Approved Professional Information for Medicines for Human Use:

PEN VK 250 AUSTELL

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

PEN VK 250 AUSTELL tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PEN VK 250 AUSTELL tablet

Each tablet contains phenoxymethylpenicillin potassium equivalent to 250 mg phenoxymethylpenicillin.

Contains sugar: lactose 52,00 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

PEN VK 250 AUSTELL tablets

Shiny, white, flat tablet with breakline on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PEN VK 250 AUSTELL is used for the 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 *Streptococcus pyogenes*; mild to moderate

pulmonary and periodontal anaerobic infections; gingivostomatitis; early Lyme disease.

Prophylactic: Recurrence of rheumatic fever.

4.2 Posology and method of administration

Posology

PEN VK 250 AUSTELL should be taken 1 hour before or at least 2 hours after meals.

Prophylactic use: 125-250 mg twice a day.

Adult therapeutic dose: 250 mg-500 mg every six hours, depending on the severity of the infection.

Streptococcal pharyngitis must be treated for a minimum of 10 days.

Method of administration

PEN VK 250 AUSTELL is for oral administration

4.3 Contraindications

PEN VK 250 AUSTELL is contraindicated in:

- Patients known to be allergic to phenoxymethylpenicillin, other penicillins or betalactam antibiotics, or any other ingredients of PEN VK 250 AUSTELL. It should be given with care to patients with a history of allergy to cephalosporins as cases of cross sensitivity have been reported.
- Babies, in the neonatal period, born of hypersensitive mothers.
- Chronic, severe or deep-seated infections such as subacute bacterial endocarditis, meningitis or syphilis.
- Dysentry and typhus, and other infections caused by penicillin resistant microbes such as Brucella and E. coli. Hypersensitivity to penicillin.
- 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. Oral penicillin should not be used as adjunctive prophylaxis for genito-urinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and childbirth.

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.

Severe empyema, bacteraemia, pericarditis, meningitis and arthritis should not be treated with penicillin during the acute phase.

All degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin. Cross sensitivity may occur with cephalosporins and other beta lactam antibiotics. These reactions are more likely to occur in individuals with a history of sensitivity to penicillins, cephalosporins 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 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 due to the increased risk of encephalopathy. As a safe dosage may be lower than usually recommended.

Phenoxymethylpenicillin may be used for prophylaxis against streptococcal infections following rheumatic fever and against pneumococcal infections following splenectomy or in sickle cell disease.

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.

Caution should be used when treating patients with a history of antibiotic-associated colitis.

Excipient lactose

This medicine contains lactose:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Probenecid delays the elimination of penicillin through the kidneys and thus prolongs its action.

Penicillins may interfere with anticoagulant control.

Phenoxymethylpenicillin reduces the excretion of the cytotoxic drug, methotrexate.

Avoid concomitant administration with bacteriostatic antibiotics such as tetracycline, erythromycin, chloramphenicol and sulphonamides because it can diminish the effect of phenoxymethylpenicillin 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 contraceptive precautions while taking phenoxymethylpenicillin.

Neomycin is reported to reduce the absorption of Phenoxymethylpenicillin The simultaneous administration of guar gum diminishes the absorption of penicillins.

Sulfinpyrazone: Excretion of penicillins reduced by sulfinpyrazone.

Typhoid vaccine (oral): Penicillins may inactivate oral typhoid vaccine.

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 to such an extent that effects on breastfed newborns are likely.

4.7 Effects on ability to drive and use machines

PEN VK 250 AUSTELL has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

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	--	--	Neutropenia, leucopenia, eosinophilia, thrombocytopenia, haemolytic anaemia, coagulation disorders, neuropathy, and nephropathy (usually associated with high doses of parenteral penicillin)
Immune system disorders	--	--	Urticaria, fever, arthralgia (joint pains), rashes, angioedema, anaphylaxis, serum sickness like reactions, haemolytic anaemia and interstitial nephritis. prostration, chills, laryngeal oedema, anaphylaxis.

Nervous system 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. Neuropathy (usually Associated with high doses of parenteral penicillin)
Cardiac disorders	--	--	Kounis syndrome
Gastrointestinal disorders	--	--	Nausea and/or vomiting, Severe and persistent diarrhoeas, epigastric distress, black hairy tongue
Hepatobiliary disorders	--	Cholestatic jaundice, hepatitis	--
Skin and subcutaneous tissue disorders	--	--	Linear IgA disease Maculopapular rash, exfoliative dermatitis, angioedema and urticaria (rashes)
Renal and urinary disorders	--	Interstitial nephritis Nephropathy (usually associated with high doses of parenteral penicillin)	--

General disorders and administration site conditions	--	--	Fever

Hypersensitivity

Although reactions have been reported much less frequently after oral than after parenteral therapy, it should be remembered that all degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin.

Pseudomembranous colitis requires immediate attention and treatment with an appropriate antibiotherapy (i.e. vancomycin).

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

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.

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 over dosage, particularly in 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 penicillins

ATC Code: J01CE02

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

Lactose

maize starch

magnesium stearate

pre gelatinised starch.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30 ºC.

Store in a cool, dry place.

Keep the container well closed.

Keep blister packs in carton until required for use.

6.5 Nature and contents of container

PEN VK 250 AUSTELL: Packed in a semi-transparent polypropylene bag, which is then sealed. The sealed bag is packed into a white, round HDPE container together with the package insert & a desiccant (silica bag).

The HDPE container is sealed with a plain aluminium tagger and is then capped with a white screw type HDPE lid. Pack size: 1000 tablets.

Aluminium foil and clear PVC blister strips containing 10 tablets. 4 or 10 blister strips are packed in an outer carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

1 Sherborne Road

Parktown

Johannesburg, 2193

Tel: +27 11 611 1400 or +27 860 287 835

8. REGISTRATION NUMBER(S)

45/20.1.2/0349

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29 July 2016

10. DATE OF REVISION OF THE TEXT

14 July 2026