Prescribing Information

Phenoxymethylpenicillin 500 mg film-coated tablets

Prescribing Information. Prescribers should consult the SmPC before prescribing.

Presentation: Each film coated tablet contains 500 mg phenoxymethylpenicillin (as phenoxymethylpenicillin potassium). For the full list of excipients, refer to SmPC.

Indications: For use in the treatment of mild to moderately severe infections caused by penicillin sensitive organisms. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Dosage and administration: *Adults:* The dosage is 250-500 mg every six hours.

Special Populations: *Elderly*: The dosage is as for adults, the dosage should be reduced if renal function is markedly impaired. *Prophylactic Use:* The dosage is 250 mg daily for long term prophylaxis of rheumatic fever. *Children* 1-5 years: 125 mg every six hours 6-12 years: 250 mg every six hours.

Method of Administration: Oral use. Each tablet should be swallowed whole with water, at least 30 minutes before food.

Fertility, pregnancy and lactation: Pregnancy: Animal studies with phenoxymethylpenicillin potassium have shown no teratogenic effects. Phenoxymethylpenicillin potassium 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: Phenoxymethylpenicillin potassium is not contraindicated with Breast feeding. Trace quantities of phenoxymethylpenicillin potassium 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.

Contraindications: Phenoxymethylpenicillin is contraindicated in patients with known penicillin hypersensitivity. 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.

Special warnings and precautions: All degree of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. These reactions are more likely occur in individuals with a history of sensitivity to penicillin, cephalosporin, and other allergens. If an 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 other corticosteroids).

Administer with caution in the presence of markedly impaired renal function, as the safe dosage may be lower than the usually recommended. 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 overgrowth of non-susceptible organisms including fungi. If super-infection occurs, appropriate measures should be taken. Each tablet of Phenoxymethylpenicillin 500 mg film-coated tablets contains 28 mg of potassium, which maybe 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. During treatment with phenoxymethylpenicillin non-enzymatic glucose tests may be false-positive.

Drug Interactions: Probenecid delays the elimination of the penicillin through the kidneys and thus prolong its action. Phenoxymethylpenicillin reduces the excretion of cytotoxic drug, methotrexate. Avoid concomitant administration with bacteriostatics antibiotics such as tetracycline, erythromycin, chloramphenicol and sulphonamides because it can diminish the effect of Phenoxymethylpeniccillin potassium. Simultaneous administration of Phenoxymethylpenicillin and oral contraceptives, the hormonal contraception can lose its efficacy. The simultaneous administration of guar gum diminishes the absorption of penicillin, the absorption of phenoxymethylpenicillin reduced by neomycin. 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 and phenindione. Excretion of penicillin reduced by sulfinpyrazone. Antibacterials inactive oral typhoid vaccine.

Effects on ability to drive/use machines: None Known

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). All degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. *Gastro-intestinal tract*: Phenoxymethylpenicillin potassium is generally well tolerated. Occasionally soft stools occur and they do not require the interruption of the treatment. Nausea, diarrhoea, vomiting, stomatitis and glossitis are sometimes seen. 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 with appropriate antibiotherapy (i.e. vancomycin). *Blood:* Eosinophilia, haemolytic anaemia, leukopenia, thrombocytopenia and agranulocytosis are extremely rare. Other possible effects on the blood composition include: neutropenia, haemolytic anaemia and coagulation disorders. *Central nervous system* toxicity, including convulsions, has been reported, especially following high doses or in severe renal impairment. Paraesthesia has been reported with prolonged use. 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. Refer SmPC for complete details.

Pack size and UK list price: Phenoxymethylpenicillin 500 mg film-coated tablets (PL 25298/0376) pack size: 20's, £ 3.99

Legal category: POM

Marketing Authorisation Holder and Distributor: Brown & Burk UK Ltd, 5 Marryat Close, Hounslow West, Middlesex, TW4 5DQ, United Kingdom

Date of Preparation: Oct 2024 **Ref:** BBUK/Phen/001

BROWN & BURK

REPORT ADVERSE EVENTS

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Brown & Burk via email to pv@bbukltd.com or via phone on +44 (0)203 384 7188

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin 500 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 500 mg phenoxymethylpenicillin (as phenoxymethylpenicillin potassium).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White to off white, circular, biconvex film coated tablet, with break line on one side and E41 on other side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For use in the treatment of mild to moderately severe infections caused by penicillin sensitive organisms.

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

4.2 Posology and method of administration

Posology

Adults: The dosage is 250-500 mg every six hours.

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

Prophylactic Use: The dosage is 250 mg daily for long term prophylaxis of rheumatic fever.

Paediatric population

Children 1-5 years: 125 mg every six hours

6-12 years: 250 mg every six hours

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.

Method of administration

Phenoxymethylpenicillin 500mg film-coated tablets are for oral use.

Each tablet should be swallowed whole with water, at least 30 minutes before food, as ingestion of phenoxymethylpenicillin with meals slightly reduces the absorption of the drug.

4.3 Contraindications

Phenoxymethylpenicillin is contraindicated in patients with known penicillin hypersensitivity.

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 degree of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. These reactions are more likely occur in individuals with a history of sensitivity to penicillin, cephalosporin, and other allergens.

Enquiry should be made for such a history before therapy with a penicillin begins. If an 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 other corticosteroids).

Oral therapy should not be relied upon in patients with severe illness, or with nausea, vomiting, gastric dilation, cardiospasm 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 the safe dosage may be lower than the usually recommended.

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 overgrowth of non-susceptible organisms including fungi. If super-infection occurs, appropriate measures should be taken.

Each tablet of Phenoxymethylpenicillin 500 mg film-coated tablets 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.

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

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid delays the elimination of the peniciilin through the kidneys and thus prolong its action.

Phenoxymethylpenicillin reduces the excretion of cytotoxic drug, methotrexate.

Avoid concomitant administration with bacteriostatics antibiotics such as tetracycline, erythromycin, chloramphenicol and sulphonamides because it can diminish the effect of Phenoxymethylpeniccillin potassium.

In case of simultaneous administration of Phenoxymethylpenicillin and oral contraceptives, the hormonal contraception can lose its efficacy. Patients should be advised to use additional forms of contraceptives precautions while taking Phenoxymethylpenicillin.

The simultaneous administration of guar gum diminishes the absorption of penicillin.

Phenoxymethylpenicillin has the following interaction information:

Neomycin - absorption of phenoxymethylpenicillin reduced by neomycin.

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.

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.

Sulfinpyrazone- excretion of penicillin reduced by sulfinpyrazone.

Typhoid Vaccines – antibacterials inactive oral typhoid vaccine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies with phenoxymethylpenicillin potassium have shown no teratogenic effects.

Phenoxymethylpenicillin potassium 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 potassium.

Trace quantities of phenoxymethylpenicillin potassium 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

None 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.

Gastro-intestinal tract
Phenoxymethylpenicillin potassium is generally well tolerated. Occasionally soft stools occur and they do not require the interruption of the treatment. Nausea, diarrhoea, vomiting, stomatitis and glossitis are sometimes seen.

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 with appropriate antibiotherapy (i.e. vancomycin).

Blood
Eosinophilia, haemolytic anaemia, leukopenia, thrombocytopenia and agranulocytosis are extremely rare. Other possible effects on the blood composition include: neutropenia, haemolytic anaemia and coagulation disorders.

Central nervous system
Central nervous system toxicity, including convulsions, has been reported, especially following high doses or in severe renal impairment. Paraesthesia has been reported with prolonged use.

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.

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 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

Cases of intended or accidental overdosage should be brought under medical supervision for symptomatic treatment. It is advisable to monitor blood levels in patients with renal malfunction.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta lactamase sensitive penicillins, ATC code: J01CE02.

Mechanism of action

Phenoxymethylpenicillin is a broad spectrum beta-lactam antibiotic with bactericidal action against Gram-positive bacteria and Gram-negative cocci. Its antimicrobial action is similar to that of benzyl penicillin. Phenoxymethylpenicillin is usually active against the following organisms:

Gram-positive aerobes and anaerobes including

Bacillus anthracis

Clostridium perfringens

Clostridium tetani

Corynebacterium diphtheriae

Erysipelothrix rhusiopathiae

Listeria monocytogenes

Peptostreptococcus spp.

*Streptococcus agalactiae (*Group *B)*

Streptococcus pneumoniae

*Streptococcus pyogenes (*Group *A)*

Gram-negative including

Neisseria meningitidis

Neisseria gonorrhoeae

Phenoxymethylpenicillin is inactivated by penicillinase and other beta-lactamases.

Phenoxymethylpenicillin binds to penicillin-binding proteins located on the inner membrane of the bacterial cell wall. Phenoxymethylpenicillin binds to and inactivates these proteins resulting in weakening of the bacterial cell wall and lysis.

5.2 Pharmacokinetic properties

Absorption

Phenoxymethylpenicillin is stable under acidic conditions so it can be administered by oral route.

Phenoxymethylpenicillin is rapidly, but incompletely absorbed after oral administration and the absorption level is around 60%. The simultaneous administration of food slightly decreases the peak plasma concentration of

phenoxymethylpenicillin, but does not appear to affect the extent of absorption. Peak plasma concentrations are reached in about 45 minutes. The peak plasma concentration increases approximately in proportion with increased doses. Peak serum concentrations of 3-6 µg per ml have been seen following dosage of 250 mg to 500 mg by mouth.

Distribution

Phenoxymethylpenicillin is widely distributed round the body tissues and fluids (volume of distribution about 0.21 kg-1 of body weight) and more readily penetrates inflamed tissues. It also diffuses across the placenta into foetal circulation and small amounts appear in the milk of nursing mothers. Eighty per cent is reported to be protein bound.

Biotransformation

Phenoxymethylpenicillin is partially metabolised to inactive penicilloic acid

by hydrolysis of the lactam ring. This metabolism occurs in the liver.

Elimination

The plasma half-life of phenoxymethylpenicillin is about 45 minutes which may increase to four hours in renal failure.

Excretion is by tubular secretion into urine. About 40% of the dose is eliminated in the urine either as under unchanged or as penicilloic acid in the first 10 hours after oral administration. Small excretion occurs in bile. Impaired absorption is seen in patients with coeliac disease.

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

Tablet core:
calcium hydrogen phosphate dihydrate
maize starch
microcrystalline cellulose
magnesium stearate

Film-coating:
macrogol polyvinyl alcohol graft copolymer (E1209),
talc (E553b),
titanium dioxide (E171),
GMCC Type 1 (E471),
polyvinyl alcohol-part. hydrolyzed (E1203).

6.2 Incompatibilities

There are no known incompatibilities.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

White opaque PVC-Al blister pack. Packs containing 10,14,20,28,30,50,56,60,84,98 & 100's 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
Micro House
5 Marryat Close, Hounslow
TW4 5DQ
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 25298/0376

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/03/2024

10 DATE OF REVISION OF THE TEXT

21/03/2024