



National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of medicinal product

MAXPEN V TABLETS

Phenoxyethyl Penicillin Tablets BP

2. QUALITATIVE & QUANTITATIVE COMPOSITION

Batch Size: 8, 00,000 Tablets

Sr. No	Ingredients	Grade	Rationale	Quantity per Unit (mg)	Quantity per Batch (Actual-Kg)
1.	Phenoxyethyl Penicillin Potassium	BP	Active	336.662	269.330
2.	Colloidal silicon dioxide	BP	Disintegrant	2.000	1.600
3.	Microcrystalline Cellulose	BP	Disintegrant	246.088	196.870
4.	Talcum	BP	Glidant	10.000	8.000
5.	Magnesium Stearate	BP	Lubricant	4.500	3.600
6.	Methyl Paraben	BP	Preservative	0.600	0.480
7.	Propyl Paraben	BP	Preservative	0.150	0.120

3. PHARMACEUTICAL DOSAGE FORM

Tablet for oral administration

Description: White circular, beveled edge uncoated tablets having embossing of “MAXPEN-V” on one side & “MAXHEAL” on other side of each tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For use in the treatment of mild to moderately severe infections caused by penicillin sensitive organisms.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and Method of Administration

Posology

Adults: The dosage is 250-500 mg every six hours.

Elderly: The dosage is as for adults. The dosage should be reduced if renal function is markedly impaired.

Prophylactic Use: The dosage is 250 mg daily for long term prophylaxis of rheumatic fever.

Paediatric population

Children 1-5 years: 125 mg every six hours

6-12 years: 250 mg every six hours

To avoid late complications (rheumatic fever), infections with β -haemolytic streptococci

should be treated for 10 days.

The treatment of acute otitis media with penicillin V should be limited to 5 days. However, 5-10 days treatment may be recommended in patients with potential for complications.

Method of administration

Penicillin VK Tablets 250 mg/Phenoxymethylpenicillin 250 mg Film-Coated Tablets are for oral use.

Each tablet should be swallowed whole with water, at least 30 minutes before food, as ingestion of phenoxymethylpenicillin with meals slightly reduces the absorption of the drug.

4.3 Contraindications

Phenoxymethylpenicillin is contraindicated in patients with known penicillin hypersensitivity. Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics e.g. cephalosporins. Severe acute infections should not be treated with phenoxymethyl penicillin.

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 (e.g. adrenaline and other pressor amines, antihistamines and other corticosteroids).

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 severe illness or with a gastrointestinal disease that causes persistent nausea, vomiting gastric dilation, cardiospasm, intestinal hypermotility or diarrhoea because absorption may be reduced. Occasionally, patients do not absorb therapeutic amounts of orally administered penicillin.

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.

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. If super-infection occurs, appropriate measures should be taken.

Caution should be used when treating patients with a history of antibiotic-associated colitis. Each tablet of Penicillin VK Tablets 250 mg/Phenoxymethylpenicillin 250 mg Film-Coated Tablets contains 28 mg 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. During treatment with phenoxymethylpenicillin non-enzymatic glucose tests may be false-positive.

4.5 Interaction with other medicinal products and other forms of interaction

As penicillins like phenoxymethylpenicillin are only active against proliferating microorganisms, phenoxymethylpenicillin should not be combined with bacteriostatic antibiotics such as tetracycline, erythromycin, chloramphenicol and sulphonamides.

Concomitant use of uricosuric drugs (e.g. probenecid and sulfinpyrazone) reduces the excretion of phenoxymethylpenicillin resulting in increased plasma levels and thus prolongs its action.

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

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

Guar gum may slow the speed of absorption of phenoxymethylpenicillin.

Phenoxymethylpenicillin has the following interaction information:

Neomycin - absorption of phenoxymethylpenicillin reduced by neomycin.

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

Coumarin – common experience in anticoagulant clinics is that INR can be altered by a course of broad-spectrum penicillins such as ampicillin, although studies have failed to demonstrate an interaction with coumarins.

Phenindione – common experience in anticoagulant clinics is that INR can be altered by a course of broad-spectrum penicillins such as ampicillin, although studies have failed to demonstrate an interaction with phenindione.

Thyphoid Vaccines – antibacterials inactive oral typhoid vaccine.

4.6 Pregnancy and lactation

Pregnancy

Animal studies with phenoxymethylpenicillin potassium have shown no teratogenic effects.

Phenoxymethylpenicillin potassium has been in extensive clinical use and suitability in human

pregnancy has been well documented in clinical trials. However, as with other drugs, caution should be exercised when prescribing to pregnant patients.

Lactation

Breast feeding is not contraindicated with phenoxymethylpenicillin potassium. Trace quantities of

phenoxymethylpenicillin potassium can be detected in breast milk. While adverse effects are apparently rare, two potential problems exist for nursing infant:

- modification of bowel flora
- direct effects on the infant such as allergy/sensitisation

Caution should therefore be exercised when prescribing for the nursing mother.

4.7 Effects on ability to drive and operate machine

Not Known.

4.8 Undesirable effects

Hypersensitivity

Potential allergic reactions include urticaria, angioneurotic oedema, erythema multiforme, exfoliative dermatitis, fever, joint pain, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis or anaphylactic shock (which could be fatal) with collapse and anaphylactoid reactions (asthma, purpura, gastrointestinal symptoms). Although these are less common, and take a milder course, in oral treatment than during parenteral penicillin treatment, it should be remembered that all degrees of hypersensitivity, including fatal anaphylaxis, have been observed with oral penicillin.

Gastro-intestinal tract

Phenoxymethylpenicillin potassium is generally well tolerated. Occasionally soft stools occur and they do not require the interruption of the treatment.

Nausea, diarrhoea, vomiting, stomatitis and glossitis are sometimes seen.

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 with appropriate antibiotherapy (i.e. vancomycin)..

Blood

Eosinophilia, haemolytic anaemia, leukopenia, thrombocytopenia and agranulocytosis are extremely rare. Other possible effects on the blood composition include: neutropenia, haemolytic anaemia and coagulation disorders.

Central nervous system

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. As with other broad-spectrum antibiotics prolonged use may result in the overgrowth of non-susceptible organisms, e.g. candida. This may present a vulvo-vaginitis.

4.9 Overdose

A large overdose may cause nausea, vomiting and diarrhoea. Rarely major motor seizures may occur. There is no known antidote. Symptomatic and supportive therapy is recommended. It is advisable to monitor blood levels in patients with renal malfunction. Phenoxymethylpenicillin may be removed by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of action

Phenoxymethylpenicillin is a broad spectrum beta-lactam antibiotic with bactericidal action against Gram-positive bacteria and Gram-negative cocci. Its antimicrobial action is similar to that of benzyl penicillin. Phenoxymethylpenicillin is usually active against the following organisms:

Gram-positive aerobes and anaerobes including

Bacillus anthracis

Clostridium perfringens

Clostridium tetani

Corynebacterium diphtheriae

Erysipelothrix rhusiopathiae

Listeria monocytogenes

Peptostreptococcus spp.

Streptococcus agalactiae (Group B)

Streptococcus pneumoniae

Streptococcus pyogenes (Group A)

Gram-negative including

Neisseria meningitidis

Neisseria gonorrhoeae

Phenoxymethylpenicillin is inactivated by penicillinase and other beta-lactamases.

Phenoxymethylpenicillin binds to penicillin-binding proteins located on the inner membrane of the bacterial cell wall. Phenoxymethylpenicillin binds to and inactivates these proteins resulting in weakening of the bacterial cell wall and lysis.

5.2 Pharmacokinetic properties

Absorption

Phenoxymethylpenicillin is stable under acidic conditions so it can be administered by oral route.

Phenoxymethylpenicillin is rapidly, but incompletely absorbed after oral administration and the absorption level is around 60%. The simultaneous administration of food slightly decreases the peak plasma concentration of phenoxymethylpenicillin, but does not appear to affect the extent of absorption. Peak plasma concentrations are reached in about 45 minutes. The peak plasma concentration increases approximately in proportion with increased doses. Peak serum concentrations of 3-6 jig per ml have been seen following dosage of 250 mg to 500 mg by mouth.

Distribution

Phenoxymethylpenicillin is widely distributed round the body tissues and fluids (volume of distribution about 0.2 l kg⁻¹ of body weight) 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. Eighty per cent is reported to be protein bound.

Biotransformation

Phenoxymethylpenicillin is partially metabolised to inactive penicilloic acid by hydrolysis of the lactam ring. This metabolism occurs in the liver.

Elimination

The plasma half-life of phenoxymethylpenicillin is about 45 minutes which may increase to four hours in renal failure.

Excretion is by tubular secretion into urine. About 40% of the dose is eliminated in the urine either as unchanged or as penicilloic acid in the first 10 hours after oral administration. Small excretion occurs in bile.

Impaired absorption is seen in patients with coeliac disease.

5.3 Pre-clinical 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

Colloidal silicon dioxide
Microcrystalline Cellulose
Talcum
Magnesium Stearate
Methyl Paraben
Propyl Paraben

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

36 months from the date of manufacture.

6.4 Special Precautions for Storage

The following applies to the storage of Penicillin VK Tablets 250 mg/Phenoxymethyl penicillin
250 mg Film-Coated Tablets:

Store below 30°C

- 'Store in the original packaging' (when packaged in blisters)
- 'Keep the container tightly closed' (when packaged in securitainers)

6.5 Nature and Contents of Container

1 X 10 Tablets in Plastic Tube

6.6 Special Precaution for Disposal

No special requirement

7. APPLICANT/MANUFACTURER

NAFDAC Reg. No. 04-7087

MAXHEAL PHARMACEUTICALS (INDIA) LTD.

95/6, M.I.D.C, SATPUR, NASHIK – 422007

MAHARASHTRA, INDIA