Approved Professional Information for Medicines for Human Use:

ATHLONE PHENOXYMETHYLPENICILLIN

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL powder for solution

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL powder for solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL powder for solution

Each 5 mL of reconstituted suspension contains the equivalent of 125 mg phenoxymethylpenicillin as phenoxymethylpenicillin potassium.

The powder contains sodium benzoate 0,32 % m/v as preservative.

Contains sugar: sucrose 2795,76 mg.

Contains sweetener: saccharin sodium 4,10 mg.

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL powder for solution

Each 5 mL of reconstituted suspension contains the equivalent of 250 mg phenoxymethylpenicillin as phenoxymethylpenicillin potassium.

The powder contains sodium benzoate 0,32 % m/v as preservative.

Contains sugar: sucrose 2898,02 mg.

Contains sweetener: saccharin sodium 4,24 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL powder for solution

A pale orange dry granular powder.

After reconstitution: A clear orange solution with orange odour & flavour.

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL powder for solution

A pale orange dry granular powder.

After reconstitution: A clear orange solution with orange odour & flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylactic: Recurrence of rheumatic fever.

Treatment of mild to moderate infections caused by sensitive organisms:

Pneumococcal infections of the middle ear; Streptococcal otitis media and sinusitis; Streptococcal pharyngitis caused by Strep pyogenes; mild to moderate pulmonary and periodontal anaerobic infections; gingivostomatitis; early Lyme disease.

4.2 Posology and method of administration

Posology

Shake the bottle before use.

Prophylactic use: 125 to 250 mg twice a day.

For adults and children 12 years and over, the usual dosage ranges from 250 mg to 500 mg every 6 hours, depending on the severity of the infection.

For infants and small children, the suggested daily dosage is 15 mg to 50 mg (25 000 to 90 000 units) per kg in 3 to 6 divided doses.

Children up to 1 year:	60 mg every six hours.
1 - 5 years:	125 mg every six hours.
6- 12 years:	250 mg every six hours.

Beta-haemolytic streptococcus infections without associated bacteraemia may be treated with 125 mg to 250 mg (200 000 to 400 000 units) every six to eight hours.

Therapy should be continued for a minimum of ten days with a therapeutic dose to prevent development of rheumatic fever and/or other serious complications. Dosage for routine streptococcus prophylaxis in patients with a history of rheumatic fever or congenital heart disease may be 125 mg (200 000 units) once or twice daily, on a continuing basis.

Special Population

Renal impairment

The dosage should be reduced if renal function is markedly impaired.

DIRECTIONS FOR RECONSTITUTING:

Athlone Phenoxymethylpenicillin 125/5 mL:

To prepare add 60 mL of water, shake until all powder is dispersed.

Athlone Phenoxymethylpenicillin 250/5 mL:

To prepare add 60 mL of water, shake until all powder is dispersed.

Method of administration

ATHLONE PHENOXYMETHYLPENICILLIN is for oral administration.

4.3 Contraindications

- Hypersensitivity to the phenoxymethylpenicillin or to any of the excipients listed in section 6.1.
- ATHLONE PHENOXYMETHYLPENICILLIN is contraindicated in patients with a history of allergy

to penicillins or cephalosporins. Cases of cross sensitivity have been reported.

- It is not recommended for chronic, severe, or deep infections such as subacute bacterial endocarditis, meningitis or syphilis. Severe empyema, bacteraemia, pericarditis and arthritis should not be treated with Phenoxymethylpenicillin during the acute phase.
- Babies born of allergic mothers in the neonatal period.
- Oral Penicillin should not be used as adjunctive prophylaxis for genito-urinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and child birth.
- Dysentry and typhus, and other infections caused by penicillin resistant microbes such as Brucella and E. coli.
- For treatment of trivial disorders.

4.4 Special warnings and 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.

Excipient sucrose

This medicine contains sucrose: patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Excipient sodium

This medicine contains less than 1 mmol sodium (23 mg) per 5 mL, that is to say essentially 'sodium-free'.

Excipient benzoic acid

Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old),

4.5 Interaction with other medicines 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.

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 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.

Breastfeeding:

Phenoxymethylpenicillin metabolites are excreted in human milk, presenting the risk of candidiasis and also of central nervous system toxicity due to prematurity of the blood brain barrier. There is a theoretical possibility of later sensitisation.

4.7 Effects on ability to drive and use machines

ATHLONE PHENOXYMETHYLPENICILLIN has no known influence on the ability to drive and use machines.

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.

Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarket spontaneous reports with phenoxymethylpenicillin.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations	--	--	Pseudomembranous colitis
Blood and lymphatic system disorders	--	Changes in blood counts, including, thrombocytopenia, neutropenia, leucopenia, eosinophilia and haemolytic anaemia.	Coagulation disorders (including prolongation of bleeding time and defective platelet function)
Immune system disorders	Allergic reactions (typically	Severe allergic reactions causing	Serum sickness-like reactions

	manifest as skin reactions (See Skin and subcutaneous disorders)).	angioedema, laryngeal oedema and anaphylaxis	characterised by fever, chills, arthralgia and oedema
Nervous system disorders	--	--	Central nervous system toxicity including convulsions (especially with high doses or in severe renal impairment); paraesthesia may occur with prolonged use, Neuropathy (usually associated with high doses of parenteral penicillin)
Cardiac disorders	--	--	Kounis syndrome
Gastrointestinal disorders	Nausea, vomiting, abdominal pain, diarrhoea	--	Sore mouth and black hairy tongue (discolouration of tongue)
Hepatobiliary disorders	--	Hepatitis and cholestatic jaundice	--
Skin and subcutaneous tissue disorders	Urticarial, erythematous or mobilliform rash and pruritus	Exfoliative dermatitis	Linear IgA disease

Renal and urinary disorders	--	Interstitial nephritis	Nephropathy (usually associated with high doses of parenteral penicillin)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Suspected adverse reactions can also be reported directly to the HCR via medsafety@austell.co.za

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 overdosage, particularly for 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

Category and Class: A 20.1.2 Penicillins

Pharmacotherapeutic group: Beta lactamase sensitive natural penicillins

ATC Code: J01C E02.

Mechanism of action

Phenoxymethylpenicillin is a narrow spectrum antibiotic inhibited by penicillinase. 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.

Mechanisms of resistance

Phenoxymethylpenicillin is inhibited by penicillinase and other betalactamases that are produced by certain micro-organisms. The incidence of beta-lactamase producing organisms is increasing.

The two main mechanisms of resistance to phenoxymethylpenicillin are:

Inactivation by bacterial penicillinases and other beta-lactamases

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 1.022.11.210) 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 nonproducers.

Streptococcus pneumoniae: For phenoxymethylpenicillin, report S. pneumoniae with benzylpenicillin MICs above 0,06mg/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, *B, C, G
Species for which acquired resistance may be a problem
Staphylococcus aureus
Streptococcus pneumonia
Staphylococcus epidermidis

* Not applicable for 125 mg.

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 125 mg, peak serum concentrations of 200 to 700 ng/ml are attained in 2 hours. After an oral dose of 500 mg, peak serum concentrations reach 3 to 5 micrograms /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 the milk; (protein binding 50 to 80 % bound plasma proteins).

Biotransformation

It is metabolised in the liver; several metabolites have been identified, including penicilloic acid.

Elimination:

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).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL powder for solution

Sodium benzoate

Saccharin sodium

Trusil orange flavour J1978

175788 Euroblend orange

Sucrose

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL powder for solution

Sodium benzoate

Saccharin sodium

Trusil orange flavour J1978

175788 Euroblend orange

Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Unopened container: Store in a dry place, at or below 25 °C. Protect from light.

Reconstituted oral solution: Store for 7 days in a refrigerator (2- 8°C)

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL powder for solution:

Clear white polyethylene bottles with a polypropylene tamper evident or HOPE polypropylene tamper evident/child resistant cap containing 60 g powder for reconstitution of 100 mL syrup.

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL powder for solution:

Natural high density polyethylene bottles with a polypropylene tamper evident or HOPE polypropylene tamper evident/child resistant cap containing 65 g powder for reconstitution of 100 mL syrup.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Shanur Healthcare (Pty) Ltd)

Loch House Unit 003

3A Eton Road, Parktown

Johannesburg, 2193

South Africa

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8. REGISTRATION NUMBER(S)

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL: 33/20.1.2/0047

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL: 33/20.1.2/0048

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

ATHLONE PHENOXYMETHYLPENICILLIN 125/5 mL: 13 July 2016

ATHLONE PHENOXYMETHYLPENICILLIN 250/5 mL: 22 December 2015

10. DATE OF REVISION OF THE TEXT

29 May 2026