SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin 125 mg/5ml Oral Solution or Tenkicin 125 mg/5ml Oral Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of Oral Solution contains 125mg of Phenoxymethylpenicillin as Phenoxymethylpenicillin Potassium Ph.Eur.

3. PHARMACEUTICAL FORM

Powder for oral solution

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Phenoxymethylpenicillin and phenoxymethylpenicillin potassium are indicated in the treatment of mild to moderately severe infections associated with micro-organisms whose susceptibility to penicillin is within the range of serum levels attained with the dosage form.

Phenoxymethylpenicillin is indicated for prophylaxis against:

- Pneumococcol infection (e.g. in asplenia and in patients with sickle cell disease).

Note: Severe empyema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with Penicillin V during the acute phase.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

The following infections will usually respond to adequate doses:
Streptococcal infections (without bacteraemia): Mild to moderate infections of the upper respiratory tract, scarlet fever and mild erysipelas.

Pneumococcal infections: mild to moderately severe infections of the respiratory tract. Staphylococcal infections sensitive to penicillin: mild infections of the skin and soft tissues. Fusospirochaetosis (Vincent's gingivitis and pharyngitis): mild to moderately severe infections of the oropharynx usually respond to therapy with oral penicillin.
Prophylactic use: prophylaxis with oral penicillin has proved effective in preventing recurrence of rheumatic fever and chorea.

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.

Note: oral penicillin should not be used as adjunctive prophylaxis for genito - urinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and child birth.

4.2 Posology and method of administration

Posology

Phenoxymethylpenicillin 125 mg/5ml Oral Solution should be given in divided doses (4 times a day) and preferably half an hour before meals or at least three hours after a meal.

The following dosage schedule applies to Phenoxymethylpenicillin 125 mg/5ml Oral Solution:

Adults (including the elderly) and children over 12 years:	250mg - 500mg every six hours
Prophylactic use	250mg twice daily is recommended for long term prophylaxis of rheumatic fever
Children:	
Infants (up to 1 year)	62.5mg every six hours
1-5 years	125mg every six hours
6-12 years	250mg every six hours

Method of Administration

For instructions of reconstitution of the medicinal product before administration, see section 6.6.

For oral administration only

Patients with Renal Impairment

Reduce dose if renal function is markedly impaired.

To avoid late complications (rheumatic fever), infections with β-haemolytic streptococci should be treated for 10 days.

4.3. Contra-Indications

Phenoxymethylpenicillin is contraindicated in patients known to be hypersensitive to Penicillin and should be used with caution in patients with known histories of allergy.

4.4 Special warnings and precautions for use

Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.
All degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. 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 with the usual agents (e.g. adrenaline and other pressor amines, antihistamines and corticosteroids).

Oral therapy should not be relied upon for 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, as safe dosage may be lower than the usually recommended doses.

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

Prolonged use of antibiotics may promote the over growth of non-susceptible organisms, including fungi. If super infection occurs, appropriate measures should be taken.

Sucrose:
This product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. Contains 2.80g of sucrose per 5ml dose. To be taken into consideration by patients with diabetes mellitus. May be harmful to the teeth.

E110 & E124:
This product contains Ponceau 4R (E124) and Sunset yellow (E110) which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Aminoglycosides: Neomycin is reported to reduce the absorption of phenoxymethylpenicillin.

Anticoagulants: Penicillins may interfere with anticoagulant control.

Bacteriostatic antibiotics: Certain bacteriostatic antibiotics such as Chloramphenicol, Erythromycin and Tetracyclines have been reported to antagonise the bactericidal activity of penicillins and concomitant use is not recommended.

Guar gum: Reduced absorption of phenoxymethylpenicillin

Methotrexate: Use of Phenoxymethylpenicillin while taking methotrexate can cause reduced excretion of methotrexate thereby increasing the risk of toxicity.

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

Sulfinpyrazone: Excretion of penicillins reduced by sulfinpyrazone.

Typhoid vaccine (oral): Penicillins may inactivate oral typhoid vaccine if ingested concomitantly.

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 newborns are likely.

4.7. Effects on Ability to Drive and Use Machines

None known

4.8 Undesirable effects

The most common reactions to oral penicillin are gastrointestinal effects and hypersensitivity reactions. Although hypersensitivity 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.

Blood and lymphatic disorders:
There have been very rare (<1/10,000) reports of changes in blood counts, including, thrombocytopenia, neutropenia, leucopenia, eosinophilia and haemolytic anaemia. Coagulation disorders (including prolongation of bleeding time and defective platelet function) have also been reported.

Gastrointestinal disorders:
Nausea, vomiting, abdominal pain, diarrhoea are common (>1/100 to <1/10). Sore mouth and black hairy tongue (discolouration of tongue) has been reported rarely (>1/10,000 to <1/1,000).

Hepatobiliary diorders:
Hepatitis and cholestatic jaundice have been reported very rarely (<1/10,000).

Immune disorders:
Allergic reactions may commonly occur (>1/100 to <1/10) and typically manifest as skin reactions (See Skin and subcutaneous disorders). Severe allergic reactions causing angioedema, laryngeal oedema and anaphylaxis have been reported rarely (>1/10,000 to <1/1,000).

Serum sickness-like reactions are characterised by fever, chills, arthralgia and oedema.

Infections and infestations:
Pseudomembranous colitis has rarely (>1/10,000 to <1/1,000) been reported.

Nervous system disorders:
Central nervous system toxicity including convulsions has been reported (especially with high doses or in severe renal impairment); paraesthesia may occur with prolonged use.
Neuropathy is an infrequent reaction and is usually associated with high doses of parenteral penicillin.

Renal and urinary disorders:
Interstitial nephritis has occurred in very rare cases (<1/10,000).
Nephropathy is an infrequent reaction and is usually associated with high doses of parenteral penicillin.

Skin and subcutaneous disorders
Urticarial, erythematous or mobilliform rash and pruritus occur commonly (>1/100 to <1/10), while exfoliative dermatitis occurs rarely (>1/10,000 to <1/1,000).

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 overdosage, particularly for 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
Phenoxymethylpenicillin is a beta-lactamase sensitive natural penicillin.

Mechanism of Action:
Phenoxymethylpenicillin 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:
Phenoxymethylpenicillin is inhibited by penicillinase and other beta-lactamases that are produced by certain micro-organisms. The incidence of beta-lactamase producing organisms is increasing.

Mechanisms of resistance
The two main mechanisms of resistance to phenoxymethylpenicillin are:

- Inactivation by bacterial penicillinases and other beta-lactamases
- 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 22.11.210) are:

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

EUCAST Species-related breakpoints (Susceptible≦/Resistant>) Units: mg/L	
Staphylococcus	≤0.12/>0.12
Streptococcus A, C, G	≤0.25/>*0.25*
S. pneumoniae	≤ 0.06/>2

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.

Commonly susceptible species
Streptococcus A, C, G
Species for which acquired resistance may be a problem
Staphylococcus aureus
Streptococcus pneumoniae
Staphylococcus epidermidis

5.2 Pharmacokinetic properties

Absorption: Rapidly but incompletely absorbed after oral administration (about 60% of an oral dose is absorbed). Calcium and potassium salts are better absorbed than the free acid. Absorption appears to be reduced in patients with coeliac disease. Absorption appears to be more rapid in fasting than non-fasting subjects.

Blood concentration: after an oral dose of 125mg, peak serum concentrations of 200 to 700ng/ml are attained in 2 hours. After an oral dose of 500mg, peak serum concentrations reach 3 to 5micrograms/ml in 30 to 60 minutes.

Half-life: Biological half-life is about 30 minutes, increased to about 4 hours in severe renal impairment.

Distribution: Widely distributed throughout the body and enters pleural and ascitic fluids and also in 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

Excretion: 20% to 35% of an oral dose is excreted in the urine in 24 hours

5.3. Pre-clinical Safety Data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Sodium Benzoate Ph.Eur.
Saccharin Sodium Ph.Eur.
Trusil Orange Flavour HSE
Orange Colour 175 78 8 HSE
(Containing sunset yellow El10 & Ponceau 4R E124)
Sucrose Ph.Eur.

6.2. Incompatibilities

None known.

6.3. Shelf-Life

Unopened container: 24 months.
Reconstituted oral solution: a shelf life of 7 days.

6.4. Special Precautions for Storage

Unconstituted powder: Store in a dry place below <25°C. Protect from light.
Reconstituted oral solution: Store for 7 days in a refrigerator ($2^{o}C – 8^{o}C$).

6.5 Nature and Contents of Container

Natural High Density Polyethylene (HDPE) 150ml Bottle with ROPP Neck containing 100ml of syrup upon reconstitution

R4 flexband (white cap with blue TE band)

CRC/TE cap - PP28 mediloc TE closure (white cap with TE band)

Hugo Meding – polypropylene spoon – Article number 7229
Or
2.5ml/5ml MediSPOON (Quatromed) double ended spoon comprised of polypropylene with CE mark

6.6. Special precautions for disposal and other handling.

To reconstitute: Loosen powder, add 63ml water and shake well.
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 06453/0024

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

09 June 1997

10. DATE OF REVISION OF THE TEXT
21 MAR 2016