Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zinnat 500mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500mg cefuroxime (as axetil).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Product imported from Belgium:
White to off-white biconvex capsule shaped tablet, plain on one face and ‘GXEG2’ engraved on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Zinnat is used in the treatment of systemic infection due to Gram-positive and Gram-negative micro organisms susceptible to this anti-infective in respiratory tract and genito-urinary tract infections.

Skin and soft tissue infections for example, furunculosis, pyoderma and impetigo. Gonorrhoea, acute uncomplicated gonococcal urethritis, and cervicitis.

Treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years old.

Cefuroxime is also available as the sodium salt (Zinacef) for parenteral administration. This permits the use of sequential therapy with the same antibiotic, when a change from parenteral to oral therapy is clinically indicated.

Where appropriate Zinnat is effective when used following initial parental therapy with Zinacef (cefuroxime sodium) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

4.2 Posology and method of administration

Route of administration: Oral

Adults (including the elderly):
Lower respiratory tract infections:
Mild to moderate lower respiratory tract infections e.g. bronchitis the usual dose is 250 mg twice daily.

More severe lower respiratory tract infections or if pneumonia is suspected the usual dose is 500 mg twice daily.

Upper respiratory tract infections the usual dose is 250 mg twice daily.

For urinary tract infections:
For urinary tract infections the usual dose is 125- 250 mg bd.

Gonorrhoea (uncomplicated) the usual dose is 1 g as a single dose.

Lyme disease in adults and children over the age of 12 years - 500 mg twice daily for 20 days.

Sequential therapy:
Pneumonia: 1.5 g Zinacef tid or bd (iv or im) for 48-72 hours, followed by 500 mg bd Zinnat (cefuroxime axetil) oral therapy for 7-10 days.

Acute exacerbations of chronic bronchitis:
750 mg Zinacef tid or bd (iv or im) for 48-72 hours, followed by 500 mg bd Zinnat (cefuroxime axetil) oral therapy for 5-10 days.
Duration of both parenteral therapy to oral therapy is determined by severity of the infection and the clinical status of the patient.

Children:
Most Infections: 125 mg twice daily (1 x 125 mg tablet) or 10 mg/kg twice daily to a maximum of 250 mg daily.
Children aged 2 years or older with otitis media or where appropriate, with more severe infections 250 mg twice daily (1 x 250 mg tablet) or 15 mg/kg twice daily to a maximum of 500 mg daily.

Renal impairment or on dialysis:
On the basis of experience to date a reduction in dosage is not deemed necessary. Optimum absorption is achieved if medication is taken after food.

4.3 Contraindications

Patients with a known hypersensitivity to cephalosporin antibiotics.

4.4 Special warnings and precautions for use

Use of cefuroxime should be reserved for serious or severe infections.

Cross-resistance and cross-sensitisation may exist between penicillins and cephalosporins. Cephalosporin antibiotics may in general be given safely to patients who are hypersensitive to penicillins, although cross reactions have been reported. Special care is indicated in patients who have experienced an anaphylactic reaction to penicillin.

As with other antibiotics, prolonged use of cefuroxime axetil may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci, Clostridium difficile) which may require interruption of treatment.

Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Therefore, it is important to consider its diagnosis in patients who develop serious diarrhoea during or after antibiotic use.

The Jarisch-Herxheimer reaction has been seen following Zinnat treatment of Lyme disease. It results directly from the bactericidal activity of Zinnat on the causative organism of Lyme disease, the spirochaete Borrelia burgdorferi. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs which reduce gastric acidity may result in a lower bioavailability of Zinnat compared with that of the fasting state and tend to cancel the effect of enhanced post-prandial absorption.

As a false negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving cefuroxime axetil. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

4.6 Pregnancy and lactation

Studies in animals do not suggest an adverse effect in reproductive studies. The drug is excreted in breast milk. There is no experience of use during pregnancy in human beings. Cefuroxime should not be used during pregnancy or lactation in breast feeding women unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Adverse drug reactions to cefuroxime axetil are generally mild and transient in nature.

The frequency categories assigned to the adverse reactions below are estimates; as for most reactions suitable data (for example from placebo-controlled studies) for calculating incidence were not available. In addition the incidence of adverse reactions associated with cefuroxime axetil may vary according to the indication.

Data from large clinical studies were used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e. those occurring at <1/1000) were mainly determined using post-marketing data and refer to a reporting rate rather than true frequency.

Placebo-controlled trial data were not available. Where indications have been calculated from clinical trial data, these were based on drug-related (investigator assessed) data.

The following convention have been used for classification of frequency:

Very common = 1/10
Common = 1/100 and <1/10
Uncommon = 1/1000 and <1/100
Rare = 1/10,000 and <1/1000
Very rare <1/10,000

Blood and lymphatic system disorders

Common:	*Eosinophilia
Uncommon:	*Positive Coombs' test, *thrombocytopenia, *leukopenia (sometimes profound)
Very rare:	*Haemolyic anaemia

Cephalosporins as a class trend tend to be absorbed onto the surface of red cells membranes and react with antibodies directed against the drug to produce a positive Coombs' test (which can interfere with cross-matching of blood) and very rarely haemolytic anaemia.

Immune system disorders

*Hypersensitivity reactions including

Uncommon:	*Skin rashes
Rare:	* Urticaria, *pruritus
Very rare:	*Drug fever, *serum sickness, *anaphylaxis

Nervous system disorders

Common:	*Headache

Gastrointestinal disorders

Common:	*Gastrointestinal disturbances including

	*diarrhoea, *nausea
Uncommon:	*Vomiting
Rare:	*Pseudomembranous colitis

Hepatobilary disorders

Common:	*Transient increased of hepatic enzyme levels. [ALT (SGPT), AST (SGOT), LDH]
Very rare:	*Jaundice (predominantly cholestatic), *hepatitis

Skin and subcutaneous tissue disorders

Very rare:	*Erythema multiforme, *Stevens-Johnson syndrome, *toxic epidermal necrolysis (exanthematic necrolysis)

See also *Immune system disorders.*

4.9 Overdose

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.
Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Bacteriology:

Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime.

Cefuroxime is a well characterised and effective antibacterial agent which has bactericidal activity against a wide range of common pathogens, including β-lactamase producing strains.

Cefuroxime has good stability to bacterial β-lactamase, and consequently is active against many ampicillin-resistant or amoxicillin-resistant strains.

The bactericidal action of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins.

The following organisms are not susceptible to Cefuroxime:

Clostridium difficile
Pseudomonas spp.
Campylobacter spp.
Acinetobacter calcoaceticus
Listeria monocytogenes
Methicillin resistant strains of Staphylococcus aureus and Staphylococcus epidermis.
Legionella spp.

Some strains of the following genera are not susceptible to Cefuroxime**:**

Enterococcus (Streptococcus) faecalis.
Morganella morganii
Proteus vulgaris
Enterobacter spp.
Citrobacter spp.
Serratia spp.
Bacteroides fragilis.

5.2 Pharmacokinetic properties

Zinnat is well absorbed after oral administration (particularly following a meal), hydrolysed in the intestinal epithelium and blood releasing cefuroxime. Peak serum levels are achieved 2-3 hours post dose and the drug is eliminated without metabolism through the kidney by glomerular filtration and active tubular secretion. Probenecid concurrently administered will delay elimination. About 50% of cefuroxime is protein bound.

5.3 Preclinical safety data

No additional data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Croscarmellose sodium type A
Sodium laurilsulfate
Hydrogenated vegetable oil
Colloidal anhydrous silica
Hypromellose
Propylene glycol
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Opaspray M-1-7120

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf-life expiry date of this product is the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Blisters packs of 10 tablets contained in an outer cardboard carton. .

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 PARALLEL PRODUCT AUTHORISATION HOLDER

PCO Manufacturing Limited,
Unit 10, Ashbourne Business Park
Rath
Ashbourne
Co. Meath

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 0465/123/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 February 2006

10 DATE OF REVISION OF THE TEXT

October 2008