Summary of Product Characteristics for Pharmaceutical Products

1 Name of the medicinal product
Cefroxym 500 Tablets.

2. Qualitative and quantitative composition:
Each film coated tablet contains:
Cefuroxime Axetil USP
Eq. to Cefuroxime .....500mg.

For full list of excipients, see section 6.1.

3. Pharmaceutical form
Tablet.

4. Clinical particulars

4.1 Therapeutic indications
Cefuroxime Axetil is indicated for the treatment of the following infections in adults and children from the age of 3 months: Acute streptococcal tonsillitis and pharyngitis, Acute bacterial sinusitis, Acute otitis media, Acute exacerbations of chronic bronchitis, Cystitis, Pyelonephritis, Uncomplicated skin and soft tissue infections, Treatment of early Lyme disease.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.
4.2 Posology and method of administration:
The usual course of therapy is seven days (may range from five to ten days) given orally. Cefuroxime Axetil tablets should be taken after food for optimum absorption.
Adults and children(≥40kg) - Indicated dosage to be given twice daily Acute tonsillitis and pharyngitis, acute bacterial sinutis-250mg;
Acute otitis media-500mg; **Acute exacerbations of chronic bronchitis**-250mg;
Cystitis-250mg; **Pyelonephritis-250mg; Uncomplicated skin and soft tissue infections-**250mg; **Lyme disease**-500mg (twice Daily for 10 to 21 days).
Children(<40kg) –Indicated dosage to be given twice daily
Acute tonsillitis and pharyngitis, acute bacterial sinusitis-10mg/kg to a maximum of 125mg B.D; **Children aged two years or older with otitis media or where appropriate, with more severe infections-**15mg/kg to a maximum of 250mg B.D**;**
Cystitis-15mg/kg to a maximum of 250mg B.D;**Pyelonephritis-**15mg/kg to a maximum of 250mg
B.D for10 to 14 days; **uncomplicated skin and soft tissue infections**-15mg/kg to a maximum of 250mg B.D; **Lyme disease**-15 mg/kg to a

maximum of 250mg B.D for 14 days (10 to 21 days). There is no experience of using Cefuroxime Axetil in children under the age of 3 months.
Renal impairment: Safety and efficacy in patients with renal failure have not been established. Cefuroxime is primarily excreted by the kidneys. In patients with markedly impaired renal function it is recommended that the dosage should be reduced to compensate for its slower excretion. Cefuroxime is effectively removed by dialysis.
Hepatic impairment: There are no data available for patients with hepatic impairment. Hepatic dysfunctions expected to have no effect on the pharmacokinetics of cefuroxime.

4.3 Contraindications:
Hypersensitivity to the active substance or to any of the excipients; Patients with known hypersensitivity to cephalosporin antibiotics; History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of betalactam antibacterial agent (penicillins, monobactams and carbapenems).

4.4 Special warnings and precautions for use:
Hypersensitivity reactions; special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactam antibiotics because there is a risk of cross-sensitivity. Serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment must be discontinued immediately and adequate emergency measures must be intiated.Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions of cefuroxime, to other cephalosporins or to any other type of beta-lactam agent.

Severe cutaneous adverse reactions (SCARS)
Severe cutaneous adverse reactions including: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with cefuroxime treatment (see section 4.8).
At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, cefuroxime should be withdrawn immediately and an alternative treatment considered. If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of cefuroxime, treatment with cefuroxime must not be restarted in this patient at any time.

Jarisch-Herxheimer reaction: This has been seen following cefuroxime Axetil treatment of Lyme disease and is usually self-limiting.
Overgrowth of non-susceptible microorganisms: Use of cefuroxime Axetil may result in the overgrowth of Candida and in the overgrowth of other non-susceptible microorganisms which may require interruption of treatment.
Pseudomembranous colitis has been reported and may range in severity

from mild to life threatening. Discontinuation of therapy and the administration of specific treatment for Clostridium difficile should be considered. Medicinal products that inhibit peristalsis should not be given.

Overgrowth of non-susceptible microorganisms

As with other antibiotics, use of cefuroxime axetil may result in the overgrowth of Candida. Prolonged use may also result in the overgrowth of other non-susceptible microorganisms (e.g. enterococci and *Clostridium difficile*), which may require interruption of treatment (see section 4.8).

Antibacterial agent–associated pseudomembranous colitis have been reported with nearly all antibacterial agents, including cefuroxime and may range in severity from mild to life threatening. This diagnosis should be considered in patients with diarrhoea during or subsequent to the administration of cefuroxime (see section 4.8). Discontinuation of therapy with cefuroxime and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given (see section 4.8).

Interference with diagnostic tests: The development of a positive Combo's Test associated with the use of cefuroxime may interfere with cross matching of blood. 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.

4.5 Interaction with other medicinal products and other forms of interaction:

- Drugs which reduce gastric acidity may result in a lower biovailability of cefuroxime Axetil compared with that of the fasting state and tend to cancel the effect of enhanced absorption after food. Concomitant use of probenecid is not recommended as it significantly increase the peak concentration time curve and elimination half-life. Concomitant use with oral anticoagulants may give rise to increased INR.

4.6 Fertility, Pregnancy and lactation:

Pregnancy:

There are limited data from the use in pregnant women. Studies in animals have shown no harmful effects on pregnancy, embryonal or foetal development, parturition or postnatal development. Cefuroxime Axetil should be prescribed to pregnant women only if the benefit outweighs the risk.

Breastfeeding: Cefuroxime is excreted in human milk in small quantities and should only be used during breastfeeding after benefit/risk assessment by the physician.

4.7 Effects on ability to drive and use machines
No effects have been observed.

4.8 Undesirable effects:
The most common adverse reactions are Candida overgrowth, eosinophilia, headache, dizziness, gastrointestinal disturbances and transient rise in liver enzymes. Uncommon adverse reactions, include positive Coomb's test, thrombocytopenia, leukopenia (sometimes profound), vomiting, skin rashes.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose
Overdose can lead to neurological sequelae e.g. encephalopathy, convulsions and coma. Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal dialysis.

5. Pharmacological properties
5.1 Pharmacodynamic properties.
Pharmacotherapeutic group: Antibacterials for systemic use, second-generation cephalosporins, **ATC-Code: J01DC02**.
Mechanism of action: Cefuroxime Axetil undergoes hydrolysis by esterase enzymes to the active antibiotic cefuroxime. Cefuroxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, leading to bacterial cell lysis and death.
Microbiological susceptibility: Cefuroxime is usually active against the following microorganism in vitro.
Commonly susceptible species: Gram-positive aerobes: Staphylococcus aureus(methicillin-susceptible) *, Coagulase negative staphylococcus (methicillin susceptible), streptococcus pyogenes, Streptococcus agalactiae: **Gram-negative aerobes**: Haemophilus influenza, Haemophilus parainfluenzae, Moraxella catarrhalis: Haemophilus influenza, Haemophilus parainfluenzae, Moraxella catarrhalis; Spirochaetes: Borrelia burgorferi.
Microorganisms for which acquired resistance may be a problem:
Gram-positive aerobes: Streptococcus pneumoniae; *Gram-negative aerobes: Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Klebsiella pneumonia, Proteus mirabillis, Proteus spp. (other than P.vulgaris), Providencia spp.: Gram-positive anaerobes: Peptostreptococcus spp., Propionibacterium spp.; Gram-negative anaerobes: Fusobacterium spp., Bacteroides spp.*
Inherently resistant microorganisms: *Gram-positive aerobes: Enterococcus faecalis, Enterococcus faecium, Gram-negative aerobes: Acinetobacter spp., Campylobacter spp., Morganella morganii, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens: Gram-negative anaerobes: Bacteroides fragitis; others: Chlamydia spp., Mycoplasma spp.,*

Legionella spp.
*all methicillin-resistant aureus are resistant to cefuroxime.

5.2 Pharmacokinetic properties

Absorption: After oral administration cefuroxime Axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood to release cefuroxime into the circulation. Optimum absorption occurs when it is administered shortly after meal. Following administration of cefuroxime Axetil tablets peak serum levels occur approximately 2.4 hours after dosing when taken with food. Pharmacokinetics is linear over the oral dosage range of 125 to 1000mg.No accumulation occurred following repeat oral doses of 250 to 500mg.

Distribution: Protein binding has been stated as 33 to 50% depending on the methodology. Following a single dose of cefuroxime Axetil 500mg tablet to 12 healthy volunteers, the apparent volume of distribution was 50L (CV%=28%). Concentrations in excess of the minimum inhibitory levels for common pathogens can be achieved in the tonsilla, sinus tissues, bronchial mucosa, bone, pleural fluid, joint fluid, synovial fluid, interstitial fluid, bile, sputum and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

Biotransformation:

Cefuroxime is not metabolised.

Elimination: The serum half-life is between 1 and 1.5 hours. Excretion is by glomerular filtration and tubular secretion .Renal clearance is 125 to 148ml/min/1.73m^2.

5.3 Preclinical safety data

There is no preclinical data of relevance for the safety-judgment beyond what has already been considered in the Summary of Product Characteristics.

6.PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium, Sodium Starch Glycolate, Sodium lauryl sulphate, Aerosil 200 pharma, Microcrystalline cellulose pH 102, Magnesium stearate, Hydroxypropyl methylcellulose (5CPS), Titanium dioxide, Ethyl cellulose, Diethyl phthalate, Isopropyl alcohol & Methylene chloride.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below
30°C.
Protected from
light.
Keep all medicine out of reach of children.

6.5 Nature and contents of the container:

1X10's Alu-Alu blister packs contained in a unit box along with literature insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Company name: Laboratory & Allied
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8. Marketing Authorization Number

H2021/CTD8724/18990

9. Date of first authorization/renewal of the authorization

September 22, 2021

10. Date of revision of the text

November 2020