1.3.1
Summary Of Product Characteristics (SPC)

1.17.1.1 Product information for health professionals

1. NAME OF THE MEDICINAL PRODUCT

1.1 Invented Name of the Medicinal Product

G-ROXIM INJECTION

Cefuroxime for Injection USP 750mg

1.2 Strength

Cefuroxime Sodium 750 mg

1.3 Pharmaceutical Form

Powder for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION Each Vial Contains:

Cefuroxime sodium USP

Equivalent to Cefuroxime ……..…750 mg.

Each ampoule contains:

Sterilised water for injections BP 10ml.

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Powder for Injection

A white or faintly yellow powder filled in clear glass vial, sealed with grey colored butyl rubber stopper and colored flip off seal.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime for Injection USP 750 mg is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. Lower Respiratory Tract Infections, including pneumonia, caused by Streptococcus pneumoniae, Haemophilus influenzae (including ampicillin-resistant strains), Klebsiella spp., Staphylococcus aureus (penicillinase- and non–penicillinase-producing strains), Streptococcus pyogenes, and Escherichia coli.
2. Urinary Tract Infections caused by Escherichia coli and Klebsiella spp.
3. Skin and Skin-Structure Infections caused by Staphylococcus aureus (penicillinase- and non–penicillinase-producing strains), Streptococcus pyogenes, Escherichia coli, Klebsiella spp., and Enterobacter spp.
4. Septicemia caused by Staphylococcus aureus (penicillinase- and non–penicillinase-producing strains), Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae (including ampicillin-resistant strains), and Klebsiella spp.
5. Meningitis caused by Streptococcus pneumoniae, Haemophilus influenzae (including ampicillin resistant strains), Neisseria meningitidis, and Staphylococcus aureus (penicillinase- and non–penicillinase-producing strains).
6. Gonorrhoeae: Uncomplicated and disseminated gonococcal infections due to Neisseria gonorrhoeae (penicillinase- and non–penicillinase-producing strains) in both males and females.
7. Bone and Joint Infections caused by Staphylococcus aureus (penicillinase- and non–penicillinase producing strains).

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Method of administration: Intravenous or Intramuscular.

After constitution, Cefuroxime for Injection may be given intravenously or by deep IM injection into a large muscle mass (such as the gluteus or lateral part of the thigh). Before injecting intramuscularly, aspiration is necessary to avoid inadvertent injection into a blood vessel.

Intravenous Administration:

The IV route may be preferable for patients with bacterial septicemia or other severe or life-threatening infections or for patients who may be poor risks because of lowered resistance, particularly if shock is present or impending.

For direct intermittent IV administration, slowly inject the solution into a vein over a period of 3 to 5 minutes or give it through the tubing system by which the patient is also receiving other IV solutions.

For direct intermittent IV infusion with a Y-type administration set, dosing can be accomplished through the tubing system by which the patient may be receiving other IV solutions. However, during infusion of the solution containing Cefuroxime for Injection, it is advisable to temporarily discontinue administration of any other solutions at the same site.

For continuous IV infusion, a solution of Cefuroxime for Injection may be added to an IV infusion pack containing one of the following fluids: 0.9% Sodium Chloride Injection; 5% Dextrose Injection; 10% Dextrose Injection; 5% Dextrose and 0.9% Sodium Chloride Injection; 5% Dextrose and 0.45% Sodium Chloride Injection; or 1/6 M Sodium Lactate Injection.

Solutions of Cefuroxime for Injection, like those of most beta-lactam antibiotics, should not be added to solutions of aminoglycoside antibiotics because of potential interaction.

However, if concurrent therapy with Cefuroxime for Injection and an aminoglycoside is indicated, each of these antibiotics can be administered separately to the same patient.

Caution:

Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.

Preparation for Administration:

1. Suspend container from eyelet support.
2. Remove protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.

Posology:

Adults:

The usual adult dosage range for Cefuroxime for Injection is 750 mg to 1.5 grams every 8 hours, usually for 5 to 10 days. In uncomplicated urinary tract infections, skin and skin-structure infections, disseminated gonococcal infections, and uncomplicated pneumonia, a 750 mg dose every 8 hours is recommended. In severe or complicated infections, a 1.5 gram dose every 8 hours is recommended. In bone and joint infections, a 1.5-gram dose every 8 hours is recommended. In clinical trials, surgical intervention was performed when indicated as an adjunct to therapy with Cefuroxime for Injection. A course of oral antibiotics was administered when appropriate following the completion of parenteral administration of Cefuroxime for Injection.

In life-threatening infections or infections due to less susceptible organisms, 1.5 grams every 6 hours may be required. In bacterial meningitis, the dosage should not exceed 3 grams every 8 hours. The recommended dosage for uncomplicated gonococcal infection is 1.5 grams given intramuscularly as a single dose at 2 different sites together with 1 gram of oral probenecid. For preventive use for clean-contaminated or potentially contaminated surgical procedures, a 1.5- gram dose administered intravenously just before surgery (approximately one-half to 1 hour before the initial incision) is recommended. Thereafter, give 750 mg intravenously or intramuscularly every 8 hours when the procedure is prolonged. For preventive use during open heart surgery, a 1.5 gram dose administered intravenously at the induction of anesthesia and every 12 hours thereafter for a total of 6 grams is recommended.

Impaired Renal Function:

A reduced dosage must be employed when renal function is impaired. Dosage should be determined by the degree of renal impairment and the susceptibility of the causative organism (see Table 1).

Table 1. Dosage of Cefuroxime for Injection in Adults with Reduced Renal Function

Creatinine Clearance (mL/min)	Dose	Frequency
> 20	750 mg - 1.5 grams	q8h
10-20	750 mg	q12h
< 10	750 mg	q24h*

* Since Cefuroxime for Injection is dialyzable, patients on hemodialysis should be given a further dose at the end of the dialysis.

When only serum creatinine is available, the following formula4 (based on sex, weight, and age of the patient) may be used to convert this value into creatinine clearance. The serum creatinine should represent a steady state of renal function.

Males: Creatinine clearance (mL/min) =	Weight (kg) x (140 - age) ---------- 72 x serum creatinine (mg/dL)

Females: 0.85 x male value

NOTE: As with antibiotic therapy in general, administration of Cefuroxime for Injection should be continued for a minimum of 48 to 72 hours after the patient becomes asymptomatic or after evidence of bacterial eradication has been obtained; a minimum of 10 days of treatment is recommended in infections caused by Streptococcus pyogenes in order to guard against the risk of rheumatic fever or glomerulonephritis; frequent bacteriologic and clinical appraisal is necessary during therapy of chronic urinary tract infection and may be required for several months after therapy has been completed; persistent infections may require treatment for several weeks; and doses smaller than those indicated above should not be used. In staphylococcal and other infections involving a collection of pus, surgical drainage should be carried out where indicated.

Pediatric Patients Above 3 Months of Age:

Administration of 50 to 100 mg/kg/day in equally divided doses every 6 to 8 hours has been successful for most infections susceptible to cefuroxime. The higher dosage of 100 mg/kg/day (not to exceed the maximum adult dosage) should be used for the more severe or serious infections.

In bone and joint infections, 150 mg/kg/day (not to exceed the maximum adult dosage) is recommended in equally divided doses every 8 hours. In clinical trials, a course of oral antibiotics was administered to pediatric patients following the completion of parenteral administration of Cefuroxime for Injection.

In cases of bacterial meningitis, a larger dosage of Cefuroxime for Injection is recommended, 200 to 240 mg/kg/day intravenously in divided doses every 6 to 8 hours.

In pediatric patients with renal insufficiency, the frequency of dosing should be modified consistent with the recommendations for adults.

Preparation of Solution and Suspension:

The directions for preparing Cefuroxime for Injection for IV and IM use are summarized in the below table.

For Intramuscular Use:

Each 750-mg vial of Cefuroxime for Injection should be constituted with 3 mL of Sterile Water for Injection. Shake gently to disperse and withdraw completely the resulting suspension for injection.

For Intravenous Use:

Each 750-mg vial should be constituted with 8.3 mL of Sterile Water for Injection. Withdraw completely the resulting solution for injection.

Preparation of Solution

Strength	**Amount of Diluent to be Added (mL)**	**Volume to be Withdrawn**	**Approximate Cefuroxime Concentration (mg/mL)**
750-mg Vial	3 (IM)	Total*	225
750-mg Vial	8.3 (IV)	Total	90

*Note: Cefuroxime for Injection is a suspension at IM concentrations.

4.3 CONTRAINDICATIONS

Cefuroxime for Injection is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

4.4 WARNING AND PRECAUTIONS

Warnings

Before therapy with cefuroxime for injection is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. This product should be given cautiously to penicillin-sensitive patients. Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to cefuroxime for injection occurs, discontinue the drug. Serious acute hypersensitivity reactions may require epinephrine and other emergency measures.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefuroxime for Injection, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

When the colitis is not relieved by drug discontinuation or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by Clostridium difficile. Other causes of colitis should also be considered.

Precautions

General:

Although Cefuroxime for Injection rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of Cefuroxime for Injection should be reduced in patients with transient or persistent renal insufficiency, because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of Cefuroxime for Injection may result in overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins.

As with other therapeutic regimens used in the treatment of meningitis, mild-to-moderate hearing loss has been reported in a few pediatric patients treated with cefuroxime. Persistence of positive CSF (cerebrospinal fluid) cultures at 18 to 36 hours has also been noted with cefuroxime injection, as well as with other antibiotic therapies; however, the clinical relevance of this is unknown.

Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous Vitamin K administered as indicated.

Prescribing Cefuroxime for Injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients:

Patients should be counseled that antibacterial drugs, including Cefuroxime for Injection, should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefuroxime for Injection is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may:

1. Decrease the effectiveness of the immediate treatment and,
2. Increase the likelihood that bacteria will develop resistance and will not be treatable by Cefuroxime for Injection or other antibacterial drugs in the future. Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

In common with other antibiotics, cefuroxime may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined estrogen/ progesterone oral contraceptives.

4.6 PREGNANCY AND LACTATION

PREGNANCY:

Teratogenic Effects:

Pregnancy Category B. Reproduction studies have been performed in mice at doses up to 6,400 mg/kg/day (6.3 times the recommended maximum human dose based on mg/m2) and rabbits at doses up to 400 mg/kg/day (2.1 times the recommended maximum human dose based on mg/m2) and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

LACTATION:

Since cefuroxime is excreted in human milk, caution should be exercised when Cefuroxime for Injection is administered to a nursing woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects of cefuroxime on the ability to drive and use machines have been performed. However, based on known adverse reactions, cefuroxime is unlikely to have an effect on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS

Cefuroxime for Injection is generally well-tolerated. The most common adverse effects have been local reactions following IV administration. Other adverse reactions have been encountered only rarely.

Local Reactions:

Thrombophlebitis has occurred with IV administration in 1 in 60 patients.

Gastrointestinal:

Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). The onset of pseudomembranous colitis may occur during or after antibacterial treatment.

Hypersensitivity Reactions:

Hypersensitivity reactions have been reported in fewer than 1% of the patients treated with Cefuroxime for Injection and include rash (1 in 125). Pruritus, urticaria, and positive Coombs' test each occurred in fewer than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylaxis, drug fever, erythema multiforme, interstitial nephritis, toxic epidermal necrolysis, and Stevens-Johnson syndrome have occurred.

Blood:

A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (fewer than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence were seen with other cephalosporins used in controlled studies. As with other cephalosporins, there have been rare reports of thrombocytopenia.

Hepatic:

Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 50 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney:

Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

Postmarketing Experience with Cefuroxime for Injection:

In addition to the adverse events reported during clinical trials, the following events have been observed during clinical practice in patients treated with Cefuroxime for Injection and were reported spontaneously. Data are generally insufficient to allow an estimate of incidence or to establish causation.

Immune System Disorders:

Cutaneous vasculitis.

Neurologic:

Seizure.

Non-site specific:

Angioedema.

Cephalosporin-class Adverse Reactions:

In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions:

Vomiting, abdominal pain, colitis, vaginitis including vaginal candidiasis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage.

Several cephalosporins, including Cefuroxime for Injection, have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests:

Prolonged prothrombin time, pancytopenia, agranulocytosis.

4.9 OVERDOSE

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: cephalosporin antibiotic

ATC code: J01DC02.

Mechanism of action

Cefuroxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

Mechanisms of resistance

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- Hydrolysis by beta-lactamases including (but not limited to) extended-spectrum beta-lactamases (ESBLs), and Amp-C enzymes, that may be induced or stably de-repressed in certain aerobic Gram-negative bacterial species;
- Reduced affinity of penicillin-binding proteins for cefuroxime;
- Outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in Gram-negative bacteria;
- Bacterial efflux pumps.

Organisms that have acquired resistance to other injectable cephalosporins are expected to be resistant to cefuroxime. Depending on the mechanism of resistance, organisms with acquired resistance to penicillins may demonstrate reduced susceptibility or resistance to cefuroxime.

Cefuroxime sodium breakpoints

The Minimum inhibitory concentration (MIC) breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are as follows:

Microorganism	**Breakpoints (mg/L)**	
	S	R
Enterobacteriaceae [1]	<8[2]	>8
Staphylococcus spp.	Note[3]	Note[3]
Streptococcus A, B, C and G	Note[4]	Note[4]
Streptococcus pneumoniae	≤0.5	>1
Streptococcus (other)	≤0.5	>0.5
Haemophilus influenzae	≤1	>2
Moraxella catarrhalis	≤4	>8
Non-species related breakpoints[1]	≤4[5]	>8[5]

[1] The cephalosporin breakpoints for *Enterobacteriaceae* will detect all clinically important resistance mechanisms (including ESBL and plasmid mediated AmpC). Some strains that produce beta-lactamases are susceptible or intermediate to 3rd or 4th generation cephalosporins with these breakpoints and should be reported as found, i.e. the presence or absence of an ESBL does not in itself influence the categorisation of susceptibility. In many areas, ESBL detection and characterisation is recommended or mandatory for infection control purposes.

[2] Breakpoint relates to a dosage of 1.5 g × 3 and to *E. coli, P. mirabilis* and *Klebsiella spp* . only.

[3] Susceptibility of staphylococci to cephalosporins is inferred from the methicillin susceptibility except for ceftazidime and cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections.

[4] The beta-lactam susceptibility of beta-haemolytic streptococci groups A, B, C and G is inferred from the penicillin susceptibility.

[5] Breakpoints apply to daily intravenous dose of 750 mg × 3 and a high dose of at least 1.5 g ×

3. S=susceptible, R=resistant.

Microbiological susceptibility

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is therefore desirable, particularly when treating severe

infections. As necessary, expert advice should be sought when the local prevalence of resistance is known and the utility of the agent in at least some types of infections is questionable. Cefuroxime is usually active against the following microorganisms *in vitro*.

Commonly susceptible species
Gram-positive aerobes: *Staphylococcus aureus (methicillin-susceptible)* * *Streptococcus pyogenes* *Streptococcus agalactiae* *Streptococcus mitis* (viridans group)
Gram-negative aerobes: *Haemophilus influenzae* *Haemophilus parainfluenzae* *Moraxella catarrhalis*
Microorganisms for which acquired resistance may be a problem
Gram-positive aerobes: *Streptococcus pneumoniae*
Gram-negative aerobes: *Citrobacter freundii* *Enterobacter cloacae* *Enterobacter aerogenes* *Escherichia coli* *Klebsiella pneumoniae* *Proteus mirabilis* *Proteus* spp. (other than *P. vulgaris*) *Providencia* spp. *Salmonella* 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. *Morganella morganii* *Proteus vulgaris* *Pseudomonas aeruginosa* *Serratia marcescens*
Gram-positive anaerobes: *Clostridium difficile*
Gram-negative anaerobes: *Bacteroides fragilis*
Others: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.

* All methicillin-resistant *S. aureus* are resistant to cefuroxime.

In vitro the activities of cefuroxime sodium and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.

5.2 Pharmacokinetic properties

Absorption

After intramuscular (IM) injection of cefuroxime to normal volunteers, the mean peak serum concentrations ranged from 27 to 35 μg/mL for a 750 mg dose and from 33 to 40 μg/mL for a 1000 mg dose, and were achieved within 30 to 60 minutes after administration. Following intravenous (IV) doses of 750 and 1500 mg, serum concentrations were approximately 50 and 100 μg/mL, respectively, at 15 minutes.

AUC and C_{max} appear to increase linearly with increase in dose over the single dose range of 250 to 1000 mg following IM and IV administration. There was no evidence of accumulation of cefuroxime in the serum from normal volunteers following repeat intravenous administration of 1500 mg doses every 8 hours.

Distribution

Protein binding has been stated as 33 to 50%, depending on the methodology used. The average volume of distribution ranges from 9.3 to 15.8 L/1.73 m^2 following IM or IV administration over the dosage range of 250 to 1000 mg. Concentrations of cefuroxime 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 humour. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

Biotransformation

Cefuroxime is not metabolised.

Elimination

Cefuroxime is excreted by glomerular filtration and renal tubular secretion. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. There is an almost complete recovery (85 to 90%) of unchanged cefuroxime in urine within 24 hours of administration. The majority of the cefuroxime is excreted within the first 6 hours. The average renal clearance ranges from 114 to 170 mL/min/1.73 m^2 following IM or IV administration over the dosage range of 250 to 1000 mg.

Special patient populations

Gender

No differences in the pharmacokinetics of cefuroxime were observed between males and females following a single IV bolus injection of 1000 mg of cefuroxime as the sodium salt.

Elderly

Following IM or IV administration, the absorption, distribution and excretion of cefuroxime in elderly patients are similar to younger patients with equivalent renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in cefuroxime dose selection, and it may be useful to monitor renal function (see section 4.2).

Paediatrics

The serum half-life of cefuroxime has been shown to be substantially prolonged in neonates according to gestational age. However, in older infants (aged >3 weeks) and in children, the serum half-life of 60 to 90 minutes is similar to that observed in adults.

Renal impairment

Cefuroxime is primarily excreted by the kidneys. As with all such antibiotics, in patients with markedly impaired renal function (i.e. $C1_{cr}$ <20 mL/minute) it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion (see section 4.2). Cefuroxime is effectively removed by haemodialysis and peritoneal dialysis.

Hepatic impairment

Since cefuroxime is primarily eliminated by the kidney, hepatic dysfunction is not expected to have an effect on the pharmacokinetics of cefuroxime.

PK/PD relationship

For cephalosporins, the most important pharmacokinetic-pharmacodynamic index correlating with *in vivo* efficacy has been shown to be the percentage of the dosing interval (%T) that the unbound concentration remains above the minimum inhibitory concentration (MIC) of cefuroxime for individual target species (i.e. %T>MIC).

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 and toxicity to reproduction and development. No carcinogenicity studies have been performed; however, there is no evidence to suggest carcinogenic potential.

Gamma glutamyl transpeptidase activity in rat urine is inhibited by various cephalosporins, however the level of inhibition is less with cefuroxime. This may have significance in the interference in clinical laboratory tests in humans.

6. PHARMACEUTICAL

PARTICULARS 6.1 List of excipients

Not Applicable

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months from the date of manufacturing.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C.

Protect from light.

Keep all medicines out of reach of children.

6.5 Nature and contents of container

15 ml glass vial with 10 ml ampoule of SWFI.

6.6 Special precautions for disposal and other Special handling None

7. Marketed by:

GREENLIFE PHARMACEUTICAL

LIMITED No.2 Bank lane.Off town Planning

Way, Ilupeju, Lagos - Nigeria