# PRESCRIBING INFORMATION

INCLUDING PATIENT MEDICATION INFORMATION

# [Pr]Penicillin G Sodium for Injection, USP

**Powder for Solution**

**1 million, 5 million and 10 million units per vial**
**Penicillin G (as penicillin G sodium)**

**For Intramuscular or Intravenous Use**

**Sterile**

**Antibiotic**

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Date of Preparation**:**
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**Control Number: 218533**

## PRESCRIBING INFORMATION

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## PHARMACOLOGICAL CLASSIFICATION

Antibiotic

## ACTIONS AND CLINICAL PHARMACOLOGY

Penicillin G is bactericidal against penicillin-susceptible microorganisms during the stage of active multiplication. It acts by inhibiting biosynthesis of cell-wall mucopeptide. It is not active against the penicillinase-producing bacteria, which include many strains of staphylococci. Penicillin G is highly active in vitro against staphylococci (except penicillinase-producing strains), streptococci (groups A, C, G, H, L and M) and pneumococci. Other organisms susceptible in vitro to penicillin G are Neisseria gonorrhoeae, Corynebacterium diphtheriae, Bacillus anthracis, Clostridia, Actinomyces bovis, Streptobacillus moniliformis, Listeria monocytogenes, and Leptospira; Treponema pallidum is extremely susceptible. Some species of gram-negative bacilli are susceptible to moderate to high concentrations of penicillin G obtained with intravenous administration. These include most strains of Escherichia coli, all strains of Proteus mirabilis, Salmonella, and Shigella; and some strains of Enterobacter aerogenes (formerly Aerobacter aerogenes) and Alcaligenes faecalis.

Aqueous penicillin G is rapidly absorbed following both intramuscular and subcutaneous injection. Approximately 60 percent of a total dose of 300 000 units is excreted in the urine within the first five-hour period. Therefore, high and frequent doses are required to maintain the elevated serum levels desirable in treating certain severe infections in individuals with normal kidney function. In neonates and young infants and in individuals with impaired kidney function, excretion is considerably delayed.

## INDICATIONS AND CLINICAL USE

Penicillin G Sodium for Injection, USP is indicated in the treatment of severe infections caused by penicillin G-susceptible microorganisms when rapid and high penicillinemia is required. Therapy should be guided by bacteriological studies, including susceptibility tests and by clinical response. The following infections will usually respond to adequate dosage:

**Streptococcal infections:** Note: Streptococci in groups A, C, G, H, L, and M are very susceptible to penicillin G. Some group D organisms are susceptible to the high serum levels obtained with aqueous penicillin G. Aqueous penicillin G sodium is the penicillin dosage form

of choice for bacteremia, empyema, severe pneumonia, pericarditis, endocarditis, meningitis, and other severe infections caused by susceptible strains of the gram-positive species listed above.

**Pneumococcal Infections: Staphylococcal infections -** Penicillin G-susceptible; **Anthrax; Actinomycosis; Clostridial infections** (including tetanus); **Diphtheria** (to prevent the carrier state); **Erysipeloid endocarditis** (*Erysipelothrix insidiosa*); **Vincent's gingivitis and pharyngitis** (fusospirochetosis) - Severe infections of the oropharynx (Note: necessary dental care should be accomplished in infections involving gum tissue) and **lower respiratory tract and genital area infections due to** *F. fusiformisans* spirochetes; **Gram negative bacillary infections** (bacteremias) - (*E. coli, E. aerogenes, A. faecalis,* Salmonella, Shigella and *P. mirabilis*); **Listeria infections** (*L. monocytogenes*); **Meningitis and endocarditis; Pasteurella infections** (*P. multocida*); **Bacteremia and meningitis; Rat bite fever** (*S. minus or S. moniliformis*); **Gonorrheal endocarditis and arthritis** (*N. gonorrhoeae*); **Syphilis** (*T. pallidum*) including congenital syphilis; **Meningococcic meningitis**.

**Prevention of Bacterial Endocarditis** (Patients unable to take oral antibiotics):
Although no controlled clinical efficacy studies have been conducted, aqueous crystalline penicillin G for injection (except penicillin G procaine suspension) has been suggested by the American Heart Association and the American Dental Association for prophylaxis against bacterial endocarditis in patients with congenital heart disease or rheumatic or other acquired valvular heart disease when they undergo dental procedures and surgical procedures of the upper respiratory tract. Since it may happen that *alpha* hemolytic streptococci relatively resistant to penicillin may be found when patients are receiving continuous oral penicillin for secondary prevention of rheumatic fever, prophylactic agents other than penicillin may be chosen for these patients and prescribed in addition to their continuous rheumatic fever prophylactic regimen. Note: When selecting antibiotics for the prevention of bacterial endocarditis, the physician or dentist should read the full joint statement of the American Heart Association and the American Dental Association.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Penicillin G Sodium for Injection, USP and other antibacterial drugs, Penicillin G Sodium for Injection, USP should be used only to treat infections that are proven or strongly suspected to be caused by 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.

## CONTRAINDICATIONS

Contraindicated in patients with a history of hypersensitivity to any penicillin.

## WARNINGS

Serious occasional fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral

administration, 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 who have experienced severe hypersensitivity reactions when treated with cephalosporins. 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. Serious anaphylactoid reactions are not controlled by antihistamines alone, and require such emergency measures as the immediate use of epinephrine, aminophylline, oxygen, and intravenous corticosteroids.

**Susceptibility/Resistance**

Development of Drug Resistant Bacteria

Prescribing Penicillin G Sodium for Injection, USP in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of resistant organisms.

## PRECAUTIONS

Penicillin G Sodium for Injection, USP should be used with caution in individuals with histories of significant allergies and/or asthma.

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

In streptococcal infections, therapy must be sufficient to eliminate the organism (10 days minimum), otherwise the sequelae of streptococcal disease may occur. Cultures should be taken following the completion of treatment to determine whether streptococci have been eradicated.

In high doses (above 10 million units), intravenous aqueous Penicillin G Sodium for Injection, USP should be administered slowly because of the adverse effects of electrolyte imbalance from the sodium content of the penicillin. The patient's renal, cardiac and vascular status should be evaluated and if impairment of function is suspected or known to exist, a reduction in the total dosage should be considered. Frequent evaluation of electrolyte balance, and renal and hematopoietic function is recommended during therapy when high doses of intravenous aqueous Penicillin G Sodium for Injection, USP are used.

Therapy of susceptible infections should be accompanied by any indicated surgical procedures. In suspected staphylococcal infections, proper laboratory studies, including susceptibility tests, should be performed.

When treating gonococcal infections in which primary or secondary syphilis may be suspected,

proper diagnostic procedures, including darkfield examinations, should be done. In all cases in which concomitant syphilis is suspected, monthly serological tests should be made for at least four months. All cases of penicillin-treated syphilis should receive clinical and serological examinations every six months for at least two or three years.

## ADVERSE REACTIONS

Penicillin is a substance of low toxicity but does possess a significant index of sensitization.

**Hypersensitivity**
The hypersensitivity reactions reported are skin rashes ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; and serum sickness-like reactions including chills, fever, edema, arthralgia, and prostration. Severe and occasionally fatal anaphylaxis has occurred (see WARNINGS).

**Hematologic Disturbances**
Hemolytic anemia, leukopenia, thrombocytopenia, neuropathy, and nephropathy are rarely observed adverse reactions and are usually associated with high intravenous dosage. Urticaria, other skin rashes, and serum sickness-like reactions may be controlled by antihistamines and, if necessary, corticosteroids. Whenever such reactions occur, Penicillin G Sodium for Injection, USP should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. High dosage of Penicillin G Sodium for Injection, USP may result in congestive heart failure due to high sodium intake.

The Jarisch-Herxheimer reaction has been reported in patients treated for syphilis.

## SYMPTOMS AND TREATMENT OF OVERDOSAGE

Prolonged use of antibiotics may promote overgrowth of non-susceptible organisms, including fungi. Should superinfection occur, appropriate measures should be taken. Indwelling intravenous catheters encourage superinfections and should be avoided whenever possible.

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

## DOSAGE AND ADMINISTRATION

**Adult Dosage**
Severe infections due to susceptible strains of streptococci, pneumococci, and staphylococci; bacteremia, pneumonia, endocarditis, pericarditis, empyema, meningitis and other severe infections: a minimum of 5 million units daily.

**Anthrax:** A minimum of 5 million units/day in divided doses until cure is effected;
**Actinomycosis**: 1 to 6 million units/day for cervicofacial cases; 10 to 20 million units/day for

thoracic and abdominal disease; **Clostridial infections** (as adjunctive therapy to antitoxin): 20 million units/day; **Diphtheria**: adjunctive therapy to antitoxin for prevention of the carrier state: 300 000 to 400 000 units/day in divided doses for 10 to 12 days; **Erysipeloid**: *Endocarditis:* 2 to 20 million units/day for four to six weeks; **Fusospirochetal infections** (*fusospirochetosis*) - severe infections of the oropharynx, lower respiratory tract and genital area: 5 to 10 million units/day; **Gram-negative bacillary infections** (*E. coli, E. aerogenes, A. faecalis,* Salmonella, Shigella and *P. mirabilis*): *Bacteremia*: 20 to 80 million units/day; **Listeria infections** (*L. monocytogenes*): *Neonates*: 500 000 to 1 million units/day; *Adults with meningitis*: 15 to 20 million units/day for two weeks; *Adults with endocarditis*: 15 to 20 million units/day for four weeks; **Pasteurella infections** *(P. multocida*); *Bacteremia and meningitis*: 4 to 6 million units/day for two weeks; **Rat bite fever** (*S. minus* or *S. moniliformis*): 12 to 15 million units/day for three to four weeks.

**Gonorrheal Endocarditis and Arthritis:** A minimum of 5 million units daily.

**Syphilis:** Aqueous Penicillin G Sodium for Injection, USP may be used in the treatment of acquired and congenital syphilis but, because of the necessity of frequent dosage, hospitalization is recommended. Dosage and duration of therapy are determined by the age of the patient and the state of the disease.

**Meningococcic Meningitis:** 1 to 2 million units intramuscular every two hours or continuous intravenous-drip of 20 to 30 million units/day.

**Prevention of Bacterial Endocarditis** (Patients unable to take oral antibiotics): For prophylaxis against bacterial endocarditis in patients with congenital heart disease or rheumatic or other acquired valvular heart disease when undergoing dental procedures or surgical procedures of the upper respiratory tract, administer 2 million units (50 000 units/kg for children) aqueous penicillin G, except penicillin G procaine suspension, intravenously or intramuscularly 30 to 60 minutes before the procedure and 1 million units (25 000 units/kg for children) six hours later. Doses for children should not exceed recommendations for adults for a single dose or for a 24-hour period.

**Infant and Children Dosage**

Usual dose 50 000 to 100 000 units/kg/day given in divided doses every four to six hours.

## ADMINISTRATION

Penicillin G Sodium for Injection, USP may be given intramuscularly or by continuous intravenous drip. The 10 million units preparation should be administered by intravenous infusion. Intramuscular doses of 100 000 units per mL will produce the minimum of discomfort. The administered volume should not exceed 4 mL per single site of intramuscular administration. Doses up to 500 000 units per mL have been administered intramuscular.

Any entry into the container to effect solution of the powder or withdrawal must be accomplished with strict aseptic technique and sterile equipment.

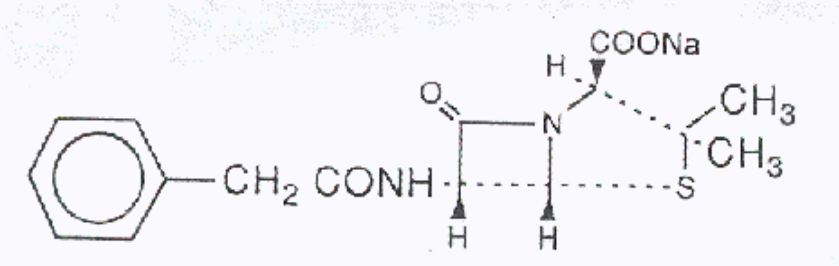
## PHARMACEUTICAL INFORMATION

**Drug Substance:**

**Proper Name** : Penicillin G Sodium

**Chemical Name** : 3,3-dimethyl-7-oxo-6[(phenylacetyl)amino]-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid monosodium salt

**Structural Formula** :




**Molecular Formula** : $C_{16}H_{17}N_2NaO_4S$

**Molecular Weight** : 356.37 g/mol

**Description** : Penicillin G Sodium is a sterile crystalline powder which is soluble in water.

## COMPOSITION

Each vial contains 1 million, 5 million, or 10 million units of penicillin G as penicillin G sodium. Each 1 million units of Penicillin G Sodium for Injection, USP contains 2 mmol of sodium.

## STABILITY AND STORAGE RECOMMENDATIONS

Store dry powder at a controlled room temperature (between 15 °C and 25 °C).

## RECONSTITUTED SOLUTIONS

Depending on the route of administration, use Sterile Water for Injection, USP, Isotonic Sodium Chloride Injection, or Dextrose Injection. Reconstituted solutions are stable for 24 hours at a

controlled room temperature (between 15 ºC and 25 °C) or for 5 days under refrigeration (between 2 ºC and 8 °C).

## RECONSTITUTION

| Potency/Vial (Million units) | Volume of Diluent (mL) | Approximate Available Volume (mL) | Approximate Concentration (units/mL) |
|---|---|---|---|
| 1 | 1.8<br>3.8 | 2<br>4 | 500 000<br>250 000 |
| 5 | 3.1<br>8.2 | 5<br>10 | 1 000 000<br>500 000 |
| 10 | 6<br>16.2 | 10<br>20 | 1 000 000<br>500 000 |

**NOTE:** Penicillins are rapidly inactivated in the presence of carbohydrate solutions at alkaline pH.

## PREPARATION OF SOLUTIONS

Solutions of penicillin should be prepared as follows: Loosen powder. Hold vial horizontally and rotate it while slowly directing the stream of diluent against the wall of the vial. Shake vial vigorously after all the diluent has been added.

## AVAILABILITY OF DOSAGE FORMS

Penicillin G Sodium for Injection, USP is supplied as a dry powder in vials containing: 1 million, 5 million, or 10 million penicillin G units as penicillin G sodium.

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

**PATIENT MEDICATION INFORMATION**

**[Pr]Penicillin G Sodium for Injection, USP**

Read this carefully before you start taking Penicillin G Sodium for Injection, USP 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 Penicillin G Sodium for Injection, USP.

**What is Penicillin G Sodium for Injection, USP used for?**

- Penicillin G Sodium for Injection, USP is used to treat infections that are caused by certain types of bacteria.
- Antibacterial drugs like Penicillin G Sodium for Injection, USP treat only bacterial infections. They do not treat viral infections.

**How does Penicillin G Sodium for Injection, USP work?**

Penicillin G Sodium for Injection, USP is an antibiotic that belongs to the penicillin class. It works by killing or stopping the growth of the bacteria that caused your infection.

**What are the ingredients in Penicillin G Sodium for Injection, USP?**

Medicinal Ingredient: penicillin G sodium

**Penicillin G Sodium for Injection, USP comes in the following dosage forms:**

Penicillin G Sodium for Injection, USP is supplied as a dry powder in vials containing: 1 million, 5 million, or 10 million penicillin G units (as penicillin G sodium).

**Do not use Penicillin G Sodium for Injection, USP if:**

- you are allergic to penicillin G sodium or other penicillin products.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Penicillin G Sodium for Injection, USP. Talk about any health conditions or problems you may have, including if you:**

- have had previous allergic reactions to other penicillins, cephalosporins, and other allergens.
- have asthma.
- have kidney disease.
- have heart disease or vascular disease (issues with your veins or arteries).
- are pregnant or planning to become pregnant.
- are breastfeeding or planning to breastfeed.

**Other warnings you should know about:**

- Your doctor may order certain tests or exams while you are taking Penicillin G Sodium for Injection, USP.

**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 Penicillin G Sodium for Injection, USP:**

- Antibiotics such as chloramphenicol, erythromycins, sulfonamides, and tetracyclines
- Probenecid (to treat gout)
- Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, phenylbutazone, and indomethacin
- Diuretics such as thiazide diuretics, furosemide, and ethacrynic acid

**How to take Penicillin G Sodium for Injection, USP:**

- Although you may feel better early in treatment, Penicillin G Sodium for Injection, USP should be used exactly as directed.
- Misuse or overuse of Penicillin G Sodium for Injection, USP could lead to the growth of bacteria that will not be killed by Penicillin G Sodium for Injection, USP (resistance). This means that Penicillin G Sodium for Injection, USP may not work for you in the future.
- Do not share your medicine.
- Your healthcare professional will prepare Penicillin G Sodium for Injection, USP before administering.

**Adult dose:**

- Your healthcare professional will decide your dose based on your infection.

**Infant and children dose:**

- Your healthcare professional will decide your child's dose based on their weight and infection.

**Overdose:**

If you think you have taken too much Penicillin G Sodium for Injection, USP, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

**What are possible side effects from using Penicillin G Sodium for Injection, USP?**

**These are not all the possible side effects you may feel when taking Penicillin G Sodium for Injection, USP. If you experience any side effects not listed here, contact your healthcare professional.**

| **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 | |
| **Jarisch–Herxheimer Reaction (Syphilis-Related Reaction):** fever, headache, shaking chills, sweating, temporary worsening of sores, seizures, stroke, muscle pain, rapid heart rate, hyperventilation, flushing, and low blood pressure | | | X |
| **Allergic Reaction:** chills, fever, hives joint pain, rash, swelling, nausea, itching, muscle spasms, low blood pressure, vascular failure, difficulty breathing, discomfort, and abdominal pain | | | X |
| **Neuropathy (Nervous System Damage):** weakness, numbness, pain, overactive reflexes, muscle twitches, seizures, and coma | X | | |
| **Congestive Heart Failure:** chest discomfort with unpleasant awareness of your heartbeat, faintness, shortness of breath, and weakness | | | X |
| **Nephropathy (Kidney Disease):** back and abdominal pain, change in the colour of urine (pale or dark), decrease in amount of urine produced, pain or discomfort when urinating, swelling of the legs and ankles, and blood in the urine | | X | |
| **Pseudomembranous Colitis (Inflammation of the Colon):** nausea, vomiting, inflammation of mouth or lips, black or hairy tongue, and gastrointestinal irritation | | X | |

| | | | |
|---|---|---|---|
| **Electrolyte Disturbances:** weakness, drowsiness, muscle pain or cramps, and irregular heartbeat | | X | |
| **Phlebitis (Swelling of a Vein):** pain, tenderness, and redness or swelling | X | | |
| **Thrombophlebitis (Blood Clots):** swelling and redness along a vein which is extremely tender or painful when touched | X | | |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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/adverse-reaction-reporting.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 **dry powder** at a controlled room temperature (between 15 °C and 25 °C).
- Store **reconstituted solution** at a controlled room temperature (between 15 °C and 25 °C) for up to 24 hours or under refrigeration (between 2 °C and 8 °C) for up to 5 days.
- Keep out of reach and sight of children.

**If you want more information about Penicillin G Sodium for Injection, USP:**

- Talk to your healthcare professional
- Find the full Prescribing Information that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); Fresenius Kabi Canada's website (http://www.fresenius-kabi.com/en-ca/), or by calling 1-877-821-7724.

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