

## **BEPEN V.K**

### **Tablets & Suspension**

#### **Composition**

##### **Bepen V.K 250 mg Syrup**

Each teaspoonful (5 ml) contains phenoxymethyl penicillin (as potassium) 250 mg.

##### **Bepen V.K 500 mg Tablets**

Each tablet contains phenoxymethyl penicillin (as potassium) 500 mg.

#### **Action**

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, 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. 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 medicine 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. About 56% of a 500 mg oral dose of the medicine is metabolised into inactive metabolite and about 23 to 36% of the medicine 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 medicine is excreted as rapidly as it is absorbed in individuals with normal kidney function; however, recovery of the medicine from the urine indicates that only about 25% of the dose given is absorbed. In neonates, young infants and individuals with impaired kidney function, excretion is considerably delayed.

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.

#### **Indications**

Bepen V.K is indicated in the treatment of mild to moderately severe infections due to penicillin G-sensitive microorganisms that are sensitive to the low serum levels of this particular form of penicillin.

### **Streptococcal Infections**

Bepen V.K is indicated for the treatment of mild to moderately severe group A  $\beta$ -haemolytic streptococcal (GABHS) infections of the upper respiratory tract.

Bepen V.K is indicated for the treatment of mild to moderately severe streptococcal infections (without bacteraemia) of the upper respiratory tract, scarlet fever and mild erysipelas.

### **Other Infections**

The following infections will usually respond to adequate dosage:

- Pneumococcal infections: mild to moderately severe infections of the respiratory tract, including otitis media.
- Penicillin G-sensitive staphylococcal infections - mild infections of skin and soft tissue.
- Fusospirochetosis (Vincent's gingivitis and pharyngitis) of the oropharynx - mild to moderately severe infections.

### **Prophylaxis against Bacterial Endocarditis**

Bepen V.K is indicated 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.

### **Other Indications**

Prevention of recurrence of infection following rheumatic fever and/or chorea.  
Prophylaxis of bacterial infections in patients with sickle cell anemia.

### **Contraindications**

- Known hypersensitivity to a penicillin-type drug.
- This drug should not be administered to babies born to mothers with a history of hypersensitivity to a penicillin type drug.

### **Warnings**

Severe pneumonia, emphysema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with oral penicillin V during the acute stage.

Serious and occasionally even fatal hypersensitivity reactions due to penicillin therapy have been reported. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients receiving oral penicillins. Such reactions are more likely to occur in individuals with a history of hypersensitivity to penicillins and/or a history of sensitivity to multiple allergens. There have also been reports of individuals with a history of penicillin hypersensitivity experiencing severe reactions when treated with cephalosporins.

Therefore, before initiating therapy with this drug, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens, because of the risk of anaphylactoid reactions.

If an allergic reaction occurs, the drug should be discontinued and 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.

### **Pregnancy**

#### *Category B*

Animal studies have not revealed evidence of fetotoxicity due to penicillin V. Although penicillin V crosses the placenta, human experience with penicillin V during pregnancy has not shown any evidence of adverse effects on the fetus.

However, since adequate and well controlled studies have not been performed in pregnant women, penicillin V should only be used during pregnancy if the benefits to the mother outweigh the potential hazards to the fetus.

### **Nursing Mothers**

Penicillin V is excreted in breast milk. Although no significant problems have been reported, risk-benefit must be considered since use by nursing mothers may lead to sensitization of the infant.

### **Use in Infants**

Penicillins are excreted largely unchanged by the kidney. Because renal function is incompletely developed in infants, the rate of elimination of the drug tends to be slow. Penicillin-type drugs should therefore be administered with caution, particularly in neonates, and organ system function should be evaluated frequently.

### **Adverse Reactions**

As with other penicillins, it may be expected that untoward reactions will be essentially limited to sensitivity phenomena. These reactions are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and in those with a history of allergy, asthma, hay fever, or urticaria.

In common with other  $\beta$ -lactam antibiotics, angioedema and anaphylaxis may occur.

The following adverse reactions have been reported as being associated with the use of penicillins.

### **Hypersensitivity**

Anaphylaxis is the most serious potential adverse reaction to a penicillin drug. It is usually associated with the administration of parenteral rather than oral dosage forms. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management including intubation, should also be administered as indicated.

Erythematous maculopapular rashes, urticaria, and occasional cases of exfoliative dermatitis, erythema multiforme and Stevens-Johnson syndrome have been reported. Laryngeal edema and serum sickness-like reactions including chills, fever, edema and arthralgia have also been reported. Such reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Whenever such reactions occur, the drug should be discontinued unless, in the opinion of the physician, the condition being treated is life threatening and amenable only to penicillin therapy.

### **Gastrointestinal**

Glossitis, stomatitis, black "hairy" tongue, nausea, vomiting, enterocolitis, pseudomembranous colitis and diarrhea have been observed.

### **Haematological**

Haematological reactions including haemolytic anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, Leukopenia, and agranulocytosis have been observed. These are believed to be hypersensitivity phenomena and are usually reversible upon discontinuation of therapy.

### **Precautions**

In the treatment of GABHS infections, therapy with this drug should be continued for at least 10 days to help prevent the occurrence of acute rheumatic fever or glomerulonephritis. Following completion of treatment, cultures should be taken to determine whether streptococci have been eradicated.

As with any potent drug, periodic assessment of renal, hepatic and hematopoietic functions should be made during prolonged therapy.

The possibility of super infection with mycotic or bacterial pathogens should be kept in mind during therapy, if super infection occurs, appropriate therapy should be instituted.

Although esophageal ulceration has been rarely reported, Bepen V.K tablets should be swallowed with sufficient liquid.

### **Drug Interactions**

*Penicillins/ Chloramphenicol/ Erythromycin/ Tetracyclines/ Sulfonamides*

Since bacteriostatic drugs may interfere with the bactericidal effect of penicillins in the treatment of meningitis or other conditions where a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy.

*Penicillins/ Probenecid*

Probenecid may decrease renal tubular secretion of penicillin-type drugs, resulting in increased blood levels.

### **Diagnostic Interference**

Treatment with penicillins may result in false positive reactions when testing for the presence of glucose in urine using Clinitest, Benedict's Solution or Fehling's Solution. Tests based on enzymatic glucose oxidase reactions such as Clinistix or Testape are not affected.

### **Dosage and Administration**

Patients should be advised to swallow Bepen V.K tablets with sufficient liquid.

The adult dosage of Bepen V.K ranges, between 125-500 mg, 4 times a day. The actual dosage of Bepen V.K to be administered is governed by the sensitivity of the pathogen, the severity of the infection and should be adjusted according to the clinical response of the patient.

The dosage for children less than 12 years of age calculated based on body weight. The suggested dosage is 25-50 mg/kg body weight/day in divided doses every 6-8 hours.

More specific dosage recommendations in definitive clinical situations are given below.

In renally impaired patients (creatinine clearance less than or equal to 10 ml/ min) do not exceed 250 mg every 6 hours.

#### **Streptococcal Infections**

In GABHS infections of the upper respiratory tract, the recommended adult dosage is 1 gram twice daily, for 10 days. The recommended dosage for children in these infections is 500 mg twice daily, for 10 days.

An alternative dosage regimen is 125-500 mg every 6-8 hours, for 10 days.

In other mild to moderately severe infections of the upper respiratory tract, scarlet fever and mild erysipelas, the dosage is 125-500 mg every 6-8 hours, for 10 days.

#### **Pneumococcal Infections**

In mild to moderately severe infections of the respiratory tract including otitis media, 250 mg every 6 hours until the patient has been afebrile for at least 2 days.

#### **Staphylococcal Infections**

In mild infections of the skin and soft tissue (culture and sensitivity tests should be performed), 250 mg every 6-8 hours.

#### **Fusospirochetosis of the Oropharynx**

250 mg every 6-8 hours, until cure is obtained.

#### **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, the dosage in adults and children over 25 kg body weight is 2 grams 1 hour before the procedure and 1 gram 6 hours later.

In children weighing less than 25 kg, half the adult dosage is recommended. Bepen V.K syrup is probably more acceptable to such patients.

**Prevention of Recurrence of Infection following Rheumatic fever and/ or Chorea**

125 mg twice daily on a continuing basis.

**Prophylaxis of Bacterial Infections in Patients with Sickle Cell Anemia**

125 mg twice daily.

**Over Dosage**

Over Dosage of penicillin, drugs may cause neuromuscular hyperirritability or convulsive seizures.

Discontinue medication, treat symptomatically, and institute supportive measures as required. In patients with renal function impairment, the antibiotic may be removed from the circulation by haemodialysis, not by peritoneal dialysis.

**Pharmaceutical Precautions**

To reconstitute Bepen V.K syrup, add purified water at intervals up to the mark on the bottle. Shake well until dissolved.

Once reconstituted, the syrup should be used within 10 days. During this period, it should be stored in a refrigerator with the cap tightly closed. After 10 days, the remaining syrup should be discarded.

**Presentation**

**Bepen V.K 250 mg Syrup**

Powder for the preparation of 100 ml syrup.

**Bepen V.K 500 mg Tablets**

Box of 16 tablets.