Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Calvepen 250 mg/5 ml Powder for Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When reconstituted each 5 ml contains 250 mg Phenoxymethylpenicillin Calcium.

Excipients with known effect
Each 5 ml contains 5 mg methyl parahydroxybenzoate (E218), 2.5 g of sucrose and 15 mg of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral suspension.

White to off-white powder which on reconstitution with water forms a homogenous suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In the treatment of infection due to micro-organisms sensitive to this anti-infective.

In the prophylactic management of patients with rheumatic fever.

4.2 Posology and method of administration

Posology

Oral penicillin should be given before meals, and in divided doses, preferably four times per day.

Adults and over 12 years:
Typical dose is 250mg to 500mg given four times daily.

See local/national prescribing guidance for further detail including weight based dosing, max daily doses and treatment duration. Doses may be modified depending on the severity of the condition.

Paediatric population

See local/national prescribing guidance for further detail including weight based dosing, max daily doses and treatment duration. Doses may be modified depending on the severity of the condition.

Children: 6-12 years:
Typical dose is 250mg given four times daily

Children: 1-6 years:
Typical dose is 125mg given four times daily

Infants under 1 year:
Typical dose is 62.5mg given four times daily

Rheumatic Fever Prophylaxis
Typical dose is 250mg twice a day.

Dosage may be modified at the discretion of the physician according to the severity of the condition.

Method of administration
For oral use.

4.3 Contraindications

Hypersensitivity to the active substance, penicillins, including ampicillin or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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.

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).

Prolonged use of an anti-infective may result in the development of superinfection due to organisms resistant to that anti-infective.

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.

Excipients
This product contains methyl parahydroxybenzoate (E218) which may cause allergic reactions (possibly delayed).

This medicinal product contains 15 mg sodium per 5ml, equivalent to 0.75 % of the WHO recommended maximum daily intake of 2g sodium for an adult.

This product contains 2.5 g of sucrose per 5 ml dose. This should be taken into account in patients with diabetes mellitus. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Penicillin V should not be combined with bacteriostatic chemotherapeutic agents/antibiotics (e.g. tetracyclines, sulphonamides or chloramphenicol), because these may have an antagonistic effect.

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.

The excretion of phenoxymethylpenicillin in urine is retarded by probenecid, as is the case for all penicillins.

Interference with laboratory tests:
Non-enzymatic methods of testing for glucose in urine may give false positive results during penicillin V therapy. Penicillin V may also interfere with urobilinogen tests.

4.6 Fertility, pregnancy and lactation

The product should not be used during pregnancy unless considered essential by the physician. The product is excreted in breast 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

Calvepen has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Gastrointestinal disorders
Penicillin V commonly (≥ 1/100, < 1/10) produces gastrointestinal side effects, including nausea, vomiting, loss of appetite, gastric discomfort, abdominal pain, flatulence and diarrhoea. These disorders are usually light and abate during or at the latest after discontinuing treatment.
Very rarely (< 1/10000) a pseudomembranous enterocolitis may occur during penicillin V therapy, mostly caused by *Clostridium difficile*, tooth discolouration.

Skin and subcutaneous tissue disorders
There have been common reports (≥ 1/100, < 1/10) of exanthema and of inflammation of mucous membranes, especially in the mouth (glossitis, stomatitis). There have been rare reports (≥ 1/10,000 to < 1/1,000) of black hairy tongue. Following penicillin V use, transiently dry mouth and taste alterations may occur. Toxic epidermal necrolysis (frequency not known). There have been very rare (< 1/10000) reports of severe skin reactions such as Stevens-Johnson syndrome

Immune system disorders
Allergic reactions may commonly (≥ 1/100, < 1/10) occur and typically manifest as skin reactions (e.g. rash, itching, urticaria). An immediate-type urticarial hypersensitivity reaction is usually indicative of true penicillin allergy and necessitates discontinuation of therapy. There have been very rare (< 1/10000) reports of serious allergic reactions due to sensitisation to the 6-aminopenicillanic acid group, including drug fever, arthralgia, eosinophilia, angioneurotic 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.

Blood and lymphatic system disorders
There have been very rare (<1/10000) reports of changes in blood counts, including granulocytopenia, agranulocytosis, thrombocytopenia, pancytopenia, haemolytic anaemia and eosinophilia. These changes are reversible.

Renal and urinary disorders
In very rare (<1/10000) cases interstitial nephritis may occur.

Hepatobiliary disorders
Transiently raised liver enzymes occur rarely.

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

There has been no experience of overdose associated with the use of Calvepen.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Therapeutic blood levels are usually achieved within half an hour and sustained for approximately four hours.

5.2 Pharmacokinetic properties

Phenoxymethylpenicillin is rapidly excreted by the kidneys with $t^{1/2}$ of 0.5 to 1 hour.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Caramel custard dry aroma
Sucrose
Hypromellose
Golden syrup flavour permaseal
Methyl parahydroxybenzoate (E218)
Sodium carraghenate
Sodium chloride
Sodium citrate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months.

The product, after reconstitution, should not be kept for more than seven days if stored at room temperature or for more than fourteen days if stored under refrigeration at a temperature between 2°C and 8°C.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions. For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Natural high-density polyethylene bottle with a tamper evident cap, containing powder for reconstitution with water to make 100 ml.

A spoon with graduations of 2.5 ml and 5 ml may be supplied with the pack of this product.

6.6 Special precautions for disposal and other handling

To reconstitute: Loosen powder, add 66 ml water and shake well.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
Waterford Road
Clonmel, Co. Tipperary
E91 D768
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/137/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20th January 1986

Date of last renewal: 20th January 2006

10 DATE OF REVISION OF THE TEXT

March 2023