SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin 125 mg/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

For Phenoxymethylpenicillin 125 mg/5ml Oral Solution

Each 5ml of reconstituted solution contains 125mg Phenoxymethylpenicillin as Phenoxymethylpenicillin Potassium as the active ingredient.

Excipients: Sucrose

Each 5ml of 125mg/5ml oral solution contains 2.6g sucrose.
For the full list of excipients, see section 6.1

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 the treatment of the following infections (see section 4.4 and 5.1)

Streptococcal infections (without bacteraemia): Mild to moderate infections of the upper respiratory tract (pharyngitis), scarlet fever and mild erysipelas.

Pneumococcal infections: mild to moderately severe infections of the respiratory tract (pneumonia and Otitis media).

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.

Phenoxymethylpenicillin is also indicated for (see section 5.1):

Prophylactic use: prophylaxis with oral penicillin has proved effective in preventing recurrence of rheumatic fever and 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 agent.

4.2 Posology and method of administration

Posology

The dosage and frequency of Phenoxymethylpenicillin depends on the severity and localisation of the infection and expected pathogens.

Phenoxymethylpenicillin Oral Solution should be given in divided doses (4 times a day) and preferably half an hour before food or at least two hours after food . Phenoxymethylpenicillin with meals slightly reduces the absorption of the drug.

The following dosage schedule applies to Phenoxymethylpenicillin 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

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.

Elderly:

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

Renal Impairment: Reduce dosage 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.

In patients with beta-haemolytic streptococcal infection, it is usual to continue treatment at the full dosage for 10 days, in order to minimise the occurrence of secondary complications such as acute nephritis and rheumatic fever.

Method of administration
For oral administration only.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
It 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.
Severe empyema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with Penicillin V during the acute phase.

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.

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

Important information regarding the ingredients in this medicine

Sucrose:
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine also contains the colouring agent Red dye Ponceau 4R Lake (E124) which may cause allergic reactions (possibly delayed).

Sodium:
This medicine contains less than 1 mmol sodium (23 mg) per 5ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

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.

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

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.

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

Anticoagulants: Penicillins may interfere with anticoagulant control.

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.

Breast-feeding:

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

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.

The following convention has been utilised for the classification of undesirable effects: -

Very common (>1/10) Common (>1/100 to <1/10) Uncommon (>1/1000 to <1/100) Rare (>1/10,000 to <1/1000) Very Rare (<1/10,000) Not known (cannot be estimated from the available date)		
SOC	LLT	Occurrence
Blood and lymphatic disorders	There have been very rare reports of changes in blood counts, including, thrombocytopenia, neutropenia, leucopenia, eosinophilia and haemolytic anaemia.	Very Rare
	Coagulation disorders (including prolongation of bleeding time and defective	Not known

	platelet function) have also been reported.	
Immune disorders	Allergic reactions may commonly occur and typically manifest as skin reactions (See Skin and subcutaneous disorders).	Common
	Severe allergic reactions causing angioedema, laryngeal oedema and anaphylaxis have been reported rarely.	Rare
	Serum sickness-like reactions are characterised by fever, chills, arthralgia and oedema	Unknown
Nervous system disorders	Central nervous system toxicity has been reported (especially with high doses or in severe renal impairment); paraesthesia with prolonged use. Neuropathy (usually associated with high doses of parenteral penicillin).	Unknown
Gastrointestinal disorders	Nausea, vomiting, abdominal pain, diarrhoea	Common
	Sore mouth and black hairy tongue (discolouration of tongue) , Superficial tooth discolouration#	Not known
Hepatobiliary disorders	Hepatitis and cholestatic jaundice have been reported.	Very rare
Infections and infestations:	Pseudomembranous colitis	Not known
Renal and urinary disorders	Interstitial nephritis.	Very rare
	Nephropathy (usually associated with high doses of parenteral penicillin)	Uncommon
Skin and subcutaneous disorders	Urticarial, erythematous or mobilliform rash and pruritus	Common
	Exfoliative dermatitis	Rare

#Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 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 adsorbed after oral administration (about 60% of an oral dose is absorbed). Calcium and potassium salts are better adsorbed 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 5µg/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 trace amounts in breast the milk; (protein binding 50 to 80% bound plasma proteins).

Biotransformation:
It is metabolised in the liver; several metabolites have been identified, including penicilloic acid.

Elimination: Unchanged drug and metabolites are excreted rapidly in urine (20% to 35% of an oral dose is excreted in the urine in 24 hours)

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of this SPC .

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Strawberry Flavour 17.41.0549
Colour Red Dye (Anstead) 1578 (E124) (Spectracol Ponceau 4R)
Saccharin Sodium
Industrial Methylated Spirit

6.2 Incompatibilities

None

6.3 Shelf life

Unopened container: 24 months
Reconstituted oral solution: 7 days

6.4 Special precautions for storage

Unconstituted powder: Do not store above 25°C. Store in a dry place.
Reconstituted oral solution: Store for 7 days in a refrigerator

6.5 Nature and contents of container

- Natural high density polyethylene bottle with a polypropylene tamper evident or HDPE/polypropylene, tamper evident/ child resistant cap containing 100ml of oral solution on reconstitution.

- Translucent HDPE bottle with polypropylene child resistant cap containing 100ml of oral solution on reconstitution**.**

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Limited
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United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0034

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