as well as closer and longer follow-up.

**Yaws, Bejel, and Pinta:** A single dose of 1.2 million I.U.

- **Prophylaxis:** for rheumatic fever and glomerulonephritis:

Following an acute attack, penicillin G benzathine (parenteral) may be given in doses of 1,200,000 I.U. once a month or 600,000 I.U. every 2 weeks.

#### Dosage Adjustment

- **Geriatric:** Dose selection should be cautious, usually starting at the low end of the dosing range.
- **Renal Impairment:** Dose selection should be cautious, usually starting at the low end of the dosing range.

#### 4.4 Administration

- BICILLIN® L-A is intended for intramuscular injection only. Do not inject into or near an artery or nerve, or intravenously, or admixed with other intravenous solutions (see [3 SERIOUS WARNINGS AND PRECAUTIONS BOX](#) and [7 WARNINGS AND PRECAUTIONS, General](#)).
- Administer by deep, intramuscular injection in the upper, outer quadrant of the buttock (dorsogluteal) or the ventrogluteal site. In infants and small children, the midlateral aspect of the thigh may be preferable.
- When doses are repeated, vary the injection site.
- Care should be taken to avoid intravenous or intraarterial administration, or injection into or near major peripheral nerves or blood vessels, since such injection may produce neurovascular damage. Discontinue delivery of the dose if the subject complains of severe immediate pain at the injection site or if, especially in infants and young children, symptoms or signs occur suggesting onset of severe pain.
- 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.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

#### 5 OVERDOSAGE

There have been no reported overdosages with Bicillin® L-A. Penicillin in overdose has the potential to cause neuromuscular hyper-irritability or convulsive seizures. Since there is no antidote, treatment should be symptomatic and supportive.

For management of a suspected drug overdose, contact your regional poison control centre.

## 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form/ Strength/Composition	Non-medicinal Ingredients
Intramuscular	Each 2 mL pre-filled syringe contains 1,200,000 IU penicillin G benzathine as an aqueous suspension	Lecithin Methylparaben Povidone USP C200 Propylparaben NF Sterile Pulverized Sodium Carboxymethylcellulose USP Sodium Citrate USP Anhydrous Water for Injection USP

Each 2 mL disposable syringe (21 gauge, thin-wall 1-1/2 inch needle) contains 1,200,000 IU penicillin G benzathine as an aqueous suspension. Supplied in packages of 10 syringes.

## 7 WARNINGS AND PRECAUTIONS

Please see [3 SERIOUS WARNINGS AND PRECAUTIONS BOX](#).

### General

- Penicillin G benzathine should only be prescribed for the indications listed in this monograph.
- 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 (see [2 CONTRAINDICATIONS](#)).

- The use of antibiotics may result in overgrowth of nonsusceptible organisms. Constant observation of the patient is essential. If new infections due to bacteria or fungi appear during therapy, the drug should be discontinued and appropriate measures taken.
- 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.

### Method of administration

Care should be taken to avoid intravenous or intraarterial administration, or injection into or near major peripheral nerves or blood vessels, since such injection may produce neurovascular damage (See

[2 CONTRAINDICATIONS, 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, 7 WARNINGS AND PRECAUTIONS](#), and [4 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 consistent with the diagnosis of Nicolau syndrome. 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 edema 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. 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 [2 CONTRAINDICATIONS, 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, 7 WARNINGS AND PRECAUTIONS](#), and [4 DOSAGE AND ADMINISTRATION](#).

Quadriceps femoris fibrosis and atrophy have been reported following repeated intramuscular injections of penicillin preparations into the anterolateral thigh. Therefore, administration in the anterolateral thigh is not recommended in adult patients.

#### **Carcinogenesis and Mutagenesis**

No long-term animal studies have been conducted with Bicillin® L-A.

#### **Gastrointestinal**

##### **Clostridioides difficile-associated disease**

*Clostridioides difficile*-associated disease (CDAD) has been reported with use of many antibacterial agents, including Bicillin® L-A (penicillin G benzathine). CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridioides difficile*. *C. difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridioides difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridioides difficile*. Surgical evaluation should be



instituted as clinically indicated, as surgical intervention may be required in certain severe cases (see [8 ADVERSE REACTIONS](#)).

## Immune

### **Hypersensitivity and anaphylaxis**

Bicillin® L-A is contraindicated in patients who are hypersensitive to this drug or have a history of a previous hypersensitivity reaction to any of the penicillins (see [2 CONTRAINDICATIONS](#)).

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of hypersensitivity 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 Bicillin® L-A, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.

If an allergic reaction occurs:

- Bicillin® L-A should be discontinued and appropriate therapy instituted.
- Serious anaphylactic reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids and airway management, including intubation should also be administered as indicated.

## Monitoring and Laboratory Tests

Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

## Renal

Dose selection in patients with renal impairment should be cautious, usually starting at the low end of the dosing range (see [4.2 Recommended Dose and Dosage Adjustment](#)).

## Sensitivity/Resistance

### **Development of drug-resistant bacteria**

Prescribing Bicillin® L-A in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

## Skin

### **Severe cutaneous adverse reactions**

Severe cutaneous adverse reactions (SCAR) such as acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) have been reported in association with beta-lactam treatment. When SCAR is suspected, Bicillin® L-A should be discontinued and appropriate therapy and/or measures should be taken.

## 7.1 Special Populations

### 7.1.1 Pregnant Women

There are no adequate and well controlled studies in pregnant women showing conclusively that harmful effects of this drug on the fetus can be excluded.

Penicillins readily cross the placenta and the effect, if any, on the fetus is not known. Although generally considered to be safe, Bicillin® L-A should be used during pregnancy only if clearly needed.

### 7.1.2 Breast-feeding

Soluble penicillin G (the hydrolysate of penicillin G benzathine) 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.

### 7.1.3 Pediatrics

Do not inject into or near an artery or nerve. Injection into or near a nerve may result in permanent neurological damage (see [3 SERIOUS WARNINGS AND PRECAUTIONS BOX](#)).

Serious complications of suspected intravascular administration have been reported and have most often occurred in infants and small children (see [7 WARNINGS AND PRECAUTIONS, General](#)).

### 7.1.4 Geriatrics

**Geriatrics (> 65 years of age):** In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. It may be useful to monitor renal function in elderly patients.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function (see [10.3 Pharmacokinetics](#)).

Clinical studies of penicillin G benzathine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

As with other penicillins, untoward reactions of the sensitivity phenomena are likely to occur, particularly in individuals who have previously demonstrated hypersensitivity to penicillins or in those with a history of allergy, asthma, hay fever or urticaria.

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

The following adverse reactions have been reported with penicillin G:

**General:** Hypersensitivity reactions including the following: skin eruptions (maculopapular to exfoliative dermatitis), erythema, cellulitis, paresthesia, urticaria, laryngeal edema, fever, eosinophilia; other serum sickness-like reactions (including chills, fever, edema, arthralgia and prostration); and anaphylaxis including shock and death.

Note: Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Whenever such reactions occur, penicillin G should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to treatment with penicillin G. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered, as indicated.

**Gastrointestinal:** Pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment.

**Hematologic:** Hemolytic anemia, leukopenia, thrombocytopenia. There has been one report of pancytopenia in an elderly patient, who received concomitant methotrexate and flucloxacillin.

**Neurologic:** Neuropathy

**Urogenital:** Nephropathy

The following adverse events have been temporally associated with parenteral administration of penicillin G benzathine, although a causal relationship has not necessarily been established.

**Body as a Whole:** Hypersensitivity reactions including allergic vasculitis, pruritus, fatigue, asthenia and pain; aggravation of existing disorder; headache, Nicolau syndrome.

**Cardiovascular:** Cardiac arrest; hypotension; tachycardia; ventricular arrhythmia, palpitations; pulmonary hypertension; pulmonary embolism; vasodilation; vasovagal reactions; cerebrovascular accident; syncope.

**Gastrointestinal:** Nausea, vomiting; blood in stool; intestinal necrosis

**Hemic and lymphatic:** Lymphadenopathy

**Injection site:** Injection site reactions including pain, inflammation, lump, abscess, cellulitis, necrosis, edema, hemorrhage, cellulites, hypersensitivity, atrophy, ecchymosis, and skin ulcer.

Neurovascular reactions including warmth, vasospasm, pallor, mottling, gangrene, numbness of the extremities, cyanosis of the extremities, and neurovascular damage.

**Metabolic:** Elevated BUN, creatinine and SGOT

**Musculoskeletal:** Joint disorder, periostitis, exacerbation of arthritis, myoglobinuria, rhabdomyolysis.

**Nervous system:** nervousness, tremors, dizziness, somnolence; confusion, memory impairment; anxiety; euphoria; transverse myelitis, seizures; coma.

A syndrome manifested by a variety of CNS symptoms, such as severe agitation with confusion, visual and auditory hallucinations, and a fear of impending death (Hoigne's syndrome), has been reported after administration of penicillin G procaine and less commonly, after injection of the combination of penicillin G benzathine and penicillin G procaine. Other symptoms associated with this syndrome, such as psychosis, seizures, dizziness, tinnitus, cyanosis, palpitations, tachycardia and/or abnormal perception in taste, also may occur.

**Respiratory:** Hypoxia, apnea, dyspnea

**Skin:** Diaphoresis

**Special Senses:** Blurred vision, blindness

**Urogenital:** Neurogenic bladder; hematuria; proteinuria; renal failure; impotence; priapism

## 9 DRUG INTERACTIONS

### 9.4 Drug-Drug Interactions

Tetracycline, a bacteriostatic antibiotic, may antagonize 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\*; probenecid prolongs, as well as increases, blood levels of the penicillins.

\*Product is not marketed in Canada.

### 9.5 Drug-Food Interactions

Interactions with food have not been established.

### 9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

### 9.7 Drug-Laboratory Test Interactions

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

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

## 10 CLINICAL PHARMACOLOGY

### 10.1 Mechanism of Action

Penicillin G exerts a bactericidal action against penicillin-susceptible microorganisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide peptidoglycan, rendering the cell wall osmotically unstable.

### 10.3 Pharmacokinetics

#### Absorption:

Intramuscular penicillin G benzathine is absorbed very slowly into the bloodstream from the intramuscular site and converted by hydrolysis to penicillin G. 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 300,000 units of penicillin G benzathine in adults results in blood levels of 0.03 to 0.05 units per mL, which are maintained for 4 to 5 days. Similar blood levels may persist for 10 days following administration of 600,000 units and for 14 days following administration of 1,200,000 units. Blood concentrations of 0.003 units per mL may still be detectable 4 weeks following administration of 1,200,000 units.

#### Distribution:

Approximately 60% of penicillin G 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. Penicillin G penetrates into all other tissues to a lesser degree with a very small level found in the cerebrospinal fluid.

#### Elimination:

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.

### 11 STORAGE, STABILITY AND DISPOSAL

Store under refrigeration (2°-8°C). May be removed from refrigerator and stored for 7 days at a temperature not exceeding 30°C. Protect from freezing.

### 12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions for this drug product.

## PART II: SCIENTIFIC INFORMATION

### 13 PHARMACEUTICAL INFORMATION

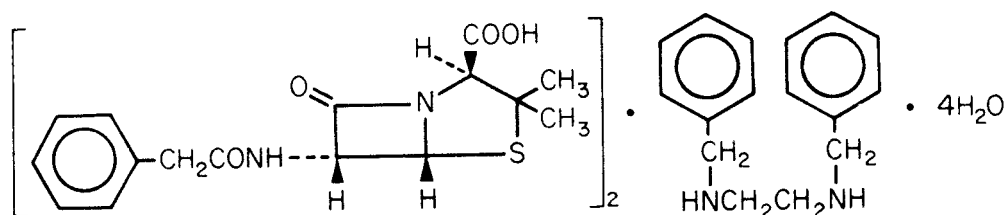
#### Drug Substance

Proper name: Penicillin G Benzathine

Chemical name: 4-Thia-1-azabicyclo [3.2.0] heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[(phenylacetyl)amino]-,[2S-(2 $\alpha$ ,5 $\alpha$ ,6 $\beta$ )]-, compounded with N,N-bis(phenylmethyl)-1, 2-ethanediamine (2:1), tetrahydrate.

Molecular formula and molecular mass: (C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>S)<sub>2</sub>·C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>·4H<sub>2</sub>O, 909.11 (dried basis), 981.19 (hydrate)

Structural formula:



Physicochemical properties:

Physical Form: White, odourless, crystalline powder.

Solubility: Very slightly soluble in water (0.15 mg/mL)

pH Values: About 6 for a saturated aqueous solution.

Melting Point: 123°-124°C.

### 14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

### 15 MICROBIOLOGY

#### Mechanism of Action

Penicillin G exerts a bactericidal action against penicillin-susceptible microorganisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall peptidoglycan, rendering the cell wall osmotically unstable.

#### Mechanism of Resistance

Penicillin is not active against penicillinase-producing bacteria or against organisms resistant to beta-lactams because of alterations in the penicillin-binding proteins. Resistance to penicillin G has not been reported in *Streptococcus pyogenes*.

## Spectrum of Activity

Penicillin has been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections as described (see [1 INDICATIONS](#)).

### Gram Positive Bacteria

Beta-haemolytic streptococci (group A, B, C, G, H, L and M)

### Other Microorganisms

*Treponema pallidum*

### **In Vitro Activity**

The following *in vitro* data are available, but their clinical significance is unknown: Penicillin G exerts high *in vitro* activity against pneumococci staphylococci (except penicillinase producing strains) and pneumococci.

Other organisms susceptible to penicillin G are *Neisseria gonorrhoeae*, *Corynebacterium diphtheriae*, *Bacillus anthracis*, Clostridia species, *Actinomyces bovis*, *Streptobacillus moniliformis*, *Listeria monocytogenes* and *Leptospira* species.

## Susceptibility Test Methods

Susceptibility to Bicillin® L-A will vary with geography and time. Local susceptibility data should be consulted where available.

### **Dilution Techniques**

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure.

### **Diffusion techniques**

Quantitative methods that require the measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized test method. This procedure uses paper discs impregnated with 10 units penicillin to test the susceptibility of microorganisms to penicillin G benzathine injectable solution. The disc diffusion interpretive criteria are provided in the table below.

### *Streptococcus pyogenes* (Group A)

**Susceptibility Test Interpretive Criteria for Penicillin**

Pathogen	MIC (mcg/mL)			Disk Diffusion (zone diameter in mm)		
	Susceptible (S)	Intermediate (I)	Resistant (R)	Susceptible (S)	Intermediate (I)	Resistant (R)
<i>Streptococcus pyogenes</i> <sup>a,b</sup>	≤ 0.12	-	-	≥ 24	-	-

<sup>a</sup>Susceptibility testing of penicillins for treatment of  $\beta$ -hemolytic streptococcal infections need not be performed routinely, because non-susceptible isolates are extremely rare in any  $\beta$ -hemolytic streptococcus and have not been reported from *Streptococcus pyogenes*. Any  $\beta$ -hemolytic streptococcal isolate found to be non-susceptible to penicillin should be re-identified, retested, and, if confirmed, submitted to a public health authority.

<sup>b</sup>The lack of data precludes defining any other interpretive criteria than 'susceptible'.

### Quality Control

Standardized 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 penicillin powder should provide the range of MIC values noted in the following table. For the diffusion technique using the 10 unit penicillin disc, the criteria in the following table should be achieved.

#### Acceptable Quality Control Ranges for Penicillin

QC Strain	MIC (mcg/mL)	Disc Diffusion (zone diameter in mm)
<i>Streptococcus pneumoniae</i> ATCC 49619	0.25-1	24 - 30

ATCC = American Type Culture Collection

## 16 NON-CLINICAL TOXICOLOGY

This information is not available for this drug product.



## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

#### PrBicillin® L-A

#### Penicillin G benzathine injectable suspension

Read this carefully before you start taking Bicillin® L-A and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Bicillin® L-A.

#### Serious Warnings and Precautions

- Your healthcare professional will inject Bicillin® L-A with an injection inside the muscle. Unintended injections of Bicillin® L-A into the blood vessels are associated with serious or life-threatening side effects. Injection into or near a nerve may result in permanent nerve damage.
- Some people taking beta-lactam antibiotics including penicillin have reported severe skin reactions and serious allergic reactions, including death.
- If you have had an allergic reaction to penicillin, or other beta-lactam antibiotics, tell your healthcare professional before you start treatment with Bicillin® L-A.
- For further information and symptoms see:
  - the “To help avoid side effects and ensure proper use...” section
  - the “What are possible side effects from using...” section

#### What is Bicillin® L-A used for?

Bicillin® L-A is used to treat bacterial infections such as:

- strep throat [a disease that causes a sore throat (pharyngitis)]
- syphilis (a disease transmitted during sex)
- yaws, bejel and pinta (skin diseases transmitted by skin-to-skin contact)

Bicillin® L-A is also used to prevent infections that may occur after a strep throat such as:

- rheumatic fever which can cause illness in the heart, joints, skin, and brain
- glomerulonephritis (an inflammation of the kidney).

Antibacterial drugs like Bicillin® L-A treat only bacterial infections. They do not treat viral infections such as the common cold. Although you may feel better early in treatment, Bicillin® L-A should be used exactly as directed. Misuse or overuse of Bicillin® L-A could lead to the growth of bacteria that will not be killed by Bicillin® L-A (resistance). This means that Bicillin® L-A may not work for you in the future. Do not share your medicine.

#### How does Bicillin® L-A work?

Bicillin® L-A is an antibiotic that belongs to the penicillin class. It works by killing or stopping the growth of the bacteria that cause your infection.

### **What are the ingredients in Bicillin® L-A?**

Medicinal ingredients: penicillin G benzathine

Non-medicinal ingredients: lecithin, methylparaben, povidone, propylparaben, sodium carboxymethylcellulose, sodium citrate, water for injection

### **Bicillin® L-A comes in the following dosage forms:**

Bicillin® L-A comes as a suspension (liquid) in a 2 mL prefilled disposable syringe

Each 2 mL prefilled syringe contains 1,200,000 IU penicillin G benzathine

### **Do not use Bicillin® L-A if you are allergic to:**

- penicillin G benzathine
- other penicillin antibiotics from the same group
- any other ingredients of Bicillin® L-A (see **Serious Warnings and Precautions** and **What are the ingredients in Bicillin® L-A?**)

### **To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Bicillin® L-A. Talk about any health conditions or problems you may have, including if you:**

- are allergic to other penicillin antibiotics, cephalosporin antibiotics such as cefazolin, cephalexin etc., or any other medications. Ask your healthcare professional if you are not sure if a medication you are allergic to belongs to one of these groups of medications.
- have allergies to any food, dyes, preservative etc., hay fever, hives or asthma.
- have kidney problems.
- are pregnant or planning to become pregnant.
- are breastfeeding or planning to breastfeed. Penicillin is passed to the infant through human breast milk.

### **Other warnings you should know about:**

Call your healthcare professional if:

- your symptoms do not improve or get worse while taking Bicillin® L-A
- you develop a severe skin rash or blisters with or without fever
- you experience any of the following symptoms during or over 2 months after your treatment with Bicillin® L-A: severe diarrhea (watery or bloody stools) with or without fever and stomach cramps

### **Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

### **The following may interact with Bicillin® L-A:**

- tetracycline (an antibiotic)
- probenecid\* (to treat gout)

\*Product is not marketed in Canada.

**How to take Bicillin® L-A:**

Your healthcare professional will inject Bicillin® L-A into a muscle of the buttocks or the hip. In infants and small children, the healthcare professional may inject Bicillin® L-A into a muscle of the thigh.

**Usual dose:**

The dose of Bicillin® L-A will depend on the type of infection you may have.

Your healthcare professional will calculate the right dose for you.

Your healthcare professional will also tell you how long to use Bicillin® L-A.

Ask your healthcare professional if you have any questions about how many doses of Bicillin® L-A you will need or when you will receive them.

**Overdose:**

If you think you, or a person you are caring for, have taken too much Bicillin® L-A, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

**What are possible side effects from using Bicillin® L-A?**

These are not all the possible side effects you may have when taking Bicillin® L-A. If you experience any side effects not listed here, tell your healthcare professional.

If you are taking this medication to treat syphilis, you may experience side effects a few hours after the beginning of the treatment, including fever, chills, headache, muscle pain and skin reactions (Jarisch-Herxheimer reaction).

Other side effects may include:

- Itching
- Skin rash
- General tiredness
- Pain
- Headache
- Nausea, vomiting
- Swollen glands
- Pain, inflammation, infection, bleeding, bruising in the area where the medication was injected
- Sweating
- Pain in your joints and bones
- Loss of muscle mass
- Nervousness
- Unintentional shaking (tremors)
- Dizziness
- Sleepiness
- Confusion

- Memory loss
- Anxiety
- Euphoria
- Ringing in your ears
- Difference in taste
- Difficulty obtaining an erection or orgasm
- Persistent and painful erection

If they occur, they are likely to be minor and temporary. However, some may be serious and need medical attention.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>COMMON</b>			
<b><i>Clostridioides difficile</i> colitis (bowel inflammation):</b> severe diarrhea (bloody or watery) with or without stomach cramps and fever			√
<b>RARE</b>			
<b>Severe allergic reaction:</b> with symptoms such as: <ul style="list-style-type: none"> <li>• Itching, skin redness</li> <li>• Widespread scaling, peeling and flaking of the skin</li> <li>• Flat red area on the skin</li> <li>• Burning or prickling feeling on your skin</li> <li>• Flu like symptoms (chills, fever, swelling, joint pain and weakness, etc.)</li> <li>• Anaphylaxis (swelling of the face, lips, tongue, back of throat, difficulty breathing or swallowing)</li> </ul>			√
<b>Heart Problems:</b> <ul style="list-style-type: none"> <li>• Heart attack</li> <li>• Abnormal heart rhythm</li> <li>• Irregularities of the heartbeat (palpitations)</li> <li>• Sudden drop in blood pressure and fainting</li> <li>• Stroke</li> </ul>			√
<b>Lung Problems:</b> <ul style="list-style-type: none"> <li>• High blood pressure in your lungs</li> </ul>			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<ul style="list-style-type: none"> <li>• Blood clots in your lungs</li> <li>• Difficulty breathing when awake or sleeping</li> </ul>			
<p><b>Nerve and blood circulation problems in the area where the medication was injected:</b></p> <ul style="list-style-type: none"> <li>• Loss of sensation and movement</li> <li>• Pallor (pale skin)</li> <li>• Blotchiness</li> <li>• Death of skin (e.g. gangrene) (Skin symptoms may include a blue or black color, pain, numbness, and sores that produce a foul-smelling discharge)</li> <li>• Numbness of the arm or leg</li> <li>• Blue or black skin on the arm or leg</li> </ul>			√
<b>Seizures</b>			√
<b>Hallucinations:</b> (seeing, hearing or even feeling something that is not really there)		√	
<p><b>Blood Problems:</b></p> <p><b>Hemolytic Anemia</b> (a condition in which red blood cells are destroyed and removed from the bloodstream before their normal lifespan is over)</p> <ul style="list-style-type: none"> <li>• Dark Urine</li> <li>• Fatigue</li> <li>• Pale skin color</li> <li>• Rapid heart rate</li> <li>• Shortness of breath</li> <li>• Yellow skin and whites of the eyes (jaundice)</li> </ul> <p><b>Low white blood cells</b></p> <ul style="list-style-type: none"> <li>• Fever</li> <li>• Frequent infections that can be serious</li> <li>• Flu-like illnesses</li> </ul> <p><b>Low platelets</b> (cells in the blood that help the blood clot)</p> <ul style="list-style-type: none"> <li>• Abnormal bleeding</li> </ul>		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<ul style="list-style-type: none"> <li>• Bleeding when you brush your teeth</li> <li>• Easy bruising</li> <li>• Pinpoint red spots on the skin (petechiae)</li> </ul>			
<p><b>Abnormal Muscle Breakdown:</b> (Rhabdomyolysis) Symptoms may include:</p> <ul style="list-style-type: none"> <li>• Dark or cola-colored urine</li> <li>• Muscle pain and weakness</li> </ul>		√	
<p><b>Kidney Problems:</b> Symptoms may include:</p> <ul style="list-style-type: none"> <li>• Any change in the amount, frequency or colour of urine</li> <li>• Fluid buildup</li> <li>• Loss of sleep</li> <li>• Poor appetite</li> <li>• Upset stomach</li> <li>• Weakness</li> <li>• Difficulty concentrating</li> </ul>			√
<p><b>Vision Changes:</b> Blurred vision</p>		√	
Blindness			√
<p><b>Severe cutaneous adverse reactions (SCAR)</b> (severe skin reactions that may also affect other organs):</p> <ul style="list-style-type: none"> <li>- skin peeling, scaling, or blistering (with or without pus) which may also affect your eyes, mouth, nose or genitals, itching, severe rash, bumps under the skin, skin pain, skin color changes (redness, yellowing, purplish)</li> <li>- swelling and redness of eyes or face</li> <li>- flu-like feeling, fever, chills, body aches, swollen glands, cough</li> <li>- shortness of breath, chest pain or discomfort</li> </ul>			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

### **Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### **Storage:**

Store under refrigeration (2°C to 8°C). May be removed from refrigerator and stored for 7 days at a temperature not exceeding 30°C. Protect from freezing.

Keep out of reach and sight of children.

### **If you want more information about Bicillin® L-A:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website <http://www.pfizer.ca>, or by calling 1-800-463-6001.

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