# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin, 250mg, Film-coated Tablets

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains phenoxymethylpenicillin 250 mg (as phenoxymethylpenicillin potassium).

For a full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

Film-coated tablet

White, circular, biconvex film coated tablets with break line on one side and ‘I 04’ on the other.

The tablet can be divided into equal halves.

## 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 in 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.

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

Method of administration

Phenoxymethylpenicillin 250 mg Film-Coated Tablets are for oral use.

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-500 mg every six hours.
***Children: Infants (up to 1 year): 62.5mg every 6 hours***
1-5 years: 125 mg every six hours
6-12 years: 250 mg every six hours

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

Prophylactic Use

Prophylaxis of rheumatic fever/ chorea: 250 mg 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.

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

The treatment of acute otitis media with Phenoxymethylpenicillin should be limited to 5 days. However, 5-10 days treatment may be recommended in patients with potential for complications.

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.

**4.3 Contraindications**

Phenoxymethylpenicillin is contraindicated in patients with known penicillin 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..

Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics e.g. cephalosporins. Severe acute infections should not be treated with phenoxymethylpenicillin.

## 4.4 Special warnings and precautions for use

All degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. Phenoxymethylpenicillin should be given with caution to patients with a history of allergy, especially to other drugs. Phenoxymethylpenicillin should also be given cautiously to cephalosporin-sensitive patients, as there is some evidence of partial cross-allergenicity between the cephalosporins and penicillins. Patients have had severe reactions (including anaphylaxis) to both drugs. If the patient experiences an allergic reaction phenoxymethylpenicillin should be discontinued and treatment with the appropriate agents initiated (e.g. adrenaline and other pressor amines, antihistamines and other corticosteroids).
Particular caution should be exercised in prescribing phenoxymethylpenicillin to patients with an allergic diathesis or with bronchial asthma.

Oral therapy should not be relied upon in patients with severe illness or with a gastrointestinal disease that causes persistent nausea, vomiting, gastric dilation, achalasia/ cardiospasm, intestinal hyper motility or diarrhoea, because absorption may be reduced. 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.
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.

In patients undergoing long-term phenoxymethylpenicillin treatment the complete and differential blood count, as well as the liver and kidney function, should be monitored.

During long-term treatment attention should also be paid to the potential overgrowth of resistant organisms including Pseudomonas or Candida. If super-infection occurs, appropriate measures should be taken.

Prolonged use of antibiotics may promote the over growth of non-susceptible organisms, including fungi.

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.

Caution should be used when treating patients with a history of antibiotic associated colitis.

Sustained severe diarrhoea should prompt suspicion of pseudomembranous colitis. As this condition may be life-threatening phenoxymethylpenicillin should be withdrawn immediately and treatment guided by bacteriologic studies.

Each tablet contains 28 mg of potassium, which may be harmful to people on low potassium diets and may cause stomach upset, diarrhoea and hyperkalaemia. High doses should be used with caution in patients receiving potassium-containing drugs or potassium sparing-diuretics.

In renal impairment the safe dosage may be lower than usually recommended.

During treatment with phenoxymethylpenicillin non-enzymatic glucose tests may be false-positive.

## 4.5 Interaction with other medicinal products and other forms of interaction

As penicillins like phenoxymethylpenicillin are only active against proliferating microorganisms, phenoxymethylpenicillin should not be combined with bacteriostatic antibiotics such as tetracycline, erythromycin, chloramphenicol and sulphonamides.

Concomitant use of uricosuric drugs (e.g. probenecid and sulfinpyrazone) reduces the excretion of phenoxymethylpenicillin resulting in increased plasma levels and thus prolongs its action.

Methotrexate: Penicillins reduce excretion of methotrexate - increased risk of toxicity.

Like other antibiotics, phenoxymethylpenicillin may reduce the effectiveness of oral contraceptives. Patients should be advised to use additional forms of contraceptive precautions while taking phenoxymethylpenicillin.

During treatment with phenoxymethylpenicillin non-enzymatic urinary glucose tests may be false-positive.

Guar gum: Reduced absorption of Phenoxymethylpenicillin.

Phenoxymethylpenicillin has the following interaction information:

Neomycin reduces the absorption of phenoxymethylpenicillin.

Combined use of phenoxymethylpenicillin and oral anticoagulants (e.g. warfarin) may prolong prothrombin time.

Coumarin - Common experience in anticoagulant clinics is that INR can be altered by a course of broad-spectrum penicillins such as ampicillin, although studies have failed to demonstrate an interaction with coumarins.

Penicillins may interfere with anticoagulant control.

Phenindione - Common experience in anticoagulant clinics is that INR can be altered by a course of broad-spectrum penicillins such as ampicillin, although studies have failed to demonstrate an interaction with phenindione.

Typhoid Vaccines - Antibacterials inactive oral typhoid vaccine.

Concurrent use of phenoxymethylpenicillin with potassium sparing diuretics (e.g Amiloride and Spironolactone) may cause hyperkalaemia, which can be life-threatening.

**4.6 Fertility, Pregnancy and lactation**

Pregnancy

Animal studies with phenoxymethylpenicillin have shown no teratogenic effects.

Phenoxymethylpenicillin has been in extensive clinical use and suitability in human pregnancy has been well documented in clinical trials. However, as with other drugs, caution should be exercised when prescribing to pregnant patients.

Lactation

Breast feeding is not contraindicated with phenoxymethylpenicillin. Trace quantities of phenoxymethylpenicillin can be detected in breast milk. While adverse effects are apparently rare, two potential problems exist for nursing infant:

- modification of bowel flora

- direct effects on the infant such as allergy/sensitisation

Caution should therefore be exercised when prescribing for the nursing mother.

### 4.7 Effects on ability to drive and use machines

Not Known.

### 4.8 Undesirable effects

Hypersensitivity

Potential allergic reactions include urticaria, angioneurotic oedema, erythema multiforme, exfoliative dermatitis, fever, joint pain, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis or anaphylactic shock (which could be fatal) with collapse and anaphylactoid reactions (asthma, purpura, gastrointestinal symptoms). Although these are less common, and take a milder course, in oral treatment than during parenteral penicillin treatment, it should be remembered that all degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin.

| Frequency categories are defined according to the following conventions:<br>Very common (≥1/10),<br>Common (≥1/100 to <1/10),<br>Uncommon (≥1/1,000 to <1/100),<br>Rare (≥1/10,000 to <1/1,000),<br>Very rare (<1/10,000),<br>Not known (cannot be estimated from the available data). | | |
|---|---|---|
| **System Organ Class** | **LLTs** | **Frequency** |
| Infections and infestations | Antibiotic associated colitis,<br>As with other broad-spectrum antibiotics prolonged use may result in the overgrowth of non-susceptible organisms, e.g. candida. This may present a vulvo-vaginitis. | Not Known |
| Blood and lymphatic system disorders | Eosinophilia, Haemolytic anaemia, leucopenia, thrombocytopenia and agranulocytosis<br>Neuropathy, and nephropathy (usually associated with high doses of parenteral penicillin) | Not Known |
| Immune system disorders | serum sickness-like reactions including interstitial nephritis, neutropenia, chills, fever, oedema, arthralgia (joint pains) and prostration; coagulation disorders laryngeal oedema, anaphylaxis. | 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 |
| Gastrointestinal disorders | Nausea, vomiting, diarrhoea, stomatitis and glossitis are sometimes seen. epigastric distress and black hairy tongue | Not Known |
| Hepatobiliary disorders | cholestatic jaundice and hepatitis | Very rare |
| Skin and subcutaneous tissue disorders | Maculopapular rash, exfoliative dermatitis, angioedema and urticaria (rashes) | Not Known |
| General disorders and | fever | Not Known |

| | | |
|---|---|---|
| administration site conditions | | |

Reporting of suspected adverse reactions

Reporting of 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 (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. It is advisable to monitor blood levels in patients with renal malfunction. Activated charcoal with a cathartic, such as sorbitol may hasten drug elimination. Phenoxymethylpenicillin may be removed by haemodialysis.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

General properties

*ATC classification:* Pharmacotherapeutic Group: Beta lactamase sensitive penicillins
ATC Code: J01CE02

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 infections 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 5 μg 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

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.

### 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

Calcium Hydrogen Phosphate Dihydrate
Maize Starch
Cellulose, Microcrystalline E460
Magnesium Stearate E572
Basic Butylated Methacrylate

Macrogol 6000
Sodium Laurilsulfate E487
Stearic Acid E570
Titanium Dioxide E171

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

3 years

### 6.4 Special precautions for storage

Do not store above 25º C.

### 6.5 Nature and contents of container

Al /PVC blister. Pack sizes of 14, 28, 42, 56, 70, 140 tablets are available
Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

No special requirements

## 7. MARKETING AUTHORISATION HOLDER

Brown & Burk UK Ltd
5, Marryat Close, Hounslow west,
Middlesex TW4 5DQ,
UK

## 8. MARKETING AUTHORISATION NUMBER(S)

PL 25298/0106

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30/04/2012

## 10. DATE OF REVISION OF THE TEXT

09/09/2024