SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Phenoxymethylpenicillin 250 mg/5ml Oral Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5ml of reconstituted solution contains 250mg of Phenoxymethylpenicillin as Phenoxymethylpenicillin Potassium as the active ingredient.

Excipients: Sucrose

Each 5ml of 250mg/5ml oral solution contains 0.255g sucrose.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Powder for oral solution.

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.

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

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.

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

### 4.2 Posology and method of administration

#### Dosage

Phenoxymethylpenicillin 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 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

**RENAL IMPAIRMENT:** Reduce dosage if renal function is markedly impaired.

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.

*For oral administration only.*
4.3 Contraindications
Phenoxymethylpenicillin is contraindicated in patients known to be hypersensitive to Penicillin and should be used with caution in patients with known histories of allergy.

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

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.

Streptococcal infections should be treated fora 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.

4.5 Interaction with other medicinal products and other forms of interaction
Guar gum: Reduced absorption of phenoxymethylpenicillin
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 bacteriocidal activity of penicillins and concomitant use is not recommended.
Aminoglycosides: Neomycin is reported to reduce the absorption of phenoxymethylpenicillin.
Penicillin may reduce the efficacy of combined oral contraceptives. Use of Phenoxy methylpenicillin while taking methotrexate can cause reduced excretion of methotrexate and thus increasing the risk of toxicity. 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
Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing to the pregnant patient.

Lactation
Phenoxy methylpenicillin is excreted in trace amounts in breast milk, presenting a risk of allergic reaction in the infant.

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.

Blood and lymphatic disorders:
There have been very rare 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.

Immune disorders:

Allergic reactions may commonly occur and typically manifest as skin reactions (See Skin and subcutaneous disorders). Severe allergic reactions
causing angioedema, laryngeal oedema and anaphylaxis have been reported rarely.

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

Nervous system disorders:

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

Gastrointestinal disorders:
Nausea, vomiting, abdominal pain, diarrhoea are common. Sore mouth and black hairy tongue (discolouration of tongue) has been reported occasionally.

Hepatobiliary disorders:
Hepatitis and cholestatic jaundice have been reported very rarely.

Infections and infestations:
Pseudomembranous colitis has occasionally been reported.

Renal and urinary disorders:
Interstitial nephritis has occurred in very rare cases. 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 most frequently, while exfoliative dermatitis occurs rarely.

4.9 Overdose

Signs and 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.
Treatment: 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.

5.1 Pharmacodynamic properties

ATC code: J01CE02

Phenoxyethylpenicillin is a beta-lactamase sensitive natural penicillin. 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.

Bacterial surface enzymes called autolysins also appear to be involved in the lethal effect of penicillins, particularly for gram-positive bacteria. In gram-negative bacilli osmotic rupture of cells may occur when the cell wall is weakened. Phenoxyethylpenicillin can also produce morphological changes in vitro including the formation of long filaments or abnormally shaped cells. Bacteria that are not growing or dividing are generally not killed by phenoxyethylpenicillin.

Mechanism(s) of Resistance:
Phenoxyethylpenicillin is inhibited by penicillinase and other beta-lactamases that are produced by certain micro-organisms. The incidence of beta-lactamase producing organisms is increasing.

EUCAST clinical MIC breakpoints to separate susceptible (S) pathogens from resistant (R) pathogens are:

EUCAST Species-related breakpoints (Susceptible≤/Resistant>) Units: mg/L

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<th>Species</th>
<th>≤0.12/&gt;0.12</th>
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<tr>
<td>S. PNEUMONIAE</td>
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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; Phenoxyethylpenicillin 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  Preclinical safety data
Not applicable

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.
6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

BRISTOL LABORATORIES LIMITED
Unit 3, Canalside, Northbridge Road
Berkhamsted, Herts, HP4 1EG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0035

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/06/2011

10 DATE OF REVISION OF THE TEXT

20/07/2012