SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin 250 mg Tablets BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Phenoxymethylpenicillin 250 mg (as Phenoxymethylpenicillin Potassium)

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet

White to off white round biconvex film-coated tablets with BL/250 debossed on one side.

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.

Recommended for use in the treatment of infections caused by susceptible organisms including Staphylococci, Pneumococci, Gonococci and Haemolytic Streptococci.

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

The usual dosage recommendations are as follows:

Adults and children over 12 years): 250-500mg every 6 hours

Children:
Infants (1 month to 1 year): 62.5mg every six hours
1 - 5 years : 125 mg every six hours
6-12 years : 250 mg 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.

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:oral
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.

4.3 Contraindications

Phenoxymethlypenicillin 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 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. 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 dilatation, 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 overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate measures should be taken.
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

Phenoxymethylpenicillin 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 phenoxymethylpenicillin during the acute phase

Important information regarding the ingredients in this medicine

This medicine contains potassium, less than 1 mmol (39 mg) per 250 mg tablet, i.e. essentially 'potassium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Guar gum: Reduced absorption of Phenoxymethylpenicillin.

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

Penicillins may interfere with anticoagulant control.

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.

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 stated

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.

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

	associated with high doses of parenteral penicillin)	

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 rare cases major motor seizures. If other symptoms are present, consideration must also be given to the possibility of an allergic reaction. Hyperkalaemia may result from overdosage, 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

Pharmacotherapeutic Group: beta lactamase sensitive penicillins.

ATC code: J01C E02

Phenoxymethylpenicillin is used in the treatment of infections caused by susceptible Staphylococci, Pneumococci, Gonococci and Haemolytic Streptococci. Unless very large doses are given, phenoxymethylpenicillin 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:
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:
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.

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; calcium and potassium salts are better absorbed that 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 5ug 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

Maize Starch
Magnesium Stearate
Povidone
Hypromellose
Purified Talc
Titanium Dioxide (E171)
Macrogol 6000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Al/PVC/PVdC blister packs: 3 years

HDPE Containers: 2 years

6.4 Special precautions for storage

Blisters: Do not store above 25ºC. Store in the original package

Containers: Do not store above 25ºC. Keep the container tightly closed

6.5 Nature and contents of container

HDPE tablet containers, pack sizes of 1000 tablets

Al /PVC/ PVdC blister, pack sizes of 28 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Limited,
Unit 3, Canalside,
Northbridge Road,
Berkhamsted,
Hertfordshire,
HP4 1EG

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0033

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first Authorisation: 26 Jan 2006

Date of Renewal of Authorisation: 22 February 2010

10 DATE OF REVISION OF THE TEXT

16/09/2021