SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenoxymethylpenicillin Sugar Free 125mg / 5ml Powder for Oral Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 138.6mg of Phenoxymethylpenicillin potassium equivalent to phenoxymethylpenicillin 125mg.

Also contains 955.5mg/5ml of Sorbitol (E420).

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution

Phenoxymethylpenicillin 125mg is a white to off-white fine powder, which when reconstituted as directed, yields a colourless to pale yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Phenoxymethylpenicillin is indicated for the treatment of the following infections (See Section 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

For oral administration

Phenoxymethylpenicillin Solution should be taken at least 30 minutes before or 2 hours after food, as ingestion of phenoxymethylpenicillin with meals slightly reduces the absorption of the drug.

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

The **usual dosage recommendations** are as follows:

Adults: 250-500 mg every six hours.

Children 1-5 years: 125 mg every six hours

6-12 years: 250 mg every six hours

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.

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

For instructions on dilution of the product before administration, see section 6.6.

4.3 Contraindications

A history of a previous hypersensitivity reaction to any penicillin is a contraindication.

4.4 Special warnings and precautions for use

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.

Particular caution should be exercised in prescribing phenoxymethylpenicillin to patients with an allergic diathesis or with bronchial asthma

Oral Penicillins are not indicated in patients with a gastrointestinal disease that causes persistent diarrhoea or vomiting, because absorption may be reduced.

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.

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. It should be noted that each 125mg dose contains about 1/3mmol 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.

Phenoxymethylpenicillin Oral Solution contains Sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

As penicillins like phenoxymethylpenicillin are only active against proliferating micro-organisms, phenoxymethylpenicillin should not be combined with bacteriostatic antibiotics.

Concomitant use of uricosuric drugs (e.g. probenecid) reduces the excretion of phenoxymethylpenicillin resulting in increased plasma levels.

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

Phenoxymethylpenicillin may reduce the excretion of methotrexate causing an increased risk of toxicity.

Like other antibiotics, phenoxymethylpenicillin may reduce the effectiveness of oral contraceptives.

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

Neomycin reduces the absorption of phenoxymethylpenicillin.

Guar gum may slow the speed of absorption of Phenoxymethylpenicillin.

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

Fertility

Fertility data for phenoxymethylpenicillin are not available.

Pregnancy:

Safe use of phenoxymethylpenicillin during pregnancy has not been definitely established. There are no adequate or controlled studies using phenoxymethylpenicillin in pregnant women and the drug should be used during pregnancy only when clearly needed.

Lactation:

Because phenoxymethylpenicillin is distributed into milk, the drug should be used with caution in nursing women.

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 penicillin therapy, it should be remembered that all degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin.

Very common (>1/10) Common (>1/100 to <1/10) Uncommon (>1/1,000 to <1/100) Rare (>1/10,000 to <1/1,000) Very rare (<1/10,000) Not known (cannot be estimated from the available data)		
Infections & infestations	Not known	Candida, Vulvo-vaginitis
Blood and lymphatic system disorders	Not known	Eosinophilia, Haemolytic anaemia Leukopenia, Thrombocytopenia, Agranulocytosis
Immune system disorders	Not known	Erythema multiforme, Anaphylactic shock (which could be fatal with collapse)
Vascular disorders	Not known	Anaphylactoid shock
Gastrointestinal disorders	Not known	Nausea, Vomiting, Diarrhoea, Stomatitis, Glossitis
Skin and subcutaneous tissue disorders	Not known	Urticaria, Angioneurotic oedema, Exfoliative dermatitis
Musculoskeletal and connective tissue disorders	Not known	Joint pains
General disorders and administration site conditions	Not known	Fever

4.9 Overdose

Overdosage may lead to gastrointestinal symptoms e.g. nausea, vomiting, epigastric pain, diarrhoea and in rare cases motor seizures. Serum potassium may need to be monitored in patients with compromised renal function and/or dehydration. General supportive measures are normally all that are required for treatment of overdosage of penicillins.

There is no known antidote. Symtomatic and supportive therapy is recommended. 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: J01C E02.

Mode of action
Phenoxymethylpenicillin exerts a bactericidal action against penicillin-susceptible bacteria by inhibition of biosynthesis of cell wall mucopeptides.

PK/PD relationship
Efficacy correlates with the time that plasma levels exceed the MIC of the pathogen under treatment.

Resistance
Resistance to phenoxymethylpenicillin is usually mediated by one or both of:

Bacterial production of β-lactamases: This family of enzymes can inactivate Phenoxymethylpenicillin by hydrolyzing the β-lactam ring

The occurrence of modified penicillin-binding proteins resulting in impaired binding of phenoxymethylpenicillin.

EUCAST recommendations for susceptibility testing:

Staphylococcus spp: Isolates positive for β- lactamase are resistant to phenoxymethylpenicillin. Isolates negative for β- lactamase and susceptible to methicillin can be reported susceptible to phenoxymethylpenicillin. Isolates resistant to methicillin are resistant to phenoxymethylpenicillin.

Streptococcus groups A, B, C and G: The β-lactam susceptibility of β-haemolytic Streptococcus groups A, B, C and G is inferred from the penicillin susceptibility.

Streptococcus pneumoniae: Isolates fully susceptible to benzylpenicillin (MIC≤ 0.064 mg/ml, susceptible by Oxacillin disk screen, Screen for β- lactam resistance with the Oxacillin 1µg disk – isolates categorized as susceptible can be reported as susceptible to phenoxymethylpenicillin irrespective of the clinical condition. Isolates categorized as Oxacillin resistant can be reported to phenoxymethylpenicillin in meningitis) can be reported susceptible to phenoxymethylpenicillin, otherwise reported as phenoxymethylpenicillin resistant without further testing.

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. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent is at least some types of infections is questionable.

Commonly susceptible species
Aerobic Gram-positive micro-organisms
Streptococcus A,B,C,G
Species for which acquired resistance may be a problem
Staphylococcus aureus
Streptococcus pneumoniae

5.2 Pharmacokinetic properties

Absorption

Following administration by mouth absorption is usually quick, complete and rapid from the gastrointestinal tract. Peak serum concentrations of 3-6 ~g per ml have been seen following dosage of 250 mg to 500 mg by mouth. The effect of food on absorption is slight and variable. Impaired absorption is seen in patients with coeliac disease.

Distribution

Eighty per cent is reported to be protein bound. Phenoxymethylpenicillin is widely distributed round the body tissues and fluids 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.

Biotransformation

Some metabolism occurs in the liver and several metabolites have been found, including penicilloic acid.

Elimination

Excretion is by tubular secretion into urine. Small excretion occurs in bile. The plasma half-life of phenoxymethylpenicillin is about 30 minutes which may increase to four hours in renal failure.

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

Sorbitol (E420)
Powdarome Strawberry Premium (Nature identical flavouring and natural flavouring, maize maltodextrin, INS1520 propylene glycol)
Sodium Saccharin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

The shelf life after reconstitution is 7 days.

6.4 Special precautions for storage

Store powder in a dry place below 25ºC

After reconstitution, phenoxymethylpenicillin oral solution must be stored between 2°C to 8°C and used within 7 days.

6.5 Nature and contents of container

150ml HDPE bottle with a 28mm child resistant cap. Each bottle contains 100 ml of reconstituted solution with a dosing syringe of 5ml.

6.6 Special precautions for disposal

No special requirements.

Add 86.0ml of water to the powder and shake vigorously. This will make 100ml of solution.

The solution should be used within 7 days of reconstitution.

Shake well before use.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 25298/0042

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26/11/2015