

Phenoxymethylpenicillin Oral Solution

Phenoxymethylpenicillin 125 mg/5 mL and 250 mg/5 mL, granules for oral solution

Presentation

Pale orange granular powder with an orange odour which when reconstituted with purified water results in a clear orange solution with an orange odour and flavour. After reconstitution, the solution provides either Phenoxymethylpenicillin 125 mg per 5 mL or 250 mg per 5 mL as appropriate.

Uses

Actions

Phenoxymethylpenicillin exerts a bactericidal action against penicillin sensitive micro-organisms during the stage of active multiplication. It is not active against the penicillinase producing bacteria, which includes many strains of staphylococci.

Sensitive organisms include the following:

- Gram-positive cocci, e.g. Streptococci (groups A,C,G,H,L and M), and non-penicillinase producing *Staphylococcus pyogenes*.
- Gram-positive bacilli, e.g. Clostridium tetani, Cl. Perfringens, Corynebacterium diphtheriae and Bacillus anthracis.
- Gram-negative bacteria, both *Neisseria meningitidis* and *N. gonorrhoeae* are sensitive to a degree but *Haemophilus influenzae* is moderately resistant and other aerobic Gram-negative bacilli are highly resistant.
- *Treponema pallidum* is sensitive, but treatment of syphilis with oral penicillins is not recommended.

Phenoxymethylpenicillin produces a bacterial effect on penicillin sensitive organisms during the stage of active multiplication through inhibition of biosynthesis of cell wall mucopeptides. The antibacterial spectrum of phenoxymethylpenicillin is similar to that of benzyl penicillin, however, it has the advantage of being acid stable and hence better absorbed from the gastrointestinal tract than benzyl penicillin.

Pharmacokinetics

Usually, up to 60% of phenoxymethylpenicillin is absorbed into the blood stream after oral administration. Absorption is usually rapid and may produce peak serum concentrations within 30 minutes and demonstrable levels are maintained for 4 hours.

Approximately 80% of phenoxymethylpenicillin is serum protein bound. Tissue levels are highest in the kidneys with lesser amounts in the liver, skin and intestines. Small amounts are found in other body tissues and the cerebrospinal fluid. About 56% of a 500mg oral dose of the medicine is metabolised into inactive metabolite and about 23

to 36% is excreted unchanged in the urine. Bile excretion is dependent upon renal function, being low in normal renal function and high in renal impairment. The oral plasma half-life is about 30 minutes in healthy adults and about 1 to 3 hours in neonates. The half life is greatly extended in patients with renal or hepatic impairment.

The medicine is excreted rapidly in individuals with normal kidney function but is considerably delayed in neonates, young infants and individuals with impaired kidney function.

Tissue levels are highest in the kidneys with lesser amounts in the liver, skin and intestines. Small amounts are found in all other body tissues and the cerebrospinal fluid.

It is resistant to inactivation by gastric acid. It may be given with meals; however, blood levels are slightly higher when given on an empty stomach. Average blood levels are two to five times higher than the levels following the same dose of oral penicillin G and show much less individual variation.

Indications

Treatment of mild to moderately severe infections caused by penicillin-sensitive organisms. The following infections will usually respond to an adequate dosage of Penicillin.

Streptococcal infections

Mild to moderate infections of the upper respiratory tract, scarlet fever and erysipelas.

Note: Streptococci in groups A C G H L and M are very sensitive to penicillin

Pneumococcal infections

Mild to moderately severe infections of the respiratory tract.

Prevention of bacterial endocarditis in patients with congenital and/or rheumatic heart lesions who are about to undergo dental procedures or minor upper respiratory tract surgery or instrumentation.

Oral penicillin should not be used as adjunctive prophylaxis for genitourinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy or complications of childbirth

Dosage and Administration

The usual dosage is 250mg every four to six hours for adults and children. For younger children the dosage is 125mg every four hours. Higher doses may be used in more severe infections. To ensure maximum absorption each dose should be taken one hour before meals. 250mg two or three times daily may be used in the prophylaxis of recurrent streptococcal infections

Contraindications

Known hypersensitivity to penicillin.

Persons who are hypersensitive to cephalosporins may also exhibit hypersensitivity to penicillin.

Warnings and Precautions

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

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including phenoxymethylpenicillin. A toxin produced with *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea of colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to medicine discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered.

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

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

Phenoxymethylpenicillin is not recommended for chronic, severe or deep seated infections as therapeutic concentrations may not be achieved in the relevant tissues.

Oral administration should not be relied upon to achieve therapeutic levels in some patients with severe illness or with nausea, vomiting, gastric dilation, cardio-spasm or intestinal hypermotility. Occasionally patients will not absorb therapeutic amounts of oral penicillin. Parenteral administration of suitable antibiotics is recommended in these patients.

In a streptococcal infection, therapy should continue for a minimum of ten days. Cultures should be taken following completion of treatment to determine whether Streptococci have been eradicated.

Use of an alternative or additional method of contraception is strongly recommended if an oestrogen containing contraceptive is taken concurrently (see Interactions).

Use during Pregnancy and Lactation

Category A.

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

Effects on ability to drive and use machines

Phenoxymethylpenicillin is unlikely to have any effect on a person's ability to drive or use machinery.

Adverse Effects

The most common reactions are nausea, vomiting, epigastric distress, diarrhoea, pruritis ani, black hairy tongue, allergic skin reactions, urticaria and other serum sickness reactions.

Hypersensitivity reactions reported are skin eruptions (macropapular to exfoliative dermatitis), urticaria and other serum sickness-like reactions, laryngeal oedema and anaphylaxis. Fever and eosinophilia may frequently be the only reaction observed. Anaphylaxis is a less common reaction.

Haemolytic anaemia, leucopenia, thrombocytopenia, neuropathy and nephropathy are uncommon reactions usually associated with high doses of parenteral penicillin.

Interactions

Bacteriostatic agents may antagonise the effect of penicillin.

Probenecid reduces the tubular excretion of penicillin, thereby increasing concentrations in the blood stream of concomitantly administered penicillin.

Food has a variable effect, generally delaying absorption.

Antacids may reduce absorption of the medicine.

When used concurrently with an oestrogen-containing oral contraceptive, the effectiveness of the oral contraceptive may be decreased because of stimulation of oestrogen metabolism or reduction of enterohepatic circulation of oestrogens, resulting in menstrual irregularities, intermenstrual bleeding and unplanned pregnancies. Patients should be advised to use an alternative or additional method of contraception while taking this penicillin.

Overdosage

Phenoxymethylpenicillin has low toxicity. However, if there is gross renal impairment, the medicine may accumulate in the blood, and the dose should be reduced accordingly. Large quantities of parenterally administered penicillin (greater than 20 million units per day) have been associated with CNS effects e.g. lethargy, confusion, epileptiform seizures.

Treatment

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

Pharmaceutical Precautions

Powder: Store below 25 °C in a dry place. Protect from light.

Reconstituted solution: Store for not more than 10 days in a refrigerator (2-8°C). Protect from light.

Solution Preparation

Add purified water up to the indicated volume and shake well. When correctly prepared, each bottle will contain 100 mL of solution.

Medicines Classification

Prescription Medicine

Package Quantities

Each bottle contain sufficient powder such that when correctly prepared, the bottle will contain 100 mL of solution.

Packs of 1 bottle.

Further Information

The product also contains sugar: approximately 2.8 g per 5 mL in the 125 mg/5 mL strength and 2.9 g per 5 mL in the 250 mg/5 mL strength.

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