tropenia, agranulocytosis, thrombocytopenia, leukopenia, anemias, lymphadenopathy, or full-blown anaphylaxis. In humans, it is estimated that up to 15% of patients hypersensitive to cephalosporins will also be hypersensitive to penicillins. The incidence of cross-reactivity in veterinary patients is unknown.

When given orally, penicillins may cause GI effects (anorexia, vomiting, diarrhea). Because the penicillins may also alter gut flora, antibiotic-associated diarrhea can occur and allow the proliferation of resistant bacteria in the colon (superinfections).

Neurotoxicity (*e.g.*, ataxia in dogs) has been associated with very high doses or very prolonged use. Although the penicillins are not considered hepatotoxic, elevated liver enzymes have been reported. Other effects reported in dogs include tachypnea, dyspnea, edema, and tachycardia.

Some penicillins (ticarcillin, carbenicillin, azlocillin, mezlocillin, piperacillin and nafcillin) have been implicated in causing bleeding problems in humans. These drugs are infrequently used systemically in veterinary species and veterinary ramifications of this effect are unclear.

Reproductive/Nursing Safety

Penicillins have been shown to cross the placenta and safe use of them during pregnancy has not been firmly established, but neither have there been any documented teratogenic problems associated with these drugs. In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy *(Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*) However, use only when the potential benefits outweigh the risks.

Penicillins are excreted in maternal milk in low concentrations; use potentially could cause diarrhea, candidiasis, or allergic response in the nursing offspring.

Overdosage/Acute Toxicity

Acute oral penicillin overdoses are unlikely to cause significant problems other than GI distress, but other effects are possible (see Adverse effects). In humans, very high dosages of parenteral penicillins, especially in patients with renal disease, have induced CNS effects.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving penicillins and may be of significance in veterinary patients:

- **AMINOGLYCOSIDES**: *In vitro* studies have demonstrated that penicillins can have synergistic or additive activity against certain bacteria when used with aminoglycosides or cephalosporins.
- **BACTERIOSTATIC ANTIBIOTICS** (*e.g.*, **chloramphenicol, erythromycin, tetracyclines**): Use with penicillins is generally not recommended, particularly in acute infections where the organism is proliferating rapidly as penicillins tend to perform better on actively growing bacteria.
- **PROBENECID**: Competitively blocks the tubular secretion of most penicillins, thereby increasing serum levels and serum half-lives.

Laboratory Considerations

- Penicillins may cause false-positive **urine glucose** determinations when using cupric-sulfate solution (Benedict's Solution, *Clinitest*®). Tests utilizing glucose oxidase (*Tes-Tape*®, *Clinistix*®) are not affected by penicillin.
- In humans, clavulanic acid and high dosages of piperacillin have caused a false-positive direct **Combs' test**.
- As penicillins and other beta-lactams can inactivate aminoglycosides *in vitro* (and *in vivo* in patients in renal failure), serum concentrations of **aminoglycosides** may be falsely decreased if the patient is also receiving beta-lactam antibiotics and the serum is stored prior to analysis. It is recommended that if the assay is delayed, samples be frozen and, if possible, drawn at times when the beta-lactam antibiotic is at a trough.

Monitoring

- Because penicillins usually have minimal toxicity associated with their use, monitoring for efficacy is usually all that is required unless toxic signs develop.
- Serum levels and therapeutic drug monitoring are not routinely done with these agents.

Client Information

- Owners should be instructed to give oral penicillins on an empty stomach, unless using amoxicillin or GI effects (anorexia, vomiting) occur.
- Compliance with the therapeutic regimen should be stressed.
- Reconstituted oral suspensions should be kept refrigerated and discarded after 14 days, unless labeled otherwise.

PENICILLIN G

(pen-i-*sill*-in *jee*)

PENICILLIN ANTIBIOTIC

Prescriber Highlights

- **Prototypical penicillin agent used for susceptible gram-positive aerobes & anaerobes; best used parenterally**
- **Contraindications: Known hypersensitivity (unless no other options)**
- **Adverse Effects: Hypersensitivity possible. Very high doses may cause CNS effects.**
- **Benzathine penicillin only effective against extremely sensitive agents**
- **Certain species may be sensitive to procaine penicillin G**

Uses/Indications

Natural penicillins remain the drugs of choice for a variety of bacteria, including group A beta-hemolytic streptococci, many gram-positive anaerobes, spirochetes, gram-negative aerobic cocci, and some gram-negative aerobic bacilli. Generally, if a bacteria remains susceptible to a natural penicillin, either penicillin G or V is preferred for treating that infection as long as adequate penetration of the drug to the site of the infection occurs and the patient is not hypersensitive to penicillins.

Pharmacology/Actions

Penicillins are usually bactericidal against susceptible bacteria and act by inhibiting mucopeptide synthesis in the cell wall resulting in a defective barrier and an osmotically unstable spheroplast. The exact mechanism for this effect has not been definitively determined, but beta-lactam antibiotics have been shown to bind to several enzymes (carboxypeptidases, transpeptidases, endopeptidases) within the bacterial cytoplasmic membrane that are involved with cell wall

synthesis. The different affinities that various beta-lactam antibiotics have for these enzymes (also known as penicillin-binding proteins; PBPs) help explain the differences in spectrums of activity the drugs have that are not explained by the influence of beta-lactamases. Like other beta-lactam antibiotics, penicillins are generally considered more effective against actively growing bacteria.

The natural penicillins (G and K) have similar spectrums of activity, but penicillin G is slightly more active *in vitro* on a weight basis against many organisms. This class of penicillin has *in vitro* activity against most spirochetes and gram-positive and gram-negative aerobic cocci, but not penicillinase producing strains. They have activity against some aerobic and anaerobic gram-positive bacilli such as *Bacillus anthracis*, *Clostridium* spp. (not *C. difficile*), Fusobacterium, and Actinomyces. The natural penicillins are customarily inactive against most gram-negative aerobic and anaerobic bacilli, and all Rickettsia, mycobacteria, fungi, Mycoplasma, and viruses.

Pharmacokinetics

Penicillin G potassium is poorly absorbed orally because of rapid acid-catalyzed hydrolysis. When administered on an empty (fasted) stomach, oral bioavailability is only about 15–30%. If given with food, absorption rate and extent will be decreased.

Penicillin G potassium and sodium salts are rapidly absorbed after IM injections and yield high peak levels usually within 20 minutes of administration. In horses, equivalent doses given either IV or IM demonstrated that IM dosing will provide serum levels above 0.5 micrograms/mL for about twice as long as IV administration [approx. 3–4 hours (IV) vs. 6–7 hours (IM)].

Procaine penicillin G is slowly hydrolyzed to penicillin G after IM injection. Peak levels are much lower than with parenterally administered aqueous penicillin G sodium or potassium, but serum levels are more prolonged.

Benzathine penicillin G is also very slowly absorbed after IM injections after being hydrolyzed to the parent compound. Serum levels can be very prolonged, but levels attained generally only exceed MIC's for the most susceptible streptococci, and the use of benzathine penicillin G should be limited to these infections when other penicillin therapy is impractical.

After absorption, penicillin G is widely distributed throughout the body with the exception of the CSF, joints and milk. In lactating dairy cattle, the milk to plasma ratio is about 0.2. CSF levels are generally only 10% or less of those found in the serum when meninges are not inflamed. Levels in the CSF may be greater in patients with inflamed meninges or if probenecid is given concurrently. Binding to plasma proteins is approximately 50% in most species.

Penicillin G is principally excreted unchanged into the urine through renal mechanisms via both glomerular filtration and tubular secretion. Elimination half-lives are very rapid and are usually one hour or less in most species (if normal renal function exists).

Contraindications/Precautions/Warnings

Penicillins are contraindicated in patients with a history of hypersensitivity to them. Because there may be cross-reactivity, use penicillins cautiously in patients who are documented hypersensitive to other beta-lactam antibiotics (*e.g.*, cephalosporins, cefamycins, carbapenems).

Do not administer systemic antibiotics orally in patients with septicemia, shock, or other grave illnesses as absorption of the medication from the GI tract may be significantly delayed or diminished; parenteral (preferably IV) routes should be used for these cases.

High doses of penicillin G sodium or potassium, particularly in small animals with a preexisting electrolyte abnormality, renal disease, or congestive heart failure may cause electrolyte imbalances. Other injectable penicillins, such as ticarcillin, carbenicillin, and ampicillin, have significant quantities of sodium per gram and may cause electrolyte imbalances when used in large dosages in susceptible patients.

Certain species (snakes, birds, turtles, Guinea pigs, and chinchillas) are reportedly sensitive to procaine penicillin G.

Adverse Effects

Adverse effects with the penicillins are usually not serious and have a relatively low frequency of occurrence.

Hypersensitivity reactions unrelated to dose can occur with these agents and can manifest as rashes, fever, eosinophilia, neutropenia, agranulocytosis, thrombocytopenia, leukopenia, anemias, lymphadenopathy, or full-blown anaphylaxis. In humans, it is estimated that up to 15% of patients hypersensitive to cephalosporins will also be hypersensitive to penicillins. The incidence of cross-reactivity in veterinary patients is unknown.

When given orally, penicillins may cause GI effects (anorexia, vomiting, diarrhea). Because the penicillins may also alter gut flora, antibiotic-associated diarrhea can occur and allow the proliferation of resistant bacteria in the colon (superinfections).

Neurotoxicity (*e.g.*, ataxia in dogs) has been associated with very high doses or very prolonged use. Although the penicillins are not considered hepatotoxic, elevated liver enzymes have been reported. Other effects reported in dogs include tachypnea, dyspnea, edema and tachycardia.

Reproductive/Nursing Safety

Penicillins have been shown to cross the placenta and safe use of them during pregnancy has not been firmly established, but neither have there been any documented teratogenic problems associated with these drugs; however, use only when the potential benefits outweigh the risks.

In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as class: ***A*** (*Probably safe. Although specific studies may not have proved he safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Penicillins are excreted in maternal milk in low concentrations; use could potentially cause diarrhea, candidiasis, or allergic responses in nursing offspring.

Overdosage/Acute Toxicity

Acute oral penicillin overdoses are unlikely to cause significant problems other than GI distress, but other effects are possible (see Adverse Effects). In humans, very high dosages of parenteral penicillins, especially those with renal disease, have induced CNS effects.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving penicillin G and may be of significance in veterinary patients:

- **AMINOGLYCOSIDES**: *In vitro* studies have demonstrated that penicillins can have synergistic or additive activity against certain bacteria when used with aminoglycosides or cephalosporins.
- **BACTERIOSTATIC ANTIBIOTICS** (*e.g.*, **chloramphenicol, erythromycin, tetracyclines**): Use with penicillins is generally not recommended, particularly in acute infections where the organism is proliferat-

ing rapidly as penicillins tend to perform better on actively growing bacteria.

- **METHOTREXATE:** Penicillins may decrease renal elimination of MTX
- **PROBENECID:** Competitively blocks the tubular secretion of most penicillins, thereby increasing serum levels and serum half-lives.

Laboratory Considerations

- As penicillins and other beta-lactams can inactivate **aminoglycosides** *in vitro* (and *in vivo* in patients in renal failure), serum concentrations of aminoglycosides may be falsely decreased if the patient is also receiving beta-lactam antibiotics and the serum is stored prior to analysis. It is recommended that if the assay is delayed, samples be frozen and, if possible, drawn at times when the beta-lactam antibiotic is at a trough.
- Penicillin G can cause falsely elevated **serum uric acid** values if the copper-chelate method is used; phosphotungstate and uricase methods are not affected
- Penicillins may cause false-positive **urine glucose** determinations when using cupric-sulfate solution (Benedict's Solution, *Clinitest*®). Tests utilizing glucose oxidase (*Tes-Tape*®, *Clinistix*®) are not affected by penicillin.

Doses

- **DOGS:**

  For susceptible infections:

  a) *Penicillin G potassium:*

  For bacteremia, systemic infections: 20,000–40,000 Units/kg IV q4–6h for as long as necessary.

  For orthopedic infections: 20,000–40,000 Units/kg IV q6h for as long as necessary.

  Prophylaxis for orthopedic surgery: 40,000 Units/kg IV one hour prior to surgery, and if surgery lasts longer than 90 minutes a second dose is given.

  For soft tissue infections: 40,000–60,000 Units/kg PO q8h for as long as necessary.

  Penicillin G procaine: 20,000–40,000 Units/kg IM, SC q12–24h for as long as necessary.

  Penicillin G benzathine: 40,000 IU/kg IM q5 days. (Greene, Hartmannn et al. 2006)

  b) *Penicillin G potassium/sodium:* 20,000 Units/kg IV, IM, or SC q6h

  Penicillin G procaine: 22,000 Units/kg IM, SC q12h. Doses may be increased to 80,000 IU/kg per day; Actinomyces infections may require 100,000–200,000 IU/kg IM daily. (Ford and Aronson 1985)

  c) *Penicillin G potassium/sodium:* 20,000 Units/kg IV, IM, q4h or 40,000 IU/kg PO on an empty stomach q6h

  Penicillin G procaine: 20,000 Units/kg IM, SC q12–24h.

  Penicillin G benzathine: 40,000 IU/kg q5 days IM (Kirk 1989)

  d) For leptospiremia: 25,000–40,000 U/kg IV or IM q12–24h for 14 days. For the renal carrier state of leptospirosis: Doxycycline 5–10 mg/kg PO twice daily of doxycycline for an additional 14 days after penicillin G therapy (Ross and Rentko 2000)

  e) For adjunctive therapy of septicemia: Penicillin G sodium/potassium: 25,000 IU/kg IV q6h. Too rapid IV infusions may cause neurologic signs; hypersensitivity may also occur. (Goodwin and Schaer 1989)

- **CATS:**

  For susceptible infections:

  a) *Penicillin G potassium:*

  For soft tissue, systemic infections: 40,000 IU/kg PO q6–8h for as long as necessary.

  Penicillin G procaine:

  For soft tissue infections: 20,000 Units/kg IM, SC q12h for as long as necessary.

  For orthopedic infections: 20,000–40,000 Units/kg IM q8h for as long as necessary.

  For resistant organisms (Actinomyces): 50,000–100,000 Units/kg IM, SC q12h for as long as necessary.

  Penicillin G benzathine: 50,000 IU/kg IM q5 days. (Greene, Hartmannn et al. 2006)

  b) *Penicillin G potassium/sodium:* 20,000–40,000 Units/kg IV, IM, q6h

  Penicillin G procaine: 22,000 Units/kg IM, SC q12h. Doses may be increased to 80,000 IU/kg per day; Actinomyces infections may require 100,000–200,000 IU/kg IM daily (Ford and Aronson 1985)

  c) *Penicillin G potassium/sodium:* 20,000 Units/kg IV, IM, q4h or 40,000 IU/kg PO on an empty stomach q6h

  Penicillin G procaine: 20,000 Units/kg IM, SC q12–24h.

  Penicillin G benzathine: 40,000 IU/kg q5 days IM (Kirk 1989)

  d) *Penicillin G sodium or potassium:* 22,000–55,000 IU/kg IV or IM q6–8h (Aronson and Aucoin 1989)

- **FERRETS:**

  For susceptible infections:

  a) Procaine Pen G: 20,000–40,000 IU/kg IM once a day to twice daily;

  Sodium or potassium Pen G: 20,000 IU/kg SC, IM or IV q4h or 40,000 IU/kg PO three times daily (Williams 2000)

- **RABBITS, RODENTS, SMALL MAMMALS:**

  a) Rabbits: Penicillin G Procaine 20,000–84,000 IU/kg SC, IM q24h for 5–7 days for venereal spirochetosis (Ivey and Morrisey 2000)

  b) Hedgehogs: 40,000 IU/kg IM once daily (Smith 2000)

- **CATTLE** (and other ruminants unless specified):

  For susceptible infections:

  a) *Penicillin G procaine:* 44,000–66,000 Units/kg IM, SC once daily

  Penicillin G benzathine: 44,000–66,000 Units/kg IM, or SC q2days (Upson 1988)

  b) For bovine respiratory disease complex: Procaine penicillin G 66,000 IU/kg IM or SC once daily. Recommend 20–day slaughter withdrawal at this dosage. (Hjerpe 1986)

  c) *Procaine penicillin G:* 40,000 IU/kg IM once daily

  Procaine penicillin G/benzathine penicillin G combination: 40,000 IU/kg IM once (Howard 1986)

  d) *Procaine penicillin G:* 10,000–20,000 IU/kg IM q12–24h.

  Benzathine penicillin G: 10,000–20,000 IU/kg, IM, SC q48h (Jenkins 1986)

- **HORSES:**

  For susceptible infections:

  a) For gram-positive aerobes: Penicillin G potassium or sodium: 10,000–20,000 Units/kg IV or IM q6h.

  For serious gram-positive infections (*e.g.,* tetanus, botulism, C. difficile enterocolitis in foals): Penicillin G sodium or potassium 22,000–44,000 Units/kg IV q6h

Susceptible bacterial infections: Penicillin G procaine: 22,000–44,000 Units/kg IM q12h (Whittem 1999)

b) Treatment of carriers with *S. equi* infections of the gutteral pouches: Administration of both systemic and topical penicillin G appears to improve treatment success rate. Before topical therapy, remove all visible inflammatory material removed from gutteral pouch. To make a gelatin/penicillin G mix of 50 mL for gutteral pouch instillation:
   1) Weigh out 2 grams gelatin (Sigma G-6650 or household) and add 40 mL of sterile water.
   2) Heat or microwave to dissolve. Cool to 45–50°C,
   3) Add 10 mL sterile water to a 10 million unit sodium penicillin G for injection vial and mix with the cooled gelatin to total volume of 50 mL.
   4) Dispense into syringes and leave overnight in the refrigerator.

   Instillation is easiest through a catheter inserted up the nose and endoscopically guided into the pouch opening with the last inch bent at an angle to aid entry under the pouch flap. Elevate horse's head for 20 minutes after infusion. (Verheyen, Newton et al. 2000)

c) For treatment of botulism: Penicillin G sodium or potassium 22,000–44,000 IU/kg IV four times daily (do not use oral penicillin therapy) (Johnston and Whitlock 1987)

d) For strangles: Early in infection when only fever and depression are present: procaine penicillin G 22,000 IU/kg IM or SC q12h, or aqueous salts (sodium or potassium) penicillin G 22,000 IU/kg IM, IV or SC q6h. If lymphadenopathy noted in otherwise healthy and alert horse do not treat. If lymphadenopathy present and horse is depressed, febrile, anorexic and especially if dyspneic, treat as above. (Foreman 1999)

e) For foals: Penicillin G Na or K: 20,000–50,000 U/kg IV q6–8h; Procaine penicillin G 22,000–50,000 U/kg IM q12h (Brumbaugh 1999)

f) For foals: Penicillin G sodium or potassium: 20,000–50,000 U/kg IV q6h Penicillin G Procaine: 20,000–50,000 U/kg IM q6h (Furr 1999)

■ **SWINE:**

For susceptible infections:

a) Procaine penicillin G: 40,000 IU/kg IM once daily.

   Procaine penicillin G/benzathine penicillin G combination: 40,000 IU/kg IM once (Howard 1986)

b) Procaine penicillin G: 6,600 IU/kg IM once daily for not more than 4 days

   Procaine penicillin G/benzathine penicillin G combination: 11,000–22,000 IU/kg IM once (Wood 1986)

■ **BIRDS:**

For susceptible infections:

a) In turkeys: Procaine penicillin G/benzathine penicillin G combination: 100 mg/kg IM of each drug once a day or every 2 days. Use cautiously in small birds as it may cause procaine toxicity. (Clubb 1986)

Monitoring

■ Because penicillins usually have minimal toxicity associated with their use, monitoring for efficacy is usually all that is required unless toxic signs develop. Serum levels and therapeutic drug monitoring are not routinely done with these agents.

Client Information

■ Owners should be instructed to give oral penicillins to animals with an empty stomach, unless using amoxicillin or if GI effects (anorexia, vomiting) occur.

■ Compliance with the therapeutic regimen should be stressed.

Chemistry/Synonyms

Penicillin G is considered natural penicillin and is obtained from cultures *Penicillium chrysogenum* and is available in several different salt forms. Penicillin G potassium (also known as benzylpenicillin potassium, aqueous or crystalline penicillin) occurs as colorless or white crystals, or white crystalline powder. It is very soluble in water and sparingly soluble in alcohol. Potency of penicillin G potassium is usually expressed in terms of Units. One mg of penicillin G potassium is equivalent to 1440–1680 USP Units (1355–1595 USP Units for the powder for injection). After reconstitution, penicillin G potassium powder for injection has a pH of 6–8.5, and contains 1.7 mEq of potassium per 1 million Units.

Penicillin G sodium (also known as benzylpenicillin sodium, aqueous or crystalline penicillin) occurs as colorless or white crystals, or white to slightly yellow, crystalline powder. Approximately 25 mg are soluble in 1 mL of water. Potency of penicillin G sodium is usually expressed in terms of Units. One mg of penicillin G sodium is equivalent to 1500–1750 USP Units (1420–1667 USP Units for the powder for injection). After reconstitution, penicillin G sodium powder for injection has a pH of 6–7.5, and contains 2 mEq of sodium per 1 million Units.

Penicillin G procaine (also known as APPG, Aqueous Procaine Penicillin G, Benzylpenicillin Procaine, Procaine Penicillin G, Procaine Benzylpenicillin) is the procaine monohydrate salt of penicillin G. *In vivo* it is hydrolyzed to penicillin G and acts as a depot, or repository form, of penicillin G. It occurs as white crystals or very fine, white crystalline powder. Approximately 4–4.5 mg are soluble in 1 mL of water and 3.3 mg are soluble in 1 mL of alcohol. Potency of penicillin G procaine is usually expressed in terms of Units. One mg of penicillin G procaine is equivalent to 900–1050 USP Units. The commercially available suspension for injection is buffered with sodium citrate and has a pH of 5–7.5. It is preserved with methylparaben and propylparaben.

Penicillin G Benzathine (also known as Benzathine Benzylpenicillin, Benzathine Penicillin G, Benzylpenicillin Benzathine, Dibenzylethylenediamine Benzylpenicillin) is the benzathine tetrahydrate salt of penicillin G. It is hydrolyzed *in vivo* to penicillin G and acts as a long-acting form of penicillin G. It occurs as an odorless, white, crystalline powder. Solubilities are 0.2–0.3 mg/mL of water and 15 mg/mL of alcohol. One mg of penicillin G benzathine is equivalent to 1090–1272 USP Units. The commercially available suspension for injection is buffered with sodium citrate and has a pH of 5–7.5. It is preserved with methylparaben and propylparaben.

Penicillin G may also be known as: benzylpenicllin, crystalline penicillin G, penicillin, *Bicillin C-R®*, *Masti-Clear®*, *Permapen®*, and *Pfizerpen®*.

Storage/Stability/Compatibility

Penicillin G sodium and potassium should be protected from moisture to prevent hydrolysis of the compounds. Penicillin G potassium tablets and powder for oral solution should be stored at room temperature in tight containers; avoid exposure to excessive heat. After reconstituting, the oral powder for solution should be stored from 2–8°C (refrigerated) and discarded after 14 days.

Penicillin G sodium and potassium powder for injection can be stored at room temperature (15–30°C). After reconstituting, the injectable solution is stable for 7 days when kept refrigerated (2–8°C) and for 24 hours at room temperature.

Penicillin G procaine should be stored at 2–8°C; avoid freezing. Benzathine penicillin G should be stored at 2–8°C.

All commonly used IV fluids (some Dextran products are physically **incompatible**) and the following drugs are reportedly physically **compatible** with penicillin G potassium: ascorbic acid injection, calcium chloride/gluconate, cephapirin sodium, chloramphenicol sodium succinate, cimetidine HCl, clindamycin phosphate, colistimethate sodium, corticotropin, dimenhydrinate, diphenhydramine HCl, ephedrine sulfate, erythromycin gluceptate/lactobionate, hydrocortisone sodium succinate, kanamycin sulfate, lidocaine HCl, methicillin sodium, methylprednisolone sodium succinate, metronidazole with sodium bicarbonate, nitrofurantoin sodium, polymyxin B sulfate, potassium chloride, prednisolone sodium phosphate, procaine HCl, prochlorperazine edisylate, sodium iodide, sulfisoxazole diolamine, and verapamil HCl.

The following drugs/solutions are either physically **incompatible** or **data conflicts** regarding compatibility with penicillin G potassium injection: amikacin sulfate, aminophylline, cephalothin sodium, chlorpromazine HCl, dopamine HCl, heparin sodium, hydroxyzine HCl, lincomycin HCl, metoclopramide HCl, oxytetracycline HCl, pentobarbital sodium, prochlorperazine mesylate, promazine HCl, promethazine HCl, sodium bicarbonate, tetracycline HCl, and vitamin B-complex with C.

The following drugs/solutions are reportedly physically **compatible** with penicillin G sodium injection: Dextran 40 10%, dextrose 5% (some degradation may occur if stored for 24 hours), sodium chloride 0.9% (some degradation may occur if stored for 24 hours), calcium chloride/gluconate, chloramphenicol sodium succinate, cimetidine HCl, clindamycin phosphate, colistimethate sodium, diphenhydramine HCl, erythromycin lactobionate, gentamicin sulfate, hydrocortisone sodium succinate, kanamycin sulfate, methicillin sodium, nitrofurantoin sodium, polymyxin B sulfate, prednisolone sodium phosphate, procaine HCl, verapamil HCl, and vitamin B-complex with C.

The following drugs/solutions are either physically **incompatible** or **data conflicts** regarding compatibility with penicillin G sodium injection: amphotericin B, bleomycin sulfate, cephalothin sodium, chlorpromazine HCl, heparin sodium, hydroxyzine HCl, lincomycin HCl, methylprednisolone sodium succinate, oxytetracycline HCl, potassium chloride, prochlorperazine mesylate, promethazine HCl and tetracycline HCl. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Note: Withdrawal times are for labeled dosages only.

Penicillin G Procaine Injection 300,000 Units/mL in 100 mL and 250 mL vials: Variety of trade names available. Depending on product, approved for use in: cattle, sheep, horses, and swine. Not intended for use in horses used for food. Do not exceed 7 days of treatment in non-lactating dairy cattle, beef cattle, swine or sheep; 5 days in lactating dairy cattle. Treatment should not exceed 4 consecutive days.

Withdrawal times vary depending on the product are for the labeled dosage of 6,600 U/kg once daily (rarely used clinically today). Actual withdrawal times may be longer. Milk withdrawal times (at labeled doses) = 48 hours. Slaughter withdrawal: Calves (non-ruminating) = 7 days; cattle = 4–10 days; sheep = 8–9 days; swine = 6–7 days; refer to label for more information.

Penicillin G Procaine Mastitis Syringes 100,000 units/mL in 10 mL units: *Go-Dry®* (G.C. Hanford) (OTC) Milk withdrawal (at labeled doses) = 72 hours. Slaughter withdrawal (at labeled doses) = 14 days. For use in dry cows only. *Masti-Clear®* (G.C. Hanford) Milk withdrawal (at labeled doses) = 60 hours. Slaughter withdrawal (at labeled doses) = 3 days. Administer no more than 3 consecutive doses or withdrawal times must lengthen.

There are also mastitis syringes in combination with novobiocin (*Albadry Plus®*) or dihydrostreptomycin (*Quartermaster®*)

Penicillin G Benzathine 150,000 U/mL with Penicillin G Procaine Injection 150,000 Units/mL for Injection in 100 mL and 250 mL vials: Variety of trade names available. Approved (most products) in horses and beef cattle. Not approved for horses intended for food use. Slaughter withdrawal: cattle = 30 days (at labeled doses). Actual species approvals and withdrawal times may vary with the product; refer to the label of the product you are using.

HUMAN-LABELED PRODUCTS:

Penicillin G (Aqueous) Sodium Powder for Injection: 5,000,000 units & 20,000,000 units in vials; *Pfizerpen®* (Pfizer); generic (Sandoz); (Rx)

Penicillin G (Aqueous) Potassium Injection (Premixed, frozen): 1,000,000 units, 2,000,000 units & 3,000,000 units in 50 mL Galaxy containers; generic (Baxter); (Rx)

Penicillin G (Procaine Injection: 600,000 Units/vial in 1 mL *Tubex* & 1,200,000 Units/vial in 2 mL *Tubex*; generic; (Monarch); (Rx)

Penicillin G Benzathine IM Injection: 600,000 units/dose in 1 mL *Tubex*; 1,200,000 units/dose in 2 mL *Tubex* and 2 mL *Isoject*; 2,400,000 units/dose in 4 mL pre-fillled syringes; *Bicillin L-A®* (Monarch); *Permapen®* (Roerig); (Rx)

Penicillin G Benzathine/Penicillin G Procaine IM Injection: 600,000 units/dose (300,000 units each penicillin G benzathine and penicillin G procaine) in 1 mL *Tubex*; 1,200,000 units/dose (600,000 units each penicillin G benzathine and penicillin G procaine) in 2 mL *Tubex*; 2,400,000 units/dose (1,200,000 units each penicillin G benzathine and penicillin G procaine) in 4 mL syringes; 1,200,000 units/dose (900,000 units penicillin G benzathine and 300,000 units penicillin G procaine) in 2 mL *Tubex*; *Bicillin C-R®* and *Bicillin C-R 900/300®* (Monarch); (Rx)

PENICILLIN V POTASSIUM

(pen-i-*sill*-in *Vee*) Phenoxymethylpenicillin

ORAL PENICILLIN ANTIBIOTIC

Prescriber Highlights

- **Oral natural penicillin**
- **Contraindications: Known hypersensitivity (unless no other options)**
- **Adverse Effects: GI effects or hypersensitivity possible**
- **Best to give on an empty stomach**

Uses/Indications

Penicillins have been used for a wide range of infections in various species. See the dosage section for more information.