SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Penicillin VK Tablets B.P.250mg or Tenkicin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 250 mg of phenoxymethylpenicillin as phenoxymethylpenicillin potassium B.P.

3 PHARMACEUTICAL FORM
Tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications
Phenoxymethylpenicillin is indicated in the treatment or prophylaxis of mild to moderately severe infections caused by penicillin sensitive organisms, i.e. those microorganisms whose susceptibility to phenoxymethylpenicillin is within the range of serum levels attained.

Phenoxymethylpenicillin is indicated for the treatment of the following infections (see section 4.4 and 5.1):
- Streptococcal infections:
  - Pharyngitis
  - Scarlet fever
- Skin and soft tissue infections (e.g. erysipelas)
- Pneumococcal infections:
  - Pneumonia
  - Otitis media
- Vincent’s gingivitis and pharyngitis

Phenoxymethylpenicillin is also indicated for (see section 5.1):
- Prophylaxis of rheumatic fever and/or chorea
- Prophylaxis of pneumococcal infection (e.g. in asplenia and in patients with sickle cell disease
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology
For oral administration only.
The dosage and frequency of Phenoxymethylpenicillin depends on the severity and localisation of the infection and expected pathogens.

Phenoxymethylpenicillin 250mg is approximately equivalent to 400,000 units.

Each tablet should be swallowed whole with water, at least 30 minutes before or 2 hours after food, as ingestion of Phenoxymethylpenicillin with meals slightly reduces the absorption of the drug.

The usual dosage recommendations are as follows:

**Adults and children over 12 years**: 250mg - 500mg every six hours

**Children**: 62.5mg every 6 hours

1-5 years: 125mg every six hours

6-12 years: 250mg every six hours

Prophylactic Use
Prophylaxis of rheumatic fever/chorea: 250mg twice daily on a continuing basis
Prophylaxis of pneumococcal infection (e.g. in asplenia and in sickle cell disease):
Adults and children over 12 years: 500mg every 12 hours
Children 6-12 years: 250mg every 12 hours
Children below 5 years: 125mg every 12 hours.

Children with difficulty in swallowing or in children younger than 5 years of age, tablets are not usually administered. The more appropriate formulation for this age group should be used.

Elderly
The dosage is as for adults. The dosage should be reduced if renal function is markedly impaired.

Renal impairment
The dosage should be reduced if renal function is markedly impaired.

Hepatic impairment
Dosage adjustment may be necessary in patients with impaired liver function when they also have renal failure. In this situation the liver may be a major excretion route.

Method of Administration
For instructions on dilution of the product before administration, see section 6.6.

4.3 Contraindications

Phenoxymethylpenicillin is contraindicated in patients known to be hypersensitive to Penicillin or any of the excipients contained in the product and should be used with caution in
4.4  Special warnings and precautions for use

Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma. Oral penicillin should not be used as adjunctive prophylaxis for genito-urinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and childbirth. Patients with a past history of rheumatic fever receiving continuous prophylaxis may harbour penicillin-resistant organisms. In these patients, the use of another prophylactic agent should be considered. Severe empyema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with Penicillin V during the acute phase.

All degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. Cross sensitivity may occur with cephalosporins and other beta lactam antibiotics.

These reactions are more likely to occur in individuals with a history of sensitivity to penicillins, cephalosporins and other allergens. Enquiries should be made for such a history before therapy is begun. If any allergic reaction occurs, the drug should be discontinued and the patient treated appropriately with the usual agents (e.g. adrenaline and other pressor amines, antihistamines and corticosteroids). Oral therapy should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilation, achalasia or intestinal hypermotility. Occasionally, patients do not absorb therapeutic amounts of orally administered penicillin. Administer with caution in the presence of markedly impaired renal function due to the increased risk of encephalopathy. A safe dosage may be lower than the usually recommended. Prolonged use of antibiotics may promote the over growth of non-susceptible organisms, including fungi. If super infection occurs, appropriate measures should be taken.

Streptococcal infections should be treated for a minimum of 10 days and post therapy cultures should be performed to confirm eradication of the organisms.

Penicillin VK Tablets BP contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Phenoxyethylpenicillin may be used for prophylaxis against streptococcal infections following rheumatic fever and against pneumococcal infections following splenectomy or in sickle cell disease.

Severe empyema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with phenoxyethylpenicillin during the acute phase.
4.5 Interaction with other medicinal products and other forms of interaction

Guar gum: Reduced absorption of Phenoxymethylpenicillin.

Penicillins may interfere with anticoagulant control.

Probenecid: Reduced excretion of phenoxymethylpenicillin by competing with it for renal tubular secretion.

Chloramphenicol, Erythromycin and Tetracyclines have been reported to antagonise the bacteriocidal activity of penicillins and concomitant use is not recommended.

Neomycin is reported to reduce the absorption of Phenoxymethylpenicillin

Use of Phenoxymethylpenicillin while taking methotrexate can cause reduced excretion of methotrexate and thus increasing the risk of toxicity.

Sulfinpyrazone: Excretion of penicillins reduced by sulfinpyrazone.

Typhoid vaccine (oral): Penicillins may inactivate oral typhoid vaccine.

4.6 Fertility, pregnancy and lactation

Pregnancy:
There are no or a limited amount of data from the use of Phenoxymethylpenicillin in pregnant women. As a precautionary measure, it is preferable to avoid the use of Phenoxymethylpenicillin during pregnancy.

Lactation:
Phenoxymethylpenicillin metabolites are excreted in human milk to such an extent that effects on breastfed new-borns are likely.

4.7 Effects on ability to drive and use machines

None Known
4.8 Undesirable effects

Although reactions have been reported much less frequently after oral than after parenteral therapy, it should be remembered that all forms of hypersensitivity, including fatal anaphylaxis have been observed with oral penicillin.

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<thead>
<tr>
<th>SOC</th>
<th>LLT</th>
<th>Occurance</th>
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<tbody>
<tr>
<td>Hepatobiliary disorders</td>
<td>cholestatic jaundice,</td>
<td>Very Rare</td>
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<tr>
<td></td>
<td>hepatitis</td>
<td></td>
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<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, vomiting, and diarrhoea,</td>
<td>Not known</td>
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<tr>
<td></td>
<td>epigastric distress,</td>
<td></td>
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<tr>
<td></td>
<td>black hairy tongue</td>
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<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Maculopapular rash, exfoliative dermatitis, angioedema and urticaria (rashes)</td>
<td>Not known</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>Antibiotic associated colitis</td>
<td>Not known</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>serum sickness-like reactions including interstitial nephritis, neutropenia, chills, fever, oedema, arthralgia (joint pains) and prostration; coagulation disorders</td>
<td>Not known</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Central nervous system toxicity including convulsions (especially with high doses or in severe renal impairment) paraesthesia with prolonged use</td>
<td>Not known</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>laryngeal oedema, anaphylaxis.</td>
<td>Not known</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>fever</td>
<td>Not known</td>
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<tr>
<td>Blood and lymphatic system disorders</td>
<td>Eosinophilia, Haemolytic anaemia, leucopenia, thrombocytopenia, neuropathy, and nephropathy (usually associated with high doses of parenteral penicillin)</td>
<td>Not known</td>
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</tbody>
</table>

**Reporting of suspected adverse reactions**  
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the yellow card scheme at www.mhra.gov.uk/yellowcard.

### 4.9 Overdose

**Symptoms:** A large oral overdose of penicillin may cause nausea, vomiting, stomach pain, diarrhoea, and rarely, major motor seizures. If other symptoms are present, consider the possibility of an allergic reaction. Hyperkalaemia may result from over dosage, particularly in patients with renal insufficiency.

**Management:** No specific antidote is known. Symptomatic and supportive therapy is recommended. Activated charcoal with a cathartic, such as sorbitol may hasten drug elimination. Penicillin may be removed by haemodialysis.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

ATC Code: J01CE02

Phenoxyethylpenicillin is used in the treatment of infections caused by susceptible Staphylococci, Pneumococci, Gonococci and Haemolytic Streptococci. Unless very large doses are given, phenoxyethylpenicillin administered by mouth is less effective than parenterally administered benzylpenicillin in the treatment of severe acute infections. It is inactivated by penicillinase.

**Mechanism of Action:** Phenoxyethylpenicillin acts through interference with the final stage of synthesis of the bacterial cell wall. The action depends on its ability to bind certain membrane-bound proteins, (penicillin-binding proteins or PBPs) that are located beneath the cell wall. These proteins are involved in maintaining cell wall structure, in cell wall
synthesis and in cell division, and appear to possess transpeptidase and carboxypeptidase activity.

PK/PD relationship
The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for phenoxymethylpenicillin.

**Mechanism(s) of Resistance:**

The two main mechanisms of resistance to phenoxymethylpenicillin are:
- Inactivation by bacterial penicillinases and other beta-lactamases. The incidence of beta-lactamase producing organisms is increasing.
- Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance.

**EUCAST clinical MIC breakpoints to separate susceptible (S) pathogens from resistant (R) pathogens (version 1.0, 22.11.2010) are:**

The susceptibility of streptococci Groups A, C and G and *S. pneumoniae* to phenoxymethylpenicillin is inferred from the susceptibility to benzylpenicillin.

<table>
<thead>
<tr>
<th>EUCAST Species-related breakpoints (Susceptible≤/Resistant&gt;) Units: mg/L</th>
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<tbody>
<tr>
<td>Staphylococcus</td>
</tr>
<tr>
<td>Streptococcus A, C, G</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
</tr>
</tbody>
</table>

**Staphylococci:** Most staphylococci are penicillinase-producers. Penicillinase-producing strains are resistant. The benzylpenicillin breakpoint (shown) will mostly, but not unequivocally, separate beta-lactamase producers from non-producers.

**Streptococcus pneumoniae:** For phenoxymethylpenicillin, report *S. pneumoniae* with benzylpenicillin MICs above 0.06 mg/L resistant.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. Expert advice should be sought as necessary when the local prevalence of resistance is such that the utility of the agent in at least some types of infection is questionable.

<table>
<thead>
<tr>
<th>Commonly susceptible species</th>
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<tr>
<td>Streptococcus A, C, G</td>
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**Species for which acquired resistance may be a problem**

<table>
<thead>
<tr>
<th>Species</th>
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<tr>
<td><em>Staphylococcus aureus</em></td>
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<tr>
<td><em>Streptococcus pneumoniae</em></td>
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<tr>
<td><em>Staphylococcus epidermidis</em></td>
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</table>
5.2 Pharmacokinetic properties

**ABSORPTION:** Rapidly but incompletely absorbed after oral administration; calcium and potassium salts are better absorbed than the free acid; Absorption appears to be reduced in subjects with coeliac disease; Absorption appears to be more rapid in fasting than in non-fasting subjects.

**BLOOD CONCENTRATION:** After an oral dose of 125mg peak serum concentration of 200 to 700ng/ml are attained in 2 hours. Peak plasma concentrations of 3 to 5µg per ml have been observed 30 to 60 minutes after a dose of 500mg.

**HALF-LIFE:** Biological half-life, about 30 minutes (increased to about 4 hours in renal failure)

**DISTRIBUTION:** Widely distributed throughout the body and enters pleural and ascitic fluids and also the cerebrospinal fluid when the meninges are inflamed; Phenoxymethylpenicillin crosses the placenta and is secreted in the milk; (Protein binding 50 to 80% bound plasma proteins)

**METABOLIC REACTIONS:** Hydroxylation may occur.
It is metabolised in the liver; several metabolites have been identified, including penicilloic acid. The unchanged drug and metabolites are eliminated rapidly in the urine, with minute concentrations excreted in bile.

**EXCRETION:** 20% - 35% of an oral dose is excreted in the urine in 24 hours.

5.3 Preclinical safety data

No relevant information additional to that already contained elsewhere in the SPC.

6. Pharmaceutical particulars

6.1 List of Excipients

Lactose B.P.
Magnesium Stearate B.P.
Purified Talc B.P.  
Maize Starch B.P.  
Ethanol B.P.  
Purified Water B.P.

6.2. Incompatibilities

None stated

6.3. Shelf-Life

36 months

6.4. Special Precautions for Storage

Store below 25°C. Protect from light and moisture

6.5. Nature and Content of Container

Polyethylene securitainers with polypropylene press on air-proof cap containing 15, 18, 20, 21, 28, 30 and 1000 tablets. Or an Opaque PVDC/PVC blister 40/250 with an Aluminium Lidding foil 20 micron containing 15, 18, 20, 21, 28, 30 and 1000 tablets

6.6. Special precautions for disposal and other handling

None stated.
No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Athlone Laboratories Limited  
Ballymurray  
Co. Roscommon  
Ireland
8. MARKETING AUTHORISATION NUMBER

PL 06453/0020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION


10. DATE OF REVISION OF THE TEXT

17/12/2015