Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kopen 250mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250 mg of phenoxymethylpenicillin (as phenoxymethylpenicillin potassium). Each tablet also contains 94.6mg of lactose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets
Circular white tablets approximately 10.5 mm in diameter, embossed 'Pen 250'.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For use in the treatment of infections caused by penicillin-sensitive gram positive bacteria and in particular Staphylococci, Pneumococci, Gonococci and Haemolytic Streptococci.

Phenoxymethylpenicillin is also indicated for:
- Prophylaxis of pneumococcal infection (e.g. in asplenia and in patients with sickle cell disease).

- Prophylaxis of rheumatic fever.

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

4.2 Posology and method of administration

Posology

Adults: 250mg or 500mg every six hours depending on the severity of the condition.

Elderly: As for adults

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

Prophylactic Use:
- Pneumococcal infection (e.g. asplenia)

Adults: 500mg every 12 hours
Children 6 - 12 years: 250mg every 12 hours
Children <5 years: 125mg every 12 hours

- Rheumatic fever

250mg twice daily is recommended for long term prophylaxis or rheumatic fever.

Children
Infants (up to 1 year): Tablets are not usually given to this age group. A liquid medicine is available.
Children 1 - 5 years: 125mg 6 hourly
Children 6 - 12 years: 250mg 6 hourly

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

For oral administration only
Ideally, each dose should be given half an hour before (or at least three hours after) a meal.
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 five days. However, 5-10 days treatment may be recommended in patients with potential for complications.

4.3 Contraindications

Phenoxymethylpenicillin is contraindicated in patients known to be hypersensitive to Penicillin, including ampicillin, and should be used with caution in patients with known histories of allergy or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Before initiation of penicillin therapy, careful enquiry should be made concerning previous hypersensitivity reaction to penicillin, cephalosporins or other drugs. Fatal anaphylaxis has been observed with oral penicillin.

Patients suffering from severe gastrointestinal impairments accompanied by vomiting and diarrhoea should not be treated with penicillin V, because sufficient absorption is not ensured. (In those cases a parenteral administration is recommended, e.g. with benzyl penicillin or another adequate antibiotic).

Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

Administer with caution in the presence of markedly impaired renal function, as safe dosage may be lower than that recommended.

In patients undergoing long-term penicillin V treatment the complete and differential blood count, as well as the liver and kidney function, should be monitored.

Prolonged use of an antibiotic may result in the development of superinfection due to organisms resistant to that anti-infective including Pseudomonas and Candida. If superinfection occurs, appropriate measures should be taken.

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

The effectiveness of oral contraceptives may be reduced in patients on concurrent penicillin V therapy. The additional use of a non-hormonal contraceptive method is therefore recommended.

Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of penicillin's. These are serious and potentially life threating cutaneous conditions. Patients should be advised of the signs and symptoms of SJS and TEN (e.g. progressive skin rash often with blisters or mucosal lesions) and instructed to discontinue use immediately and seek urgent medical attention.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of oral penicillins may be reduced if a non-absorbable aminoglycoside (e.g. neomycin) was used immediately before oral penicillin therapy or is still being used for bowel antisepsis.

Bacteriostatic antibacterials: Bacteriostatic antibacterials such as Chloramphenicol, Erythromycin, Sulphonamides and Tetracyclines have been reported to antagonise the bactericidal activity of penicillins and concomitant use is not recommended.

Guar Gum: Reduces the absorption of phenoxymethylpenicillin.

Methotrexate: Use of phenoxymethylpenicillin while taking methotrexate can cause reduced excretion of methotrexate thereby increasing the risk of toxicity.

Probenecid: Reduces excretion of phenoxymethylpenicillin by blocking renal tubular secretion.

Laboratory tests: Non enzymatic methods of detecting glucose in the urine may show false positive results during treatment with phenoxymethylpenicillin. Phenoxymethylpenicillin may also interfere with tests for urobilinogen.

4.6 Fertility, pregnancy and lactation

Pregnancy:
The product should not be used during pregnancy unless considered essential by the physician.
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.

Lactation:
The product is excreted in breast milk, presenting the risk of candidiasis and also to 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

Kopen 250mg Tablets has no or negligible influence on the ability todrive 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.

The following convention has been utilised for the classification of undesirable effects:-
Very common (≥1/10), Common (≥1/100, <1/10), Uncommon (≥1/1000, <1/100), Rare (≥1/10,000, <1/1000), Very rare (<1/10,000), not known (cannot be estimated from the available data).

Blood and lymphatic disorders:
Very Rare: Changes in blood counts, including, thrombocytopenia, granulocytopenia, agranulocytosis, neutropenia, leucopenia, eosinophilia, pancytopenia and haemolytic anaemia. These changes are reversible on discontinuation.

Gastrointestinal disorders:
Common: Gastric discomfort, flatulence, Nausea, vomiting, loss of appetite, abdominal pain, diarrhoea, glossitis, stomatitis.
Uncommon
Very rarely: a pseudomembranous enterocolitis may occur during penicillin V therapy, mostly caused by Clostridium difficile, tooth discolouration.

Hepatobiliary disorders:
Rare: Transient induction of liver enzymes occurs rarely.

Skin and subcutaneous tissue disorders:
Common: exanthema, inflammation of mucous membranes especially in the mouth (glossitis, stomatitis),
Rare: black hairy tongue, transiently dry mouth and taste alterations may occur.
Very Rare: Severe skin reactions such as Stevens-Johnson syndrome
Unknown: Toxic epidermal necrolysis

Immune system disorders:
Common: Allergic reactions (typically manifest as skin reactions), Urticarial, erythematous or mobilliform rash, itching, pruritus may occur. An immediate-type urticarial hypersensitivity reaction is usually indicative of true penicillin allergy and necessitates discontinuation of therapy.
Very Rare: Reports of serious allergic reactions due to sensitisation to the 6-aminopenicillanic acid group, including drug fever, arthralgia, eosinophilia, angineurotic oedema, laryngeal oedema, bronchospasm, tachycardia, dyspnoea, serum sickness, allergic vasculitis and dropping of blood pressure up to life threatening shock.
Hypersensitivity reactions of all intensities to the point of anaphylactic shock have also been observed after oral penicillin use. Severe anaphylactoid reactions, which occur significantly less often after oral administration of penicillin than after intravenous or intramuscular administration, may necessitate appropriate emergency management.
Very Rare: Serum sickness-like reactions (characterised by fever, chills, arthralgia and oedema)

Infections and infestations:
Very Rare: Pseudomembranous colitis

Renal and urinary disorders:
Very Rare: Interstitial nephritis.

Investigations:
Rare: Raised liver enzymes

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance Website: www.hpra.ie.

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

ATC code: J01CE02

Phenoxymethylpenicillin is a beta-lactamase sensitive natural penicillin.
Mechanism of Action:
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.

Bacterial surface enzymes called autolysins also appear to be involved in the lethal effect of penicillins, particularly for gram-positive bacteria. In gram-negative bacilli osmotic rupture of cells may occur when the cell wall is weakened.

Phenoxymethylpenicillin is a narrow spectrum antibiotic and is, therefore, less likely to cause the potentially harmful modifications of bowel flora associated with oral administration of 'broad spectrum' antibiotics. Therapeutic blood levels are usually achieved within half an hour and sustained for approximately four hours.

One gram of phenoxymethylpenicillin is the equivalent of 1.7 million units of penicillin.

Phenoxymethylpenicillin can also produce morphological changes in vitro including the formation of long filaments or abnormally shaped cells. Bacteria that are not growing or dividing are generally not killed by phenoxymethylpenicillin.

Mechanism(s) of Resistance:
Phenoxymethylpenicillin is inhibited by penicillinase and other beta-lactamases that are produced by certain micro- organisms. The incidence of beta-lactamase producing organisms is increasing.

Susceptibility testing breakpoints
MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for {INN} and are listed here:
https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

5.2 Pharmacokinetic properties

ABSORPTION: Rapidly but incompletely absorbed after oral administration; calcium and potassium salts are better absorbed than the free acid; Absorption appears to be reduced in subjects with coeliac disease; Absorption appears to be more rapid in fasting than in non-fasting subjects.

BLOOD CONCENTRATION: After an oral dose of 125mg peak serum concentration of 200 to 700ng/ml are attained in 2 hours and after an oral dose of 500mg peak serum concentrations reach 2 to 5ug/ml in 2 to 4 hours.

HALF-LIFE: Biological half-life, about 30 minutes.

DISTRIBUTION: Widely distributed throughout the body and enters pleural and ascitic fluids and also the 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).

METABOLIC REACTIONS: Hydroxylation may occur.

EXCRETION: 20% - 35% of an oral dose is excreted in the urine in 24 hours.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Magnesium stearate
Talc
Maize starch

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C. Store in the original container to protect from moisture.

6.5 Nature and contents of container

An opaque white polypropylene securitainer with a polyethylene press on air proof cap.
100 or 500 tablet pack sizes contain a polyethylene jayfilla.
1000 tablet pack size contain a polyethylene bag.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Athlone Pharmaceuticals Limited
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Dublin 4
D04 C5Y6
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1418/014/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 24 July 2007

10 DATE OF REVISION OF THE TEXT

December 2025