National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

[Instructions in this font/colour are from the World Health Organisation Public Assessment Report WHOPAR guidelines.]

[Additional instructions and examples]
{<example text>}

1. NAME OF THE MEDICINAL PRODUCT

{(ZADIP) Ampicillin 250 mg & Cloxacillin 250 mg Capsule}

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[API and strength:
Each hard gelatin capsule contains:
Ampicillin Trihydrate BP Eq. to Ampicillin 250 mg
Cloxacillin Sodium BP Eq. to Cloxacillin 250 mg
Excipients Q.S.]

3. PHARMACEUTICAL FORM

[Includeadescriptionofthevisualappearanceoftheproductpharmaceuticalformasmarketed,including information on pH and osmolarity asrequired.

[e.g.: Black/Purple Color size '0' capsule printed on cap 'ZADIP' & '500' on body containing white color powder.]

<The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.>

<The capsule can be divided into equal halves.>

<The capsule should not be divided.>

[Product scoring may be recommended or required when a WHO Prequalified product is scored, or scoring is specified for an innovator or comparator product(s), or when division into fractional doses may be necessary according to recommended posology.

4. Clinical particulars

ZADIP is indicated for the treatment of the following infections including mixed Grampositive (except methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococcus (MRCoNS)) and Gram-negative infections:

Surgery: post-operative wound infections, post-operative pulmonary infections.

2 Respiratory infections: bronchopneumonia, acute exacerbations of chronic bronchitis.

Obstetrics: puerperal fever.

Other infections such as septicaemia, bone infections e.g., osteomyelitis, ear, nose and throat infections.

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to ZADIP. Where treatment is initiated before results are available expert advice should be sought when the local prevalence of resistance is such that the utility of ZADIP is questionable (see Pharmacological properties, Pharmacodynamics).

ZADIP neonatal oral drops are indicated for the prophylaxis or treatment of bacterial infections in premature babies or neonates , caused by known susceptibile strains of bacteria

4.1 Therapeutic indications

Product Name: Zadip Ampicillin 250 mg & Cloxacillin 250 mg Capsule

Adults and elderly: Ampicillin 250 mg and cloxacillin 250 mg 1 capsule 4 time daily. If severe infection, the dose can be increased up to 12 capsule daily.

Children: Per dose contain Ampicillin 125 mg and cloxacillin 125 mg: 1 dose 4 time daily.

Neonates to 2 years: 0.6mL (90mg) of reconstituted suspension every 4 hours. Administer 0/5 to 1 hour prior to feeding

4.2 Posology and method of administration

Posology

Pediatric population

<No data are available.>

Method of administration

4.3 Contraindications

The following statements reflect the information available on the adverse reaction profile of the individual constituents (ampicillin and cloxacillin) and/or the combination in ZADIP. The majority of the adverse reactions listed below are not unique to ampicillin - cloxacillin and may occur when using other penicillins.

4.4 Special warnings and precautions for use

4.5 Interaction with other medicinal products and other forms of interaction

<No interaction studies have been performed.>

<Interaction studies have only been performed in adults.>

4.6 Pregnancy and Lactation

Adequate human data on use during pregnancy are not available. However, animal studies have not identified any risk to pregnancy or embryo-foetal development.

Adequate human and animal data on use during lactation are not available

[See prequalification guidance: Section Guidance for Part 4 — Summary of Product Characteristics (SmPC) — Of a WHO Public Assessment Report (WHOPAR).*]*

4.7 Effects on ability to drive and use machines

No Study

4.8 Undesirable effects

[See prequalification guidance: Section Guidance for Part 4 — Summary of Product Characteristics (SmPC) — Of a WHO Public Assessment Report (WHOPAR).*]*

<Pediatric population>

4.9 Overdose

Overdosage with oral ZADIP is unlikely to cause serious reactions if renal function is normal. Very high dosage of i.v. administered ampicillin and/or high dosage of cloxacillin in renal failure may provoke neurotoxic reactions similar to those seen with benzylpenicillin in excess.

Gastrointestinal effects such as nausea, vomiting, and diarrhoea may be evident. These symptoms should be treated symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Mechanism of action:

Both Ampicillin and Cloxacillin are bacterial agents.

They act by interfering with synthesis of the peptidoglycan layer of the cell wall, which normally protects the bacterium from its environment. Defective wall synthesis renders the cell incapable of withstanding the osmotic gradient between the cell and its environment so that it swells and explodes.

Synergy has been demonstrated between Ampicillin and Cloxacillin against some beta lactamase producing organisms.

Pharmacodynamic effects:

ZADIP is a combination of ampicillin and cloxacillin. Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal betalactamases. Ampicillin is a broad-spectrum antibiotic of the aminopenicillin group; it is not resistant to beta-lactamases.

Both ampicillin and cloxacillin are bactericidal antibiotics and act by interfering with the formation of new bacterial cell wall by dividing organisms.

The prevalence of acquired resistance is geographically variable and for select species may be very high. Local information on resistance is desirable, particularly when

treating severe infections.

ZADIP susceptibility rates are higher than ampicillin rates due to the cloxacillin activity against β-lactamase producing staphylococci. Methicillin-susceptible Staphylococcus aureus (MSSA) and methicillin-susceptible coagulase-negative staphylococcus (MSCoNS) are commonly susceptible to ZADIP. MRSA and MRCoNS are resistant to ZADIP. For all other indicated bacterial species, the susceptibility of ZADIP is similar to ampicillin including limited activity against Gram-negative organisms.

Clinical efficacy and safety

Resistance

Pediatric population

5.2 Pharmacokinetic properties

Absorption and Bioavailability

Both ampicillin and cloxacillin are stable in the gastric environment resulting in good absorption. Neither component of the combination of ampicillin and cloxacillin interferes with the absorption or excretion of the other.

The total quantity absorbed by the oral route represents 50% (cloxacillin) and 40% (ampicillin) of the quantity administered.

The presence of food in the stomach may depress oral absorption and ZADIP should therefore be taken 0.5 to 1 hour before meals.

Distribution

ZADIP diffuses well into most tissues and body fluids including, among others, bronchial secretions, sinuses, saliva, cerebrospinal fluid (variable percentage depending on the degree of meningeal inflammation), bile, serous membranes and middle ear.

Crossing the meningeal barrier: ZADIP diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.

Crossing into breast milk: ZADIP is excreted in small quantities in breast milk.

Plasma half-life for cloxacillin is 0.5 to 1 hour and 1 to 1.5 hour for ampicillin.

Protein binding: the serum protein binding proportion is approximately 94% for cloxacillin and 18% for ampicillin.

Metabolism

In normal subjects approximately 20% (cloxacillin) and 40% (ampicillin) of the dose administered is metabolised.

Elimination

ZADIP is eliminated mainly through the kidney. Approximately 30% of the dose administered orally and over 60% of the ampicillin dose administered parenterally is eliminated in active form in the urine within 24 hours. The equivalent percentages for cloxacillin are approximately 20% and 30% respectively. A small proportion (10%) of the dose administered is excreted in bile.

Special Population

5.3 Preclinical safety data

<Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.>

<Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>

<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:>

<Mutagenicity and Carcinogenicity>

<Reproductive toxicology>

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Megnesium Stearete BP

Talcum BP

[List all excipients **except solvents removed during processing**.]

Iso Propyl alcohol

Methylene Di Chloride

Black Color Cap And Purple color body "0" size capsule

6.2 Incompatibilities

<Not applicable.>

6.3 Shelf life

3 years

6.4 Special precautions for storage

Ampicillin - cloxacillin should be stored in a dry place below 25°C.

Do not use after expiry date.

All medicines should be kept out of reach of children.

Reconstitution of ampicillin - cloxacillin injections and preparation of ampicillin - cloxacillin infusion solutions must be carried out under appropriate aseptic conditions if extended storage periods are required.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

[All pack sizes must be listed. If applicable, add:]

<Not all pack sizes may be marketed.>

[The container/closure description should include all parts of the primary packaging including desiccant, void filler or adsorbent cotton filler and dosing device(s) if relevant. Dimensions/volume/capacity may be listed. Shape and colour of the bottle and the cap type (including plastic e.g. PP), should be stated.

[Printed Foil, PVC Clear, Leaflet, Printed Carton having 10× 10 Capsule]

[For blisters in cartons where the carton is necessary for light protection, the carton is an important aspect of the package description.]

<Not all pack sizes may be marketed.>

6.6 Special precautions for disposal <and other handling>

[Include practical instructions for preparation and handling of the product including disposal of the medicinal product, and waste materials derived from the used medicinal product.]

<No special requirements.>

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

7. <APPLICANT/MANUFACTURER>

{Name and address}

Imported by:

ZADIP PHARMA NIG. LTD.

68 B, Coker road, llupeju, Lagos.

Zadip.pharma@gmail.com

Exported by:

ATHENA PHARMA PVT. LTD.

620, Prestige Indl. Estate.

Bawdi cross Lane, Off. Marve Road,

Malad (West), Mumbai-400064, India.

Manufacturer By:

Brusseles Laboratories Pvt. Ltd.

33, Changodar Industrial Estate, Sarkhej- Bavla Road,

Changodar: 382210, Ahmedabad, Gujrat, India.