IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PPA1328/004/001
Case No: 2034068

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

B & S Healthcare

Unit 4, Bradfield Road, **Ruislip**, **Middlesex**, **HA4 0NU**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Zinnat 250 mg Film-coated Tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **26/03/2007** until **14/09/2011**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zinnat 250 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250mg cefuroxime (as axetil.)
Excipients: Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.

Product imported from Italy and the UK:
White to off-white film-coated biconvex capsule-shaped tablets marked ‘GX ES7’ on one side and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Zinnat tablets are indicated in the treatment of systemic infections 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 parenteral Zinacef (cefuroxime sodium) in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

4.2 Posology and method of administration

Adults (including the elderly):
Lower respiratory tract infections:
Mild to moderate lower respiratory tract infections e.g. bronchitis - the usual dose is 250mg twice daily.
More severe lower respiratory tract infections or if pneumonia is suspected - the usual dose is 500mg twice daily.

Upper respiratory tract infections:
Upper respiratory tract infections - the usual dose is 250mg twice daily.
Urinary tract infections:
For urinary tract infections the usual dose is 125 - 250mg bd.
Gonorrhoea (uncomplicated) - the usual dose is 1g as a single dose.
Lyme disease in adults and children over the age of 12 years - 500mg twice daily for 20 days.
Sequential therapy:
Pneumonia:- 1.5g Zinacef tid or bd (iv or im) for 48-72 hours, followed by 500mg bd Zinnat (cefuroxime axetil) oral therapy for 7-10 days.

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

Children:

Most infections - 125mg (1 x 125mg tablet) twice daily, or 10mg/kg twice daily to a maximum of 250mg daily.
Children aged two years or older with otitis media or where appropriate, with more severe infections - 250mg (1x 250mg tablet) twice daily, or 15mg/kg twice daily to a maximum of 500mg 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 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 reactions to cefuroxime axetil have been generally mild and transient in nature.

As with other cephalosporins, there have been rare reports of erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (exanthematic necrolysis) and hypersensitivity reactions including skin rashes, urticaria, pruritus, drug fever, serum sickness, and very rarely anaphylaxis.
A small proportion of patients receiving cefuroxime axetil have experienced gastrointestinal disturbances, including diarrhoea, nausea and vomiting. As with other broad-spectrum antibiotics, there have been reports of pseudomembranous colitis. Headache has also been reported.

Eosinophilia and transient increases of hepatic enzyme levels, [ALT (SGPT), AST (SGOT) and LDH] have been noted during Zinnat therapy. There have been rare reports of thrombocytopenia and leukopenia (sometimes profound). As with other cephalosporins, jaundice has been reported very rarely.
Cephalosporins as a class 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.

4.9 Overdose

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions.
Serum levels of cefuroxime can be reduced by haemodialysis and 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 amoxycillin-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 epidermidis.
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

Tablet core:

Microcrystalline cellulose
Croscarmellose sodium type A
Sodium laurilsulfate
Hydrogenated vegetable oil
Colloidal anhydrous silica

Film coat:

Hypromellose
Propylene glycol
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Titanium dioxide (E171)
Sodium benzoate (E211)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

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

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Zinnat tablets are packed in double foil blisters of 12 and 14 tablets.

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

B&S Healthcare
Unit 4
Bradfield Road
Ruislip
Middlesex
HA4 0NU
United Kingdom

8 Parallel Product Authorisation Number

PPA 1328/4/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 15th September 2006

10 DATE OF REVISION OF THE TEXT

February 2006