

PRODUCT INFORMATION

NAME OF THE DRUG

Proprietary name: Abbocillin V 150 mg/5 mL;

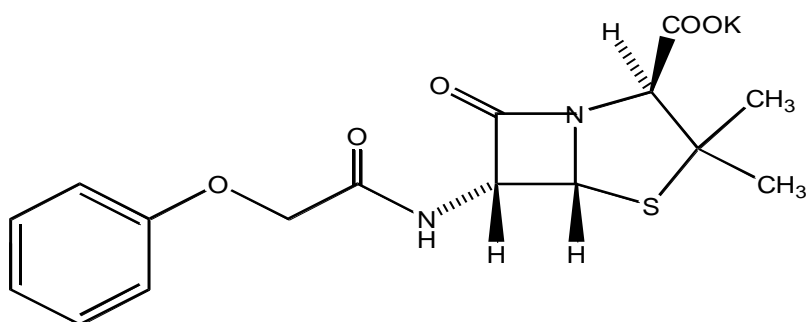
Non-proprietary name: phenoxymethylpenicillin (as benzathine) 150 mg/5 mL oral suspensions

Proprietary name: Abbocillin VK tablets 250 mg; Abbocillin VK tablets 500 mg

Non-proprietary name: phenoxymethylpenicillin (as potassium) 250 mg and 500 mg tablets

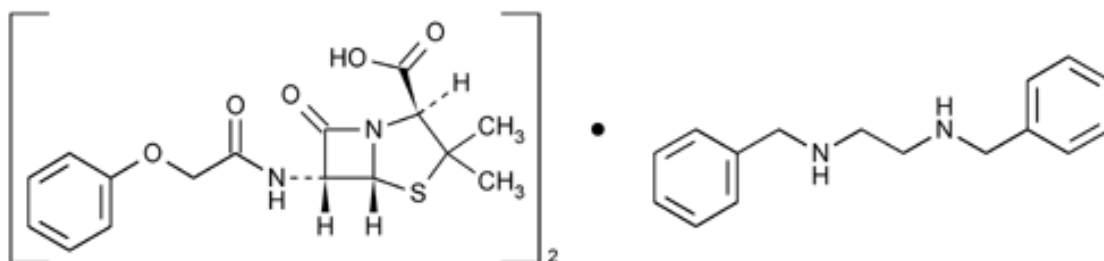
The structural formula of **phenoxymethylpenicillin potassium** is:

CAS number is 132-98-9



The structural formula of **phenoxymethylpenicillin benzathine** is:

CAS RN: 63690-57-3



DESCRIPTION:

Phenoxymethylpenicillin (or penicillin V) potassium is the potassium salt of the phenoxymethyl analog of penicillin G. It is a white crystalline powder and is soluble in water and polar organic solvents but practically insoluble in vegetable oils and liquid paraffins. Its chemical name is potassium (6R)-6-(2-phenoxyacetamido) penicillanate with an empirical formula of $C_{16}H_{17}KN_2O_5S$ and a molecular weight of 388.5.

Benzathine phenoxymethylpenicillin has an empirical formula of $(C_{16}H_{18}N_2O_5S)_2 \cdot C_{16}H_{20}N_2$ and a molecular weight of 941.1. It is an almost white powder, almost insoluble in water and soluble in alcohol, chloroform ether and acetone.

Abbocillin V Oral suspension 150 mg/5 mL: is a beige liquid and contains phenoxymethylpenicillin 150 mg as the benzathine salt. Excipients include. Butylated

hydroxyanisole, Sodium methyl hydroxybenzoate, Sodium propyl hydroxybenzoate, Potassium sorbate, Sodium citrate, Sucrose, Xanthan gum, Apricot flavour, Polysorbate 80-

Abbecillin VK tablets 250 mg, 500 mg are film coated tablets and contains phenoxymethylpenicillin 250 mg or 500 mg as the potassium salt. Excipients include sodium citrate, maize starch, povidone, talc, magnesium stearate colourings.

PHARMACOLOGY

Microbiology: Penicillin V exerts a bactericidal action against penicillin sensitive microorganisms during the stage of active multiplication. It is not active against the penicillinase producing bacteria, which include 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: Some isolates of both *Neisseria meningitidis* and *N. gonorrhoeae* remain sensitive to penicillin while most strains of *Haemophilus influenzae* and *Moraxella catarrhalis* are now resistant. Other aerobic Gram-negative bacilli are highly resistant.

Treponema pallidum is sensitive, but treatment of syphilis with oral penicillins is not recommended

Susceptibility test

Dilution or diffusion techniques- either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of “susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “intermediate” indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors from causing major discrepancies in interpretation. A report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

Pharmacology: Phenoxymethylpenicillin produces a bactericidal 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. 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.

Pharmacokinetics

Usually, up to 60% of the drug 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. Penicillin levels are highest in the kidney tissues, with lesser amounts in the liver, skin and intestines. Small amounts are found in other body tissues and the cerebrospinal fluid.

Approximately 80% of phenoxymethylpenicillin is serum protein bound. About 56% of a 500 mg oral dose of the drug is metabolised into inactive metabolite and about 23 to 36% of the drug is rapidly excreted in the unchanged form in the urine. Bile excretion depends on 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 drug is excreted as rapidly as it is absorbed in individuals with normal kidney function; however, recovery of the drug from the urine indicates that only about 25% of the dose given is absorbed, however, in neonates, young infants and individuals with impaired kidney function, excretion is considerably delayed.

INDICATIONS

Treatment of mild to moderately severe infections caused by penicillin sensitive staphylococci, pneumococci, gonococci and haemolytic streptococci infections. Therapy should be guided by bacteriological studies, including sensitivity tests, and by clinical response.

For prophylactic use in recurrent streptococcal infections including the prevention of recurrence following rheumatic fever and/or Sydenham's chorea and to prevent bacterial endocarditis in patients with rheumatic fever and/or congenital heart disease who are about to undergo dental or upper respiratory surgery or instrumentation.

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

CONTRAINDICATIONS

Known hypersensitivity to penicillin and/or cephalosporin.

PRECAUTIONS

Risk-benefit should be considered when the following medical problems exist:

History of sensitivity (allergy to penicillins/cephalosporins)

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 drug 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.

Gastrointestinal disease (pseudomembranous colitis):

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 drug 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.

Drugs 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 below).

History of bleeding disorders: Some penicillins may cause platelet dysfunction and haemorrhage.

Renal Function Impairment: Because most penicillins are excreted through the kidneys, a reduction in dosage, or increase in dosing interval, is recommended in patients with renal function impairment; and the potassium content of high doses of phenoxymethylpenicillin potassium, should be considered in patients with severe renal function impairment.

Prolonged use: prolonged use of penicillins may lead to the development of oral candidiasis.

Carcinogenicity

Long term studies have not been performed in animals

Genotoxicity

The genotoxic potential of phenoxymethylpenicillin has not been examined.

Effects on Fertility

Reproductive studies performed in the mouse, rat and rabbit have revealed no evidence of impaired fertility due to phenoxymethylpenicillin.

Use in Pregnancy

Category A

Human experience with the penicillins during pregnancy has not shown any positive evidence of adverse effects on the fetus. There are, however, no adequate and well controlled studies in pregnant women showing conclusively that harmful effects of these drugs on the fetus can be excluded. Because animal reproduction studies are not always predictive of human response, penicillin should be used during pregnancy only if clearly needed.

Use in Lactation

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

Paediatric Use:

The half-life of Phenoxymethylpenicillin is prolonged in premature infants and neonates up to 3 months of age. Consequently only three doses a day may be adequate to maintain plasma levels in these infants.

Use in the elderly

There are no age specific problems documented with the use of Phenoxymethylpenicillin, However, the elderly are more likely to have age-related renal function impairment, which may require dosage adjustment

Renal or Hepatic Impairment:

The half-life is greatly extended in these patients.

Interactions:

Bacteriostatic drugs 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 drug.

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. This interaction may be of greater clinical significance with long-term use of this penicillin; patients should be advised to use an alternative or additional method of contraception while taking this penicillin.

Aminoglycosides: mixing penicillins with aminoglycosides in vitro has resulted in substantial mutual inactivation.

Methotrexate: concurrent use with penicillins has resulted in decreased clearance of methotrexate toxicity; probably due to competition for renal tubular secretion; patients should be closely monitored.

Laboratory value alterations:

With diagnostic test results:

Glucose, urine: High urinary concentrations of penicillin may produce false positive or elevated test results with copper sulfate tests (Benedict's, Clinitest or Fehling's).

Direct antiglobulin (Coombs') tests: False positive results may occur during therapy with any penicillin.

White blood cell count: leukopenia or neutropenia is associated with the use of all penicillins; the effect is more likely to occur with prolonged therapy and severe hepatic function impairment.

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.

The 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.

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

Anaphylaxis is a less common reaction.

OVERDOSAGE

Phenoxymethylpenicillin has low toxicity. However, if there is gross renal impairment, the drug may accumulate in the blood, and the dose should be reduced accordingly.

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

Contact the Poison Information Centre on 131 126 for advice on management

DOSAGE AND ADMINISTRATION

Adults: 250 mg to 500 mg every four to six hours, preferable one hour before food. The dosage should be determined according to sensitivity of the organisms and severity of the infection.

Prevention of recurrence following rheumatic fever: 250 mg twice a day continuously.

Children: *Infants and small children* - 15 to 50 mg/Kg in three to six divided doses. If not calculated by bodyweight the following dosage schedule may be used.

Up to 1 year. 60 mg every six hours.

1 to 5 years. 120 mg every six hours.

6 to 12 years. 120 to 270 mg every six hours.

PRESENTATION

Abbecillin V Oral suspension

150mg/5mL apricot flavoured, beige colour, 100 mL

Abbecillin VK Tablets, 250 mg

Bright yellow, plain on both sides, smooth, round film coated tablet; 25's.

Abbecillin VK Tablets, 500 mg

Bright yellow, one side plain and the other side with a break bar, smooth, film coated capsule-shaped tablet; 25's.

STORAGE

Oral suspension: store between 2 - 8°C

Tablets: store below 30°C

POISON SCHEDULE

S4

SPONSOR

Aspen Pharma Pty Ltd
34-36 Chandos Street,
St. Leonards NSW 2065
Australia

Approved by Therapeutic Goods Administration on

26 May 2010