ZINNAT Tablets and Suspension

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

ZINNAT® TABLETS 125 mg

ZINNAT® TABLETS 250 mg

ZINNAT® TABLETS 500 mg

ZINNAT® SUSPENSION 125 mg (Granules for oral suspension)

COMPOSITION:

ZINNAT TABLETS 125 mg: Each tablet contains cefuroxime 125 mg (as cefuroxime axetil).

ZINNAT TABLETS 250 mg: Each tablet contains cefuroxime 250 mg (as cefuroxime axetil).

ZINNAT TABLETS 500 mg: Each tablet contains cefuroxime 500 mg (as cefuroxime axetil).

Tablets excipients:

Core: microcrystalline cellulose, croscarmellose sodium, colloidal silicon dioxide, sodium lauryl sulphate, hydrogenated vegetable oil.

Coating: propylene glycol, methylhydroxypropylcellulose, methylparahydroxybenzoate, propylparahydroxybenzoate, hypromellose, titanium dioxide, sodium benzoate.

ZINNAT SUSPENSION 125 mg: Reconstitution of the contents of the multidose bottle as directed yields a suspension containing 125 mg of cefuroxime (as cefuroxime axetil) in each 5 ml.

ZINNAT Suspension excipients: aspartame, xanthan gum, acesulfame potassium, povidone K30, stearic acid, sucrose and tutti frutti flavour.

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION:

Cefuroxime axetil is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime.

Bacteriology:

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

Cefuroxime has bactericidal activity against a wide range of common organisms, including beta-lactamase producing strains.

Cefuroxime has stability to bacterial beta-lactamase.

The bacterial 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 faecalis

Morganella morganii

Proteus vulgaris

Enterobacter spp

Citrobacter spp

Serratia spp

Bacteroides fragilis.

Pharmacokinetics:

After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation.

Optimum absorption occurs when it is administered after a meal. Peak serum levels (2-3 mg/ml for a 125 mg dose, 4-5 mg/ml for a 250 mg dose, 5-7 mg/ml for a 500 mg dose) occur approximately two to three hours after dosing when taken after food. The serum half-life is between 1 and 1,5 hours. Protein binding has been variously stated as 33-50 %, depending on the methodology used. Cefuroxime is not metabolised and is excreted by glomerular filtration and tubular secretion.

Concurrent administration of probenecid increases the area under the mean serum concentration time-curve by 50 %.

Serum levels of cefuroxime are reduced by dialysis.

INDICATIONS:

ZINNAT is indicated for the treatment of patients with infections caused by susceptible organisms in the following diseases:

Pharyngitis and Tonsillitis caused by *Streptococcus pyogenes*. (Penicillin is the usual medicine of choice in the treatment and prevention of Streptococcal infections, including the prophylaxis of rheumatic fever. ZINNAT is generally effective in the eradication of streptococci from the oral pharynx. ZINNAT is not indicated for the prophylaxis of subsequent rheumatic fever because data to support such use is not available).

Otitis Media caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (ampicillin-susceptible and ampicillin-resistant strains), *Moraxella (Branhamella) catarrhalis*, and *Streptococcus pyogenes*.

Sinusitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*.

Acute and chronic bronchitis caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (ampicillin-susceptible strains), and *Haemophilus parainfluenzae* (ampicillin-susceptible strains).

Acute uncomplicated cystitis caused by *Escherichia coli* and *Klebsiella pneumoniae*.

Lyme Disease caused by the spirochaete *Borrelia burgdorferi*. ZINNAT is indicated for the treatment of early Lyme disease and subsequent prevention of late Lyme disease in adults and children over 12 years old.

CONTRA-INDICATIONS:

ZINNAT is contra-indicated in patients with a history of hypersensitivity to cefuroxine axetil, other cephalosporin antibiotics or to any of the other components of ZINNAT.

WARNINGS:

ZINNAT Suspension contains aspartame, which is a source of phenylalanine and so should be used with caution in patients with phenylketonuria.

The sucrose content of ZINNAT suspension should be taken into account when treating diabetic patients, and appropriate advice provided.

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.

INTERACTIONS:

Cefuroxime axetil may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

Concomitant use of ZINNAT and furosemide should be avoided when possible, and the combined use of cephalosporins and aminoglycosides should be undertaken with caution. (Refer to Special Precautions).

ZINNAT must not be administered simultaneously with other medicines.

Cefuroxime does not interfere in enzyme-based tests for glucosuria. Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. However, this should not lead to false-positive results. Cefuroxime may cause false-negative reactions in the ferricyanide test. ZINNAT can cause a falsely high reading in the alkaline picrate assay for

creatinine, although the degree of elevation is unlikely to be of clinical importance. It is possible that cefuroxime may also interfere with this determination.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Adults:

Sinusitis:	250 mg twice daily
Acute and chronic bronchitis:	250 mg twice daily
Acute uncomplicated cystitis:	125 mg twice daily
Lyme disease:	500 mg twice daily for 20 days.

Children:

Usual dose - 125 mg twice daily.

For otitis media in children less than 2 years of age the usual dose is 125 mg twice daily and in children over 2 years of age 250 mg twice daily.

For Lyme disease in children over the age of 12 years the usual dose is 500 mg twice daily for 20 days.

There is no experience in children under the age of 3 months.

Because of the bitter taste of cefuroxime axetil, ZINNAT tablets should not be crushed.

The usual course of therapy is seven days (range 5-10 days).

Note: Cefuroxime axetil should be taken half an hour after food for optimum absorption.

Directions for use of suspension:

1. Shake the bottle to loosen the granules and remove the cap.
2. Fill the measuring cup with water to the line (20 ml of water for 50 ml pack and 37 ml of water for the 100 ml pack).
3. Add the water to the bottle all at once and replace the cap.

4. Invert the bottle and rock the bottle vigorously until the sound of the granules in the container disappears.
5. Turn the bottle into an upright position and shake vigorously.
6. Once mixed with the correct amount of water, ZINNAT suspension must be immediately stored in the fridge between 2 °C and 8 °C. Throw away the bottle 10 days after first opening it.

Patient Instructions:

Shake the bottle vigorously until the suspension can be heard moving in the bottle before each dose is withdrawn.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side effects:

Clinical Trial data:

The following convention has been used for the classification of frequency: very common ≥1/10, common ≥1/100 to <1/10, uncommon ≥1/1 000 to <1/100, rare ≥1/10 000 to <1/1 000, very rare <1/10 000.

Infections and infestations:

Common: candida overgrowth.

Blood and lymphatic system disorders:

Common: eosinophilia

Uncommon: positive Coombs' test, thrombocytopenia, leucopenia (sometimes profound)

Immune system disorders:

Hypersensitivity reactions including:

Uncommon: skin rashes

Nervous system disorders:

Common: headache, dizziness

Gastrointestinal disorders:

Common: diarrhoea, nausea, abdominal pain

Uncommon: vomiting

Hepatobiliary disorders:

Common: increases of hepatic enzyme levels, [alanine aminotransferase, (serum glutamic pyruvic acid transaminase), aspartate aminotransferase (serum glutamic oxaloacetic transaminase), and LDH].

Side effects reported from post-marketing spontaneous reports:

Blood and lymphatic system disorders:

Haemolytic anaemia.

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

Immune system disorders:

Urticaria, pruritus, drug fever, serum sickness, anaphylaxis.

Gastrointestinal disorders:

Pseudomenbranous colitis.

Hepatobiliary disorders:

Jaundice (predominantly cholestatic), hepatitis.

Skin and subcutaneous tissue disorders:

Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (exanthematic necrolysis) (see also Immune system disorders).

Special Precautions:

Patients who experience anaphylactoid reactions to penicillins may experience a similar reaction when cephalosporins (such as cefuroxime) are administered. Should anaphylaxis occur, ZINNAT should be discontinued and the patient treated with the usual agents (corticosteroids and antihistamines).

Use of ZINNAT may result in the overgrowth of candida. Prolonged use may also result in the overgrowth of other non-susceptible organisms (e.g. Enterococci and *Clostridium difficile*), which may require discontinuation 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 ZINNAT 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.

It is recommended that either glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving ZINNAT. ZINNAT does not interfere in the alkaline picrate assay for creatinine.

Serum levels of cefuroxime are reduced by dialysis.

ZINNAT Suspension contains aspartame, which is a source of phenylalanine and so should be used with caution in patients with phenylketonuria.

Effects on ability to drive and use machines:

As ZINNAT may cause dizziness, patients should be warned to be cautious when driving or operating machinery.

KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT:

See SIDE EFFECTS AND SPECIAL PRECAUTIONS.

Treatment is symptomatic and supportive.

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

IDENTIFICATION:

ZINNAT TABLETS 125 mg:	White to off-white film-coated, capsule-shaped tablets, engraved ‘GXES5’ on one side and plain on the other.
ZINNAT TABLETS 250 mg:	White to off-white film-coated, capsule-shaped tablets, engraved ‘GXES7’ on one side and plain on the other.

ZINNAT TABLETS 500 mg:	White to off-white film-coated, capsule-shaped tablets, engraved ‘GXEG2’ on one side and plain on the other.
ZINNAT SUSPENSION 125 mg:	White to off-white free-flowing granules for preparing a suspension, producing a white to pale yellow suspension on reconstitution.

PRESENTATION:

All strengths of ZINNAT tablets are supplied in foil strips or double foil blister packs of 10 tablets.

ZINNAT Suspension 125 mg: Granules for reconstitution are supplied in bottles of 50 ml and 100 ml. A 5 ml dosing spoon and measuring cup are provided in the carton.

STORAGE INSTRUCTIONS:

ZINNAT tablets should be stored at or below 30 °C.

ZINNAT Suspension 125 mg:

The granules (unconstituted suspension) must be stored at or below 30 °C.

The reconstituted suspension can be kept for up to 10 days when refrigerated immediately between 2 °C and 8 °C.

Keep out of reach of children.

REGISTRATION NUMBER:

ZINNAT TABLETS 125 mg:	V/20.1.1/362
ZINNAT TABLETS 250 mg:	V/20.1.1/363
ZINNAT TABLETS 500 mg:	V/20.1.1/364
ZINNAT SUSPENSION 125 mg:	Z/20.1.1/148

NAME AND BUSINESS ADDRESS OF THE HOLDER OF CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460.

DATE OF PUBLICATION OF THE PACKAGE INSERT:

Registration date:

ZINNAT TABLETS 125 mg: 25 September 1989

ZINNAT TABLETS 250 mg: 25 September 1989

ZINNAT TABLETS 500 mg: 25 September 1989

ZINNAT SUSPENSION 125 mg: 10 August 1993

Revision approval date:

1 March 2013

GDS023

Botswana:
Zinnat 250 mg Tablet - Reg No B9304175 S2
Zinnat 500 mg Tablet - Reg No B9304180 S2
Zinnat 125 mg/5 ml Suspension - Reg No BOT0200518 S2

Namibia:
Zinnat 125 mg Tablet - Reg No 90/20.1.1/00598 NS2
Zinnat 250 mg Tablet - Reg No 90/20.1.1/00599 NS2
Zinnat 500 mg Tablet - Reg No 90/20.1.1/00600 NS2
Zinnat 125 mg/5 ml Suspension - Reg No 04/20.1.1/0915 NS2

Zimbabwe:
Zinnat 250 mg Tablet - Reg No 88/7.2.2/2192 PP
Zinnat 500 mg Tablet – Reg No 88/7.2.2/2191 PP
Zinnat 125 mg/5 ml Suspension – Reg No 92/7.2.2/2576 PP