# ZINACEF INJECTION

**SCHEDULING STATUS:**

S4

**PROPRIETARY NAME AND DOSAGE FORM:**

**ZINACEF 250 mg INJECTION** (Powder for Injection)

**ZINACEF 750 mg INJECTION** (Powder for Injection)

**ZINACEF 1,5 g INJECTION** (Powder for Injection)

**COMPOSITION:**

Vials containing 250 mg, 750 mg or 1,5 g cefuroxime as cefuroxime sodium.

Sugar-free.

**PHARMACOLOGICAL CLASSIFICATION:**

A 20.1.1. Antimicrobial agents. Broad and medium spectrum antibiotics.

**PHARMACOLOGICAL ACTION:**

Cefuroxime is a bactericidal semi-synthetic cephalosporin antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms. Peak serum levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. Concurrent administration of probenecid produces an elevated peak serum level and restricts the excretion of the antibiotic. There is almost complete recovery of unchanged cefuroxime in the urine within 24 hours of administration, the major part being eliminated in the first six hours. The tubular excretion component of renal clearance of cefuroxime is of the order of 50 %.

**INDICATIONS:**

Cefuroxime is indicated for the treatment of the following infections when caused by susceptible strains of the designated micro-organisms:

Respiratory tract infections.

Ear, nose and throat infections.

Urinary tract infections.

Soft tissue infections.

Obstetrics and gynaecological infections.

Gonorrhoea.

Prophylaxis against infection in abdominal, gynaecological, cardiac and pulmonary surgery where there is increased risk from infection.

**Bacteriology:**

Sensitivity tests should be carried out whenever possible.

Cefuroxime has activity against:

*Staphylococcus aureus* including penicillin-resistant strains but not the rare methicillin-resistant strains.

*Escherichia coli.*

*Klebsiella* spp.

*Enterobacter* spp.

*Streptococcus pyogenes.*

*Streptococcus viridians.*

*Clostridium* spp.

*Proteus mirabilis.*

*Proteus rettgeri.*

*Proteus vulgaris.*

*Proteus morganii.*

*Neisseria* spp - including β-lactamase producing strains of *N. gonorrhoeae.*

*Haemophilus influenzae.*

*Bacteroides fragilis.*

*Staphylococcus epidermidis.*

**CONTRA-INDICATIONS:**

Hypersensitivity to cephalosporin antibiotics.

**WARNINGS AND SPECIAL PRECAUTIONS:**

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

Prolonged use may result in the overgrowth of non-susceptible organisms. Patients developing frequent loose stools should be carefully monitored for the possible development of an antibiotic colitis.

Concomitant use of ZINACEF and furosemide should be avoided when possible. If they are used together renal function should be monitored closely as furosemide may enhance the nephrotoxic potential of the cephalosporins.

The combined use of cephalosporins and aminoglycosides seems to increase the risk of nephrotoxicity and should be undertaken with caution and with close monitoring of renal function.

As a precaution, renal function should be monitored if this is already impaired.

**INTERACTIONS:**

ZINACEF 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. ZINACEF may cause false-negative reactions in the ferricyanide test. Some cephalosporins 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.

ZINACEF must not be administered simultaneously with other medicines.

**PREGNANCY AND LACTATION:**

Safety in pregnancy and lactation has not been established.

**DOSAGE AND DIRECTIONS FOR USE:**

**General dosage recommendation:**

**Adults:**

The dosage range for cefuroxime lies between 1,5 to 6,0 g/day. Many infections will respond to 750 mg three times daily by intramuscular or intravenous injection. For more severe infections, this dose should be increased to 1,5 g three times daily intravenously. The frequency of intramuscular or intravenous injection can be increased to six hourly if necessary.

**Infants and children:**

Doses of 30 to 100 mg/kg/day, given as 3 or 4 divided doses. A dose of 60 mg/kg/day will be appropriate for most infections.

**Other recommendations:**

*Gonorrhoea:*

1,5 g cefuroxime should be given as a single dose. This may be given as 2 x 750 mg injections into different sites, e.g. each buttock.

*Prophylaxis:*

The usual dose is 1,5 g intravenously with induction of anaesthesia for abdominal and gynaecological operations, but may be supplemented with two 750 mg intramuscular doses 8 and 16 hours later. In cardiac and pulmonary operations, the usual dose is 1,5 g

intravenously with induction of anaesthesia continuing with 750 mg intramuscularly three times daily for a further 24 to 48 hours.

*Dosage in impaired renal function:*

Cefuroxime is excreted by the kidneys. Therefore, in patients with markedly impaired renal function it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the dose until the GFR falls below 20 ml/min. In adults with marked impairment (GFR 10 to 20 ml/min), 750 mg twice daily is recommended and with severe impairment (GRF less than 10 ml/min) 750 mg once daily is adequate. For patients on dialysis, a further 750 mg dose should be given at the end of each dialysis. When continuous peritoneal dialysis is being used, a suitable dosage is usually 750 mg twice daily.

**Administration:**

*Intramuscular injection:*

Add 1 ml sterile Water for Injections to 250 mg cefuroxime or 3 ml sterile Water for Injections to 750 mg cefuroxime. Shake gently to produce an opaque suspension. Suspensions which appear granular must be discarded.

*Intravenous injection:*

Dissolve cefuroxime in sterile Water for Injections using at least 2 ml for 250 mg, at least 6 ml for 750 mg, or 15 ml for 1,5 g. Solutions which appear turbid must be discarded.

*Intravenous infusion:*

For short intravenous infusion (30 to 60 minutes) 1,5 g may be dissolved in 50 ml sterile Water for Injections. These solutions may be given directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluids. Solutions which appear turbid must be discarded.

Suspensions of cefuroxime for intramuscular injection and aqueous solutions for direct intravenous injection should be used within 5 hours if kept below 25 °C or within 48 hours if refrigerated. Some increase in colour may occur on storage. Solutions for short

intravenous infusion (1,5 g plus 50 ml sterile Water for Injections) which show less increase in colour, should be used within 24 hours if kept below 25 °C or within 72 hours if refrigerated.

Cefuroxime is compatible with the more commonly used intravenous fluids. It will retain potency for up to 24 hours at room temperature in Sodium Chloride Injection B.P. 0,9 % *m/v*, 5 % Dextrose Injection B.P., 0,18 % *m/v* Sodium Chloride plus 4 % Dextrose Injection B.P. and Compound Sodium Lactate Injection B.P. (Hartmann's solution). The pH of 2,74 % *m/v* Sodium Bicarbonate Injection B.P. considerably affects the colour of the solution and therefore this solution is not recommended for the dilution of cefuroxime. However, if required for patients receiving Sodium Bicarbonate Injection by infusion the cefuroxime may be introduced into the tube of the giving set. The stability of cefuroxime in Sodium Chloride Injection B.P. 0,9 % *m/v* and in 5 % Dextrose Injection is not affected by the presence of hydrocortisone sodium phosphate. Cefuroxime is also compatible with aqueous solutions containing up to 1 % lignocaine hydrochloride.

**SIDE EFFECTS:**

Effects reported include rashes, thrombophlebitis after intravenous injection, gastrointestinal disturbance and *Candida intertrigo*. The principal changes in haematological parameters seen in some patients have been of unexplained decreased haemoglobin concentration and of eosinophilia. Patients developing eosinophilia should have renal function closely monitored since hypersensitivity with acute renal failure has previously been documented. Patients developing decreased haemoglobin concentration should have bone marrow response monitored. Leucopenia and neutropenia have also been noted.

A positive Coombs' test has been found in patients treated with cefuroxime; this phenomenon can interfere with the cross-matching of blood. There are sometimes rises in serum liver enzymes or serum bilirubin particularly in patients with pre-existing liver

disease. There may also be some variation in the results of biochemical tests of renal function but these do not appear to be of clinical importance.

Hypersensitivity reactions including skin rashes (maculopapular and urticarial), drug fever and anaphylaxis have been reported. Transient pain may be experienced at the site of intramuscular injection. This is more likely to occur with higher doses. However, it is unlikely to be a cause for discontinuation of treatment.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**

See SIDE EFFECTS.

Serum levels of cefuroxime are reduced by dialysis. Treatment is supportive and symptomatic.

**IDENTIFICATION:**

Cefuroxime sodium is a white to cream powder.

**PRESENTATION:**

Vials containing 250 mg, 750 mg and 1,5 g of cefuroxime as the sodium salt packed singly.

**STORAGE INSTRUCTIONS:**

The dry powder in vials should be stored at or below 25 °C and protected from light.

Keep out of reach of children.

**REGISTRATION NUMBER:**

ZINACEF 250 mg INJECTION: L/20.1.1/0096

ZINACEF 750 mg INJECTION: L/20.1.1/0097

ZINACEF 1,5 g INJECTION: L/20.1.1/0098

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

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

**DATE OF PUBLICATION OF THE PACKAGE INSERT:**

Registration date: 4 September 1978

Revision approval date: 28 September 2000

Date of implementation of Regulation 11: 9 March 2018



**MANUFACTURER:**

GlaxoSmithKline Manufacturing S.p.A., Via Alessandro Fleming 2, 37135 Verona, Italy

Botswana:

Zinacef 250 mg Injection - Reg No B9304185 S2

Zinacef 750 mg Injection - Reg No B9304190 S2

Zinacef 1,5 g Injection - Reg No B9304200 S2

Malawi:

Zinacef 750 mg Injection – Reg No PMPB/PL270/66 POM

Namibia:

Zinacef 250 mg Injection - Reg No 90/20.1.1/00596 NS2

Zinacef 750 mg Injection - Reg No 90/20.1.1/00597 NS2

Zinacef 1,5 g Injection - Reg No 90/20.1.1/00595 NS2

Zambia:

Zinacef 750 mg Injection – Reg No 179/016 POM

Zimbabwe:

Zinacef 750 mg Injection - Reg No 80/7.2.2/1367 PP

**SKEDULERINGSTATUS:**

S4

**EIENDOMSNAAM EN DOSEERVORM:**

**ZINACEF 250 mg INJECTION** (Poeier vir Inspuiting)

**ZINACEF 750 mg INJECTION** (Poeier vir Inspuiting)

**ZINACEF 1,5 g INJECTION** (Poeier vir Inspuiting)

**SAMESTELLING:**

Flessies bevattende 250 mg, 750 mg of 1,5 g kefuroksiem as natriumkefuroksiem.

Suikervry.

**FARMAKOLOGIESE KLASSIFIKASIE:**

A 20.1.1. Antimikrobiese middels. Breë- en mediumspektrum antibiotika.

**FARMAKOLOGIESE WERKING:**

Kefuroksiem is 'n bakteriedodende, half-sintetiese kefalosporien-antibiotikum wat weerstand teen die meeste β-laktamases bied, en is aktief teen 'n groot verskeidenheid van Gram-positiewe en Gram-negatiewe organismes. Piek serumvlakke van kefuroksiem word bereik binne 30 tot 45 minute na die intramuskulêre toediening van die middel. Die serum-halfleeftyd na intramuskulêre of intraveneuse inspuiting is ongeveer 70 minute. Die gelyktydige toediening van probenesied sorg vir 'n verhoogde piek serumvlak en beperk die uitskeiding van die antibiotikum. Daar is byna algehele herwinning van die onveranderde kefuroksiem in die urien binne 24 uur na toediening, en die grootste deel word gedurende die eerste ses uur uitgeskei. Die tubulêre

uitskeidingskomponent vir die renale opruiming van kefuroksiem is in die omtrek van 50 %.

**INDIKASIES:**

Kefuroksiem word aangedui vir die behandeling van die volgende infeksies as hulle veroorsaak word deur vatbare stamme van die genoemde mikro-organismes:

Infeksies van die lugweë.

Infeksies van die oor, neus en keel.

Urienweginfeksies.

Sagteweefselsinfeksies.

Obstetriese en ginekologiese infeksies.

Gonoree.

Profilakse teen infeksie in abdominale, ginekologiese, kardiale en pulmonêre chirurgie waar daar verhoogde risiko van infeksie bestaan.

**Bakteriologie:**

Sensitiwiteitstoetse moet waar moontlik uitgevoer word.

Kefuroksiem toon aktiwiteit teen:

*Staphylococcus aureus* insluitende die penisillienweerstandige stamme maar nie die raar metisillienweerstandige stamme nie.

*Escherichia coli.*

*Klebsiella* spp.

*Enterobacter* spp.

*Streptococcus pyogenes.*

*Streptococcus viridans.*

*Clostridium spp.*

*Proteus mirabilis.*

*Proteus rettgeri.*

*Proteus vulgaris.*

*Proteus morganii.*

*Neisseria* spp - insluitende β-laktamase-produserende stamme van *N*. *gonorrhoeae*.

*Haemophilus influenzae.*

*Bacteroides fragilis.*

*Staphylococcus epidermidis.*

**KONTRA-INDIKASIES:**

Hipersensitiwiteit teenoor kefalosporien-antibiotika.

**WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:**

Spesiale sorg is aangedui in pasiënte wat ’n allergiese reaksie teenoor penisilliene of ander β-laktam antibiotika getoon het.

Langdurige gebruik kan aanleiding gee tot die oorgroei van nie-vatbare organismes. Pasiënte wat herhaalde los ontlastings ondervind, moet sorgvuldig gemonitor word vir die moontlike ontwikkeling van antibiotiese kolitis.

Die gelyktydige gebruik van ZINACEF en furosemied moet, waar moontlik, vermy word. Indien hulle wel gelyktydig gebruik word, moet die nierfunksie sorgvuldig gemonitor word aangesien furosemied moontlik die nefrotoksiese potensiaal van die kefalosporiene kan verhoog.

Dit blyk asof die gesamentlike gebruik van kefalosporiene en aminoglikosiede die gevaar van nefrotoksisiteit verhoog, en dit moet derhalwe onderneem word met versigtigheid en met die sorgvuldige monitering van nierfunksie.

As ’n voorsorgmaatreël moet die nierfunksie gemonitor word as dit reeds verswak is.

**INTERAKSIES:**

ZINACEF versteur nie ensiem-gebaseerde toetse vir glukosurie nie. Geringe versteuring van die koperreduksiemetodes (Benedict, Fehling, Clinitest) kan waargeneem word. Dit behoort egter nie aanleiding te gee tot vals-positiewe resultate nie. ZINACEF kan 'n vals-negatiewe reaksie in die ferrisianiedtoets lewer. Sommige kefalosporiene kan foutiewelik 'n hoë lesing lewer in die alkaliese pikraattoets vir kreatinien, hoewel die mate van hierdie verhoging waarskynlik nie van kliniese belang sal wees nie. Dit is moontlik dat kefuroksiem ook hierdie vasstelling kan belemmer.

ZINACEF moet nie gelyktydig met ander medisyne toegedien word nie.

**SWANGERSKAP EN LAKTASIE:**

Veiligheid gedurende swangerskap en borsvoeding is nog nie vasgestel nie.

**DOSIS EN GEBRUIKSAANWYSINGS:**

**Algemene dosisaanbevelings:**

**Volwassenes:**

Die kefuroksiem-dosisreikwydte is tussen 1,5 en 6,0 g/dag. Talle infeksies sal reageer op 750 mg drie maal per dag by wyse van intramuskulêre of intraveneuse inspuiting.

In die geval van ernstiger infeksies kan hierdie dosis vermeerder word tot 1,5 g drie maal per dag intraveneus toegedien. Die frekwensie van intramuskulêre of intraveneuse inspuitings kan, indien nodig, tot ses-uurliks verhoog word.

**Babas en kinders:**

Dosisse van 30 tot 100 mg/kg/dag, toegedien in 3 of 4 verdeelde dosisse. 'n Dosis van 60 mg/kg/dag behoort voldoende vir die meeste infeksies te wees.

**Ander aanbevelings:**

*Gonoree:*

1,5 g kefuroksiem moet as 'n enkeldosis toegedien word. Dit kan as 2 x 750 mg inspuitings elk op verskillende plekke, bv. een inspuiting in elke boud, toegedien word.

*Profilakse:*

Die gewone dosis is 1,5 g intraveneus met induksie van narkose vir abdominale en ginekologiese operasies, maar kan later aangevul word met twee 750 mg intramuskulêre dosisse 8 en 16 uur later. By kardiale en pulmonêre operasies is die gewone dosis 1,5 g intraveneus met induksie van narkose gevolg met 750 mg intramuskulêr drie maal daagliks vir ’n verdere 24 tot 48 uur.

*Dosis as die nierfunksie verswak is:*

Kefuroksiem word deur die niere uitgeskei. In die geval van pasiënte met ’n besliste verswakking van nierfunksie, word daar derhalwe aanbeveel dat die kefuroksiem-dosis veminder moet word om vir die stadiger uitskeiding daarvan te vergoed. Dit is egter nie nodig om die dosis te verminder totdat die GFR laer as 20 ml/min daal nie. By volwassenes met ’n besliste verswakking van nierfunksie (GFR 10 tot 20 ml/min), word 750 mg twee maal daagliks aanbeveel, en by dié met ’n ernstige verswakking (GFR minder as 10 ml/min), is 750 mg daagliks voldoende. Pasiënte wat dialise ondergaan, behoort na afloop van iedere dialise ’n verdere dosis van 750 mg te ontvang. Wanneer voortdurende peritoneale dialise gebruik word, is ’n dosis van 750 mg twee maal daagliks gewoonlik geskik.

**Toediening:**

*Intramuskulêre inspuiting:*

Voeg 1 ml steriele Water vir Inspuitings by 250 mg kefuroksiem, of 3 ml steriele Water vir Inspuitings by 750 mg kefuroksiem. Skud saggies totdat ’n ondeursigtige suspensie gevorm het. Suspensies wat korrelrig vertoon moet vernietig word.

*Intraveneuse inspuiting:*

Los kefuroksiem in steriele Water vir Inspuitings op. Gebruik ten minste 2 ml vir elke 250 mg, ten minste 6 ml vir 750 mg, of 15 ml vir 1,5 g. Oplossings wat troebelrig vertoon moet vernietig word.

*Intraveneuse infusie:*

Vir kortstondige intraveneuse infusie (30 tot 60 minute) kan 1,5 g opgelos word in 50 ml steriele Water vir Inspuitings. Hierdie oplossings kan direk in die aar toegedien word. As die pasiënt parenterale vloeistowwe ontvang, kan dit ook deur die buis van die toedieningstel toegedien word. Oplossings wat troebelrig vertoon moet vernietig word.

Kefuroksiemsuspensies vir intramuskulêre inspuiting en waterige oplossings vir regstreekse intraveneuse inspuiting moet binne 5 uur gebruik word as dit benede 'n temperatuur van 25 °C gebêre word, of binne 48 uur as dit in 'n yskas bewaar word. 'n Verandering in kleur mag voorkom met berging. Oplossings vir kortstondige intraveneuse infusie (1,5 g plus 50 ml steriele Water vir Inspuitings) wat minder opvallende kleurveranderings toon, moet gebruik word binne 24 uur as dit benede 25 °C bewaar word, of binne 72 uur as dit in 'n yskas bewaar word.

Kefuroksiem is verenigbaar met die meeste intraveneuse vloeistowwe wat algemeen gebruik word. Teen kamertemperatuur sal dit sy potensie tot 24 uur lank behou in Natriumchloried-inspuiting B.P. 0,9 % *m/v*, 5 % Dekstrose-inspuiting B.P., 0,18 % *m/v* Natriumchloried plus 4 % Dekstrose-inspuiting B.P. en Saamgestelde Natriumlaktaat-inspuiting B.P. (Hartmann se oplossing). Die pH van 2,74 % *m/v* Natriumbikarbonaat-inspuiting B.P. het 'n aansienlike uitwerking op die kleur van die oplossing en hierdie oplossing word derhalwe nie vir die verdunning van kefuroksiem aanbeveel nie. Indien nodig kan die kefuroksiem egter deur die buis van die toedieningstel toegevoeg word in die geval van pasiënte wat 'n infusie van Natriumbikarbonaat-inspuiting ontvang. Die stabiliteit van kefuroksiem in Natriumchloried-inspuiting B.P. 0,9 % *m/v* en in 5 % Dekstrose-inspuiting word nie deur die aanwesigheid van hidrokortisoon natriumfosfaat geaffekteer nie. Kefuroksiem is ook verenigbaar met waterige oplossings bevattende tot 1 % lignokaïenhidrochloried.

**NEWE-EFFEKTE:**

Newe-effekte wat gerapporteer is, sluit in veluitslag, tromboflebitis na intraveneuse inspuiting, gastroïntestinale versteurings en *Candida intertrigo*. Die vernaamste veranderings in hematologiese parameters wat by sommige pasiënte waargeneem is, was ’n onverklaarbare vermindering van die hemoglobienkonsentrasie en eosinofilie. Die nierfunksie van pasëinte wat eosinofilie ontwikkel, moet sorgvuldig gemonitor word, aangesien hipersensitiwiteit met akute nierversaking voorheen gedokumenteer is. Die beenmurg-reaksie van pasiënte wat ’n verlaagde hemoglobienkonsentrasie toon, moet gemonitor word. Leukopenie en neutropenie is al aangeteken.

’n Positiewe Coombs-toets is aangetref by sommige pasiënte wat met kefuroksiem behandel is; ’n verskynsel wat kruisproewe met bloed kan belemmer. Styging in serumlewerensieme of serumbilirubien word soms waargeneem, veral by pasiënte met ’n reeds bestaande lewersiekte. Daar kan ook sekere verskille in die resultate van biochemiese toetse vir nierfunksie wees, maar dit skyn nie asof hierdie verskille van kliniese belang is nie.

Hipersensitiwiteitsreaksies, insluitend veluitslae (makulopapulêr en urtikaries), geneesmiddelkoors en anafilakse is al aangemeld. Verbygaande pyn kan ondervind word by die plek waar ’n intramuskulêre inspuiting toegedien is. Dit kom meer dikwels met groot dosisse voor. Dit is egter onwaarskynlik dat dit die staking van die behandeling sal noodsaak.

**BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:**

Sien NEWE-EFFEKTE.

Serum vlakke van kefuroksiem word verminder deur dialise. Behandeling is ondersteunend en simptomaties.

**IDENTIFIKASIE:**

Natriumkefuroksiem is ’n wit tot roomwit poeier.

**AANBIEDING:**

Flessies bevattende 250 mg, 750 mg of 1,5 g kefuroksiem as die natriumsout, enkel verpak.

**BERGINGSINSTRUKSIES:**

Die droë poeier in die flessies moet bewaar word by of benede 25 °C en teen lig beskerm word.

Hou buite bereik van kinders.

**REGISTRASIENOMMER:**

ZINACEF 250 mg INJECTION: L/20.1.1/0096

ZINACEF 750 mg INJECTION: L/20.1.1/0097

ZINACEF 1,5 g INJECTION: L/20.1.1/0098

**NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:**

GlaxoSmithKline South Africa (Edms) Bpk.

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**DATUM VAN PUBLIKASIE VAN DIE VOUBILJET:**

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Weergawe goedgekeur: 28 September 2000

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