

SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin 250mg/5ml Oral Solution Sugar Free BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of Oral Solution contains 250mg of Phenoxymethylpenicillin as Phenoxymethylpenicillin Potassium Ph. Eur.

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.

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.

Fusospirochetosis (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.

4.2 Posology and Method of Administration

Dosage

Phenoxymethylpenicillin Sugar Free 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 Phenoxyethylpenicillin Sugar Free:

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 dose 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 Contra-indications

Phenoxyethylpenicillin is contraindicated in patients known to be hypersensitive to Penicillin and should be used with caution in patients with known histories of allergy.

Sorbitol:

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.4 Special Warnings and Special 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.

4.5 Interaction with other Medicaments and Other Forms of Interaction

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

Anticoagulants: Penicillins may interfere with anticoagulant control.

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.

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.

Oral Contraceptives: Penicillin may reduce the efficacy of combined oral contraceptives.

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

Sulfinpyrazone: Excretion of penicillins reduced by sulfinpyrazone.

Typhoid vaccine (oral): Penicillins may inactivate oral typhoid vaccine if ingested concomitantly.

4.6 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:

Phenoxymethylpenicillin 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

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.

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.

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.

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.

Infections and infestations:

Pseudomembranous colitis has occasionally been reported.

Nervous system disorders:

Central nervous system toxicity including convulsions has been reported (especially with high doses or in severe renal impairment); paraesthesia may occur with prolonged use.

Neuropathy is an infrequent reaction and is usually associated with high doses of parenteral penicillin.

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 morbilliform rash and pruritus occur most frequently, while exfoliative dermatitis occurs rarely.

4.9 Overdosage

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 overdose, 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. PHARMACEUTICAL PARTICULARS

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.

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. Phenoxymethylpenicillin 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 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.

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

EUCAST Species-related breakpoints (Susceptible \leq /Resistant $>$) Units: mg/L	
Staphylococcus	$\leq 0.12 / > 0.12$
Streptococcus A, B, C, G	$\leq 0.25 / > 0.25$
S. pneumoniae	$\leq 0.5 / > 2$

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.

Streptococci: Strains with MIC values above the S/I breakpoint are very rare or not yet reported. Until there is evidence regarding clinical response for confirmed isolates with MIC above the current resistant breakpoint (in italics) they should be reported resistant. Streptococci groups A, B, C and G do not produce beta-lactamase. The addition of a beta-lactamase inhibitor does not add clinical benefit.

Streptococcus pneumoniae: For phenoxymethylpenicillin, report *S. pneumoniae* with benzylpenicillin MICs above 0.06 mg/L resistant.

5.2 Pharmacokinetic Properties

Absorption: Rapidly but incompletely absorbed after oral administration (about 60% of an oral dose is absorbed). Calcium and potassium salts are better absorbed 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 5micrograms/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 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.

Excretion: Unchanged drug and metabolites are excreted rapidly in the urine. (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

Sodium Benzoate Ph. Eur.

Saccharin Sodium Ph. Eur.

Trusil Orange Flavour HSE

Orange Colour 175 78 8 HSE

(Containing sunset yellow E110 & Ponceau 4R E124)

Sorbitol 60W

Mono Ammonium Glycyrrhizinate

6.2 Incompatibilities

None known

6.3 Shelf life

Unopened container: 24 months

Reconstituted oral solution: a shelf life of 7 days

6.4 Special Precautions for Storage

Unconstituted powder: Store in a dry place below 25°C. Protect from light

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.

May also contain

Hugo Meding – polypropylene spoon – Article number 7229

Or

5ml Medispoon

Or

A dosing syringe with bottle neck adaptor

6.6 Instructions for use/handling

No special instructions

7. Marketing Authorisation Holder

Athlone Laboratories Limited,
Ballymurray,
Co. Roscommon,
Ireland

8. Marketing Authorisation Number

PL 6453/0053

9. Date of First Authorisation/Renewal of Authorisation

1 December 1998

10. Date of Partial Revision of Text

11th May 2012