Approved Professional Information for Medicines for Human Use:

METPEN 125/250

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

METPEN 125 (POWDER FOR ORAL SOLUTION)

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2. QUALITATIVE AND QUANTITATIVE COMPOSITION

METPEN 125 powder for oral solution

Each 5 mL after reconstitution contains phenoxymethylpenicillin potassium equivalent to phenoxymethylpenicillin 125 mg.

Contains sugar (castor grade): 2610,00 mg

Contains sweetener: Saccharin sodium: 0,50 mg

METPEN 250 powder for oral solution

Each 5 mL after reconstitution contains phenoxymethylpenicillin potassium equivalent to phenoxymethylpenicillin 250 mg.

Contains sugar (castor grade): 2550,00 mg

Contains sweetener: Saccharin sodium: 1,00 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution

METPEN 125/250 is a light pink powder with an odour of strawberry, when reconstituted, a clear pink solution is obtained.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

METPEN is used prophylactically to prevent recurrence of rheumatic fever.

It is also indicated in the treatment of:

- Mild to moderate infections caused by sensitive organisms,
- Pneumococcal infections of the middle ear,
- Streptococcal otitis media and sinusitis,
- Sore throat due to Group A haemolytic streptococci,
- Streptococcal pharyngitis caused by *Streptococcus pyogenes.*

4.2 Posology and method of administration

Method of administration

METPEN is for oral administration.

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

4.3 Contraindications

- Hypersensitivity to the phenoxymethylpenicillins, cephalosporin or to any of the excipients listed in section 6.1.
- Use in dysentery and typhus, and other infections caused by penicillin resistant microbes such as *Brucella an 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 medicine 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 sure infection occurs, appropriate measures should be taken.

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.

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 precaution measure, it is preferable to avoid the use of Phenoxymethylpenicillin during pregnancy.

Breastfeeding

Phenoxymethylpenicillin metabolites are excreted in human milk to such an extent that effects on breastfed newborns are likely.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

a) Summary of the safety profile

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.

b) Tabulated list of adverse reactions

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

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).
Gastrointestinal disorders	Nausea, vomiting, abdominal pain, diarrhoea.		Sore mouth and black hairy tongue (discolouration of tongue).
Hepatobiliary disorders		Hepatitis and cholestatic jaundice.	
Cardiac disorders			Kounis syndrome
Immune disorders	Allergic reactions (typically manifest as skin reactions) (See Skin and subcutaneous disorders).	Severe allergic reactions causing angioedema, laryngeal oedema and anaphylaxis.	Serum sickness-like reactions 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).
Renal and urinary disorders		Interstitial nephritis, nephropathy (usually associated with high doses of parenteral penicillin).	
Skin and subcutaneous tissue disorders	Urticarial, erythematous or morbilliform rash and pruritus	Exfoliative dermatitis	Linear IgA

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

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 overdosage, 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 haemodialyses.

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.

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for phenoxymethylpenicillin.

Mechanism(s) of Resistance:

Phenoxymethylpenicillin is inhibited by penicillinase and other betalactamasess that 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 penicillinase and other beta-lactamases
- Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacterial 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 sreptococci 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 strain 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 0,06 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 local prevalence of resistance is such that the utility of the medicine 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 mg/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 ascetic fluids and also in cerebrospinal fluid when the meanings are inflamed; Phenoxymethylpenicillin crosses the placenta and is secreted in the milk; (proteins binding 50 to 80 % bound plasma proteins).

Biotransformation

It is metabolised in the liver. Several metabolites have been identified including penicilloic acid.

Elimination

The unchanged medicine and metabolites are excreted rapidly in the urine. Only small amounts are excreted in the bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

strawberry flavour 17.41.05

red dye (Anstead) 1578 E 124

sucrose (castor grade)

saccharin sodium

purified water

industrial methylated spirit

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Unconstituted powder: Store in a dry place at or below 25 °C.

Reconstituted oral solution: Store for 7 days in a refrigerator.

Shake bottle before use.

Keep well closed.

6.5 Nature and contents of container

White-Opaque HDPE bottle of 100 ml, with a tamper evident cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Direction for reconstitution: 100 ml syrup. Add 65 ml water and shake well to dissolve. Shake the bottle well before use.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Laboratories (Pty) Ltd.

52 Mineral Crescent,

Crown ext 3,

Johannesburg, 2092,

South Africa

8. REGISTRATION NUMBER(S)

METPEN 125: 42/20.1.2/0038

METPEN 250: 42/20.1.2/0039

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05 August 2011

10. DATE OF REVISION OF THE TEXT

30 January 2026