

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Calvepen 333 and 666 mg Tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Calvepen 333 mg Tablets:

Each tablet contains 333mg of Phenoxymethylpenicillin Calcium equivalent to 300mg (500,000 i.u.) of Phenoxymethylpenicillin.

Calvepen 666 mg Tablets:

Each tablet contains 666mg of phenoxymethylpenicillin calcium equivalent to 600 mg (1,000,000 i.u.) of phenoxymethylpenicillin.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablets.

Calvepen 333 mg tablets: White, oval, film-coated tablet having "105" engraved on one side and Clonmel logo on the other.

Calvepen 666 mg tablets: White, oval, film-coated tablet having "104" engraved on one side and Clonmel logo on the other side.

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

Oral penicillin should ideally be given in divided doses (3 - 4 times daily) and preferably half an hour before meals.

Adults

The usual total daily dose is 1000 to 2000 mg in divided doses.

Children

Aged over 6 years

The usual total daily dose is 500 to 1000 mg in divided doses.

Aged under 6 years

The usual total daily dosage is 250 to 500 mg.

Rheumatic Fever Prophylaxis

The usual total daily dose is 250 to 500 mg.

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

4.3 Contraindications

Known hypersensitivity to penicillins, including ampicillin.

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.

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

Presumed to be safe or unlikely to produce an effect.

4.8 Undesirable effects

Gastrointestinal tract

Penicillin V commonly ($\geq 1/100$, $< 1/10$) 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 ($< 1/10,000$) a pseudomembranous enterocolitis may occur during penicillin V therapy, mostly caused by *Clostridium difficile*.

Skin and tissue (Hypersensitivity reactions)

There have been common reports ($\geq 1/100$, $< 1/10$) of exanthema and of inflammation of mucous membranes, especially in the mouth (glossitis, stomatitis). There have been rare reports (\geq

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).

Hypersensitivity phenomena

Allergic reactions may commonly ($\geq 1/100$, $< 1/10$) 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 ($< 1/10,000$) 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 blood cells

There have been very rare ($< 1/10,000$) reports of changes in blood counts, including granulocytopenia, agranulocytosis, thrombocytopenia, pancytopenia, haemolytic anaemia and eosinophilia. These changes are reversible.

Kidneys, urogenital tract

In very rare ($< 1/10,000$) cases interstitial nephritis may occur.

Hepato-biliary

Transient induction of liver enzymes occurs rarely.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacodynamic group: Beta-lactamase sensitive penicillins.

ATC Code: JO1CE02

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.

5.2 Pharmacokinetic properties

Phenoxymethylpenicillin is well absorbed after oral administration. The calcium salt is relatively insoluble and stable at low pH and therefore, phenoxymethylpenicillin escapes destruction in gastric juice but enters into solution in the duodenum and upper small intestine from which it is well absorbed. Peak levels are reached one to two hours later and the drug is rapidly excreted in the bile and urine 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

Crospovidone
Gelatin
Magnesium stearate
Maize starch
Hypromellose
Colloidal anhydrous silica
Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Glass bottles: No special storage precautions.
Blisters: Do not store above 25°C.
Securitainers: Do not store above 25°C.

6.5 Nature and contents of container

Calvepen 333 mg tablets:
Glass bottles of 100 and 500 tablets. PVC/aluminium blister packs of 4, 100 and 500 tablets. High density polypropylene tubes with low density polyethylene caps (securitainers) of 4, 10, 100 and 500 tablets.

Calvepen 666 mg tablets:
Glass bottles of 150 tablets. PVC/aluminium blister pack of 4 and 100 tablets. High density polypropylene tubes with low density polyethylene caps (securitainers) of 4, 100 and 500 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product.

No special requirements

7. MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Limited,
Waterford Road,
Clonmel,
Co. Tipperary

8. MARKETING AUTHORISATION NUMBER(S)

Calvepen 333 mg tablets: PA 126/137/1
Calvepen 666 mg tablets: PA 126/137/2

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st April 1977
Date of last renewal: 1st April 2007

10. DATE OF REVISION OF THE TEXT

February 2011