**FINAL PACKAGE INSERT**

**SCHEDULING STATUS:** S4

**PROPRIETARY NAMES AND DOSAGE FORMS:**

**SEFTRY 0,5 g(Powder for solution for injection)**
**SEFTRY 1,0 g (Powder for solution for injection)**
**SEFTRY 2,0 g (Powder for solution for injection)**

**Composition:**
**SEFTRY 0,5 g:** Each vial contains: dry, sterile ceftriaxone sodium equivalent to 0,5 g Ceftriaxone.
**SEFTRY 1,0 g:** Each vial contains: dry, sterile ceftriaxone sodium equivalent to 1,0 g Ceftriaxone.
**SEFTRY 2,0 g:** Each vial contains: dry, sterile ceftriaxone sodium equivalent to 2,0 g Ceftriaxone.

Sugar free.

**PHARMACOLOGICAL CLASSIFICATION:**
A 20.1.1 Broad and medium spectrum antibiotics

**PHARMACOLOGICAL ACTION:**
Ceftriaxone is a third generation cephalosporin. The bactericidal activity of ceftriaxone results from inhibition of bacterial cell wall synthesis.

***Pharmacokinetic properties:***
*Absorption:*
The maximum concentration after a single intramuscular (IM) dose of 1,0 g is about 81 mg/l and is reached within 2 to 3 hours after administration.
The area under the plasma concentration versus time curve (AUC) after intramuscular (IM) administration is equivalent to that after intravenous (IV) administration of an equivalent dose, indicating 100 % bioavailability of intramuscularly administered ceftriaxone.

*Distribution:*
The apparent volume of distribution of ceftriaxone is 0,13 to 0,19 l/kg. Ceftriaxone shows good tissue penetration and body-fluid distribution after a dose of 1 to 2 g; concentrations well above the minimum inhibitory concentrations of most pathogens responsible for infection are detectable for more than 24 hours in body-fluids or tissues including lung, heart, biliary tract/liver, tonsil, middle ear and nasal mucosa, bone as well as cerebrospinal, pleural, prostatic and synovial fluids.

*Protein binding:*
Ceftriaxone is reversibly bound to albumin. There is proportionally decreased albumin binding with an increase in plasma concentration of ceftriaxone.

*Penetration into particular tissues:*
Paediatrics:
Ceftriaxone penetrates the inflamed meninges of neonates, infants and children. Ceftriaxone concentrations exceed 1,4 mg/l in the cerebrospinal fluid (CSF) 24 hours after IV injection in doses of 50 mg/kg in neonates to 100 mg/kg in infants. Peak concentration in CSF with a mean of 18 mg/l is reached about 4 hours after intravenous injection.

Mean CSF concentrations are 17 % of plasma concentrations in patients with bacterial meningitis and 4 % in patients with aseptic meningitis.

The mean values of maximum plasma concentration, elimination half-life, plasma clearance and volume of distribution after a 50 mg/kg IV dose and after a 75 mg/kg IV dose in paediatric patients suffering from bacterial meningitis are shown in the table below.

*Mean pharmacokinetic parameters of ceftriaxone in paediatric patients with meningitis:*

| | ***50 mg/kg IV*** | ***75 mg/kg IV*** |
|---|---|---|
| Maximum plasma concentrations (μg/ml) | 216 | 275 |
| Elimination half-life (h) | 4,6 | 4,3 |
| Plasma clearance (ml/h/kg) | 49 | 60 |
| Volume of distribution (ml/kg) | 338 | 373 |
| CSF concentration – inflamed meninges (μg/ml) | 5,6 | 6,4 |
| Range (μg/ml) | 1,3 to 18,5 | 1,3 to 44 |
| Time after dose (h) | 3,7 (± 1,6) | 3,3 (± 1,4) |

Adults:
In meningitis in adults, administration of 50 mg/kg leads within 2 to 24 hours to CSF concentrations several times higher than the minimum in-vitro inhibitory concentrations required for the most common meningitis pathogens.
Ceftriaxone crosses the placental barrier and is excreted in the breast milk in low concentrations.

In healthy, young adult volunteers the total plasma clearance is 10 to 22 ml/min.

The renal clearance is 5 to 12 ml/min. 50 to 60 % of ceftriaxone is excreted unchanged in the urine, while 40 to 50 % is excreted unchanged in the bile. The elimination half-life in adults is about 8 hours.

***Pharmacokinetics in special clinical situations:***
*Neonates:*
Urinary recovery accounts for about 70 % of the dose.
*Infants less than eight days old and elderly persons aged over 75 years:*
Elimination half-life is usually 2 to 3 times that in young adults.
*Patients with renal or hepatic dysfunction:*
The pharmacokinetics of ceftriaxone are only minimally altered and the elimination half-life is only slightly increased.
*Impaired kidney function alone:*
Billiary elimination of ceftriaxone is increased.
*Impaired liver function alone:*
Renal elimination of ceftriaxone is increased.

***Micro-organisms resistant to ceftriaxone:***
Methicillin-resistant Staphylococcus species; *Enterococcus faecum; Listeria monocytogenes; Pseudomonas aeruginosa; Ureaplasma urealyticum; Mycoplasma species; Mycobacterium species;* some isolates of Bacteroides species (bile sensitive); and most strains of Clostridium difficile.

**INDICATIONS:**
***SEFTRY is indicated for the treatment of the following infections:***
Bacterial septicaemia caused by:
Methicillin-sensitive *Staphylococcus aureus* (MSSA), *Streptococcus pneumoniae, Haemophilus influenzae, Escherichia coli or Klebsiella pneumoniae.*

*Meningitis caused by:*
*Haemophilus influenzae, Neisseria meningitides, or Streptococcus pneumoniae.*

*Intra-abdominal infections caused by:*
*Escherichia coli, Klebsiella pneumoniae, or Peptostreptococcus species.*

*Skin and skin structure infections caused by:*
Methicillin-sensitive *Staphylococcus aureus* (MSSA), *Streptococcus pyogenes, Streptococcus viridans* group*, Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii, Serratia marcescens,* or *Peptostreptococcus* species.

*Bone and joint infections caused by:*
Methicillin-sensitive *Staphylococcus aureus* (MSSA)*, Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, or Enterobacter species.*
*Renal and urinary tract infections (complicated and uncomplicated) caused by:*
*Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii, or Klebsiella pneumoniae.*

*Respiratory tract infections caused by:*
*Streptococcus pneumoniae,* Methicillin-sensitive *Staphylococcus aureus* (MSSA), *Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis, or Serratia marcescens.*

*Ear, nose and throat infections (acute bacterial otitis media) caused by:*
*Streptococcus pneumoniae, Haemophilus influenzae, (including beta- lactamase-producing strains), or Moraxella catarrhalis* (including beta-lactamase-producing strains).

*Uncomplicated gonorrhoea (cervical/urethral and rectal) caused by:*
*Neisseria gonorrhoeae,* including both beta- lactamase-, and non-beta-lactamase-producing strains, and pharyngeal gonorrhoea caused by non-beta-lactamase-producing strains of *Neisseria gonorrhoeae.*

*Peri-operative infection prophylaxis.*

**CONTRAINDICATIONS:**
SEFTRY is contraindicated in patients with known hypersensitivity to beta-lactam antibiotics. In patients hypersensitive to penicillin, the possibility of allergic cross-reactions should be borne in mind.
Hyperbilirubinemic neonates, especially prematures, should not be treated with SEFTRY. *In-vitro* studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin and bilirubin encephalopathy can possibly develop in the patients.
SEFTRY is contraindicated in:
- Premature newborns up to a corrected age of 41 weeks (weeks of gestation + weeks of life),
- Full-term newborns (up to 28 days of age) with jaundice, or who are hypoalbuminaemic or acidotic because these are conditions in which bilirubin binding is likely to be impaired.
- Full-term newborns (up to 28 days of age) if they require (or are expected to require) IV calcium treatment, or calcium-containing infusions because of the risk of precipitation of ceftriaxone-calcium.

Contraindications of lignocaine must be excluded before intramuscular injection of SEFTRY when lignocaine is used as solvent.

**WARNINGSAND SPECIAL PRECAUTIONS:**

**In patients of any age SEFTRY must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites. However, in patients older than 28 days of age SEFTRY and calcium-containing solutions may be administered sequentially one after another if infusion lines at different sites are used, or if the infusion lines are replaced or thoroughly flushed between infusions with physiological salt-solution to avoid precipitation. In patients requiring continuous infusion with calcium-containing TPN solutions, healthcare professionals may wish to consider the use of alternative antibacterial treatments which do not carry a similar risk of precipitation. If use of SEFTRY is considered necessary in patients requiring continuous nutrition, TPN solutions and SEFTRY can be administered simultaneously, albeit via different infusion lines at different sites.Alternatively, infusion of TPN solution could be stopped for the period of SEFTRY infusion, considering the advice to flush infusion lines between solutions. Cases of fatal reactions with calcium-ceftriaxone precipitates in lungs and kidneys in both premature and full-term newborns aged less than 1 month have been described. In somecases the infusion lines and times of administration of ceftriaxone and calcium-containing solutions differed. In the available scientific data, there are no reports of confirmed intravascular precipitations in patients, other than newborns, treated with SEFTRY and calcium-containing solutions or any other calcium-containing products. In vitro studies demonstrated that newborns have an increased risk of precipitation of ceftriaxone-calcium compared to other age groups.** (see "CONTRAIDICATIONS" and "SIDE EFFECTS")

**Do not use diluents containing calcium, such as Ringer's solutions or Hartman's solution to reconstitute SEFTRY or to further dilute a reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone-calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same IV administration line. Therefore, ceftriaxone and calcium-containing solutions must not be mixed or administered simultaneously.**

***Interaction with calcium-containing products:***
There are no reports to date of intravascular or pulmonary precipitations in patients, other than neonates, treated with ceftriaxone and calcium-containing IV solutions. However, the theoretical possibility exists for an interaction between ceftriaxone and IV calcium-containing solutions in patients other than neonates. Therefore, SEFTRY and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age even via different infusion lines at different sites. As a further theoretical consideration and based on 5 half-lives of ceftriaxone, SEFTRY and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient (see "CONTRAINDICATIONS" and "DOSAGE AND DIRECTIONS FOR USE").

No data are available on potential interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and calcium-containing products

(IV or oral).

***Special Precautions:***
Pseudomembranous enterocolitis and coagulation disorders have been reported with SEFTRY. It is important to consider pseudomembranous enterocolitis in patients who present with diarrhoea subsequent to the administration of SEFTRY. Superinfections with non-susceptible micro-organisms may occur.
Shadows, which have been mistaken for gallstones, have been detected on sonograms of the gallbladder, usually following doses higher than the standard recommended dose.

These shadows are however precipitates of calcium ceftriaxone, which disappear on completion or discontinuation of SEFTRYtherapy. In symptomatic cases, conservative non-surgical management is recommended.

Cases of pancreatitis, possibly of biliary obstruction aetiology, have been reported in patients treated with SEFTRY. Most patients who developed pancreatitis have had risk factors associated with biliary stases and biliary sludge, e.g. severe illness and total parenteral nutrition.

**Ceftriaxone displaces bilirubin from serum albumin.**

**SEFTRYis not recommended for use in neonates (especially premature) at risk of developing bilirubin encephalopathy.**(See CONTRAINDICATIONS)

**Effects on ability to drive and use machinery:**
Since SEFTRY sometimes induces dizziness the ability to drive and use machines can be impaired.

**INTERACTIONS:**
Interactions of SEFTRY with calcium containing products (See WARNINGS AND SPECIAL PRECAUTIONS, DOSAGE AND DIRECTIONS FOR USE)
Renal function impairment has not been observed after concurrent administration of large doses of SEFTRY and potent diuretics (e.g. furosemide). There is no evidence that SEFTRY increases renal toxicity of aminoglycosides.

No effect similar to that of disulfiram has been demonstrated after ingestion of alcohol subsequent to the administration of SEFTRY.

Ceftriaxone does not contain an N-methylthiotetrazole moiety associated with possible ethanol intolerance and bleeding problems of certain other cephalosporins.

In an in vitro study antagonistic effects have been observed with the combination of chloramphenicol and SEFTRY.

The elimination of SEFTRY is not altered by probenecid.

SEFTRY may adversely affect the efficacy of oral hormonal contraceptives. Consequently, it is advisable to use supplementary (non-hormonal) contraceptive measures during treatment and in the month following treatment.

***Interaction with laboratory tests:***
In patients treated with SEFTRY the Coombs' test and tests for galactosaemia may in rare cases be false-positive.
Non-enzymatic methods for glucose determination in urine may give false-positive results.

**HUMAN REPRODUCTION:**
SEFTRY crosses the placental barrier, and is excreted in breast-milk.
Safety in pregnancy and lactation has not been established.

**DOSAGE AND DIRECTIONS FOR USE:**
Do not use diluents containing calcium, such as Ringer's solution or Hartman's solution to reconstitute SEFTRY vials or to further dilute a reconstituted vial for IV administration because a precipitate can form.

Precipitation of ceftriaxone-calcium can also occur when ceftriaxone is mixed with calcium-containing solutions in the same IV administration line. Therefore, ceftriaxone and calcium-containing solutions must not be mixed or administered simultaneously.SEFTRY and calcium-containing infusions such as parental nutrition, should not be mixed or co-administered to any patient irrespective of age even via different infusion lines at different infusion times at different sites (see "CONTRAINDICATIONS" and "WARNINGS AND SPECIAL PRECAUTIONS").

***Standard dosage:***
*Adults and children over 12 years:*
The usual dosage is 1 to 2 g SEFTRY once daily. In severe cases or in infections caused by moderately sensitive organisms, the dosage may be raised to 4 g, once daily.
*Neonates, infants and children up to 12 years:*
The following dosage schedules are recommended for once daily administration:
*Neonates (up to 14 days):*
20 to 50 mg/kg body weight once daily. The daily dose should not exceed 50 mg/kg. It is not necessary to differentiate between premature and term infants.
*Infants and children (15 days to 12 years):*
20 to 80 mg/kg once daily. For children with bodyweights of 50 kg or more, the usual adult dose should be used. Intravenous doses of ≥ 50 mg/kg body weight should be given by infusion over at least 30 minutes.
*Elderly patients:*
No dose modification is needed in the elderly.

***Duration of therapy:***
The duration of therapy varies according to the course of the disease. Administration of SEFTRYshould be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

***Special dosage instructions:***
*Meningitis:*
In bacterial meningitis in infants and children, treatment begins with doses of 100 mg/kg (not to exceed 4 g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dose can be adapted accordingly. For bacterial meningitis in adults, the recommended dose is 4 g once daily.

*Gonorrhoea:*
For the treatment of uncomplicated gonorrhoea (both beta-lactamase-producing and non-beta-lactamase-producing strains), a single intramuscular (IM) dose of 250 mg SEFTRY is recommended.

*Peri-operative infection prophylaxis:*
A single dose of 1 to 2 g SEFTRY administered 30 to 90 minutes prior to surgery.
In colorectal surgery, administration of SEFTRYwith or without a 5-nitroimidazole, e.g. metronidazole, has been proven effective, (separate administration: see "Method of administration").

*Impaired renal and hepatic function:*
In patients with impaired renal function, there is no need to reduce the dosage of SEFTRY provided that hepatic function is intact.
In cases of severe renal failure (creatinine clearance < 10 ml/min) the SEFTRY dosage should not exceed 2 g daily.
In patients with liver damage, there is no need for the dosage to be reduced, provided that renal function is intact.

***Method of administration:***
SEFTRY must be reconstituted prior to use. Reconstituted solutions retain their physical and chemical stability for 24 hours when kept at or below 25 °C or 48 hours in the refrigeratorat 2 to 8 °C. As a general rule, however, the solutions should be used immediately after preparation. The solutions range in colour from pale yellow to amber, depending on the concentration and length of storage. The colouration of the solutions is of no significance for the efficacy or tolerance of the medicine.

*Intramuscular injection:*
For IM injection, SEFTRY 1 g is dissolved in 3,5 ml of water for injection.
Intramuscular administrations, of some cephalosporins, cause pain at the injection site. This can be reduced greatly by administering in combination with a local anesthetic.
SEFTRY dissolved in 3,5 ml of a 1 % lignocaine solution instead of water for injection can reduce pain at the site of injection. It is recommended that not more than 1 g be injected at one site.
Reconstitution with 1 % lignocaine (without adrenaline) has no effect on the absorption or the elimination of SEFTRY.
In case lignocaine is used as a solvent SEFTRY solutions should only be used for intramuscular injection.

**The lignocaine solution must never be administered intravenously.**

*Intravenous injection:*
For IV injection SEFTRY 0,5 g is dissolved in 5 ml, and SEFTRY 1 g in 10 ml, sterile water for injection. The intravenous administration should be given over 2 to 4 minutes.

*Intravenous infusion:*
The infusion should be given over a period of at least 30 minutes. For IV infusion, 2 g SEFTRY is dissolved in approximately 40 ml of one of the following calcium-free infusion solutions:
- Sodium chloride 0,9 %
- Sodium chloride 0,45 % + dextrose 2,5 %
- Dextrose 5 %
- Dextrose 10 %
- Dextran 6 % in dextrose 5 %
- Hydroxy ethyl starch 6 – 10 % infusions

Sterile water for injection.
SEFTRY should not be mixed with or piggybacked into solutions containing other antimicrobial medicines or into diluent solutions other than those listed above, owing to possible incompatibility.

***Incompatibilities:***
SEFTRY should not be added to solutions containing calcium, such as Hartmann's solution and Ringer's solution or to further dilute a reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone-calcium can also occur when SEFTRY is mixed with calcium-containing solutions in the same IV administration line.

SEFTRY must not be administered simultaneously with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, SEFTRY and calcium-containing solutions may be administered sequentially, of one another, if the infusion lines are thoroughly flushed between infusions with a compatible fluid. In vitro studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone-calcium.

SEFTRYis incompatible with amsacrine, vancomycin, fluconazole and aminoglycosides.

**SIDE EFFECTS**
*Gastrointestinal system:*
Less frequent: Loose stools/diarrhoea, nausea, vomiting, stomatitis, glossitis, precipitation of ceftriaxone calcium salts in the gallbladder, precipitation of ceftriaxone calcium salt in the gallbladder has been observed, mostly in patients treated with doses higher than the recommended standard dose. In children, prospective studies have shown a variable incidence of precipitation with intravenous application, in some studies to above 20 %.
The incidence seems to be lower with slow infusion (20-30 minutes). This effect is usually asymptomatic, but in rare cases, the precipitations have been accompanied by clinical symptoms such as pain, nausea and vomiting.
Symptomatic treatment is recommended in these cases. Precipitation is usually reversible upon discontinuation of SEFTRY. Increase in liver enzymes, pseudomembranous colitis.

*Haematological system:*
Less frequent: Eosinophilia, leucopenia, granulocytopenia, hemolytic anemia, thrombocytopenia, Unknown frequency: Isolated cases of agranulocytosis (< 500 $mm^3$) have been reported, most of them following total doses of 20 g or more.
Haematoma or bleeding, lymphopenia, prolongation of prothrombin time.

*Skin and appendages:*
Urticaria, Exanthema, allergic dermatitis, pruritus, oedema. Unknown frequency: Isolated cases of severe cutaneous adverse reactions (erythema multifome, Stevens-Johnson syndrome or Lyell's syndrome/toxic epidermal necrolysis) have been reported.

*Central nervous system:*
Rare: Headache and dizziness.

*Urogenital system:*
Rare: Oliguria, genital mycosis.
Cases of drug precipitation in the kidneys have been reported, mostly in children older than 3 years and who have been treated with either high daily doses (e.g. ≥ 80 mg/kg/-day) or total doses exceeding 10 g and presenting with other risk factors (e.g. fluid restrictions, confinement to bed, etc.). The risk of precipitate formation is increased in immobilized or dehydrated patients. This event may be symptomatic or asymptomatic, may lead to renal insufficiency and is usually reversible upon discontinuation of SEFTRY.

*Hypersensitivity reactions:*
Rare: Anaphylactic shock and anaphylactoid reactions e.g., bronchospasms

*Local reactions:*
Phlebitic reactions may occur after IV administration. These may be minimised by slow (2 to 4 minutes) injection of the medicine. Intramuscular injection without lignocaine solution is painful, (see "DOSAGE AND DIRECTIONS FOR USE").

*Other:*
Rare: Fever, Vertigo, Increase in serum creatinine, shivering.
SEFTRY must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines.
Rarely, severe, and in some cases fatal, adverse reactions have been reported in preterm and full-term newborns (aged < 28 days) who had been treated with intravenous SEFTRY and calcium. Precipitation of ceftriaxone-calcium salt have been observed in lung and kidney post-mortem.
The high risk of precipitation in newborns is due to their low blood volume and the longer half life of SEFTRY compared with adults.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**
In the case of overdosage nausea, vomiting, diarrhea, can occur. SEFTRY concentration cannot be reduced by haemodialysis or peritoneal dialysis. There is no specific antidote. Treatment is symptomatic.

**IDENTIFICATION:**
SEFTRY 0,5 g Powder for solution for injection:
White to yellowish powder in a 10 or 15 ml injection vial made of colourless glass, with a grey rubber stopper and aluminium cap with a grey flip-off seal.
SEFTRY 1,0 g Powder for solution for injection:
White to yellowish powder in a 15 ml injection vial made of colourless glass, with a grey rubber stopper and aluminium cap with a light blue flip-off seal.
SEFTRY 2,0 g Powder for solution for injection:
White to yellowish powder in a 30 ml injection vial made of colourless glass, with a grey rubber stopper and aluminium cap with a orange flip-off seal.
On constitution, a yellowish to brown-yellow clear solution is obtained.

**PRESENTATION:**
Packs for IM, IV or for IV infusion containing:
SEFTRY 0,5 g, 1,0 g and 2,0 g Powder for solution for injection is packed in cartons containing 1 or 10 single dose glass vial with a grey rubber stopper and aluminium cap with a flip-off seal.

**STORAGE INSTRUCTIONS:**
Store in the original packaging (in the carton) at or below 25 °C and protect the vials from light.
The reconstituted solution is intended for immediate use, but the solution may be stored in the original vials in the refrigerator at 2 to 8°C for 48 hours or at or below 25 °C for 24 hours.
After use, discard any remaining solution.

KEEP OUT OF THE REACH OF CHILDREN.

**Registration numbers:**
SEFTRY 0,5 g: 41/20.1.1/0869
SEFTRY 1,0 g: 41/20.1.1/0870
SEFTRY 2,0 g: 41/20.1.1/0871

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:**
Oethmaan Biosims (Pty) Ltd
14 Komatie Road, Emmarentia
Johannesburg 2195

**DATE OF PUBLICATION OF THIS PACKAGE INSERT:**
25 November 2011

**FINALE VOUBILJET**

**SKEDULERINGSTATUS:** S4

**EIENDOMSNAME EN DOSEERVORMS**

**SEFTRY 0,5 g poeier vir oplossing vir inspuiting**
**SEFTRY 1,0 g poeier vir oplossing vir inspuiting**
**SEFTRY 2,0 g poeier vir oplossing vir inspuiting**

**Samestelling**

**SEFTRY 0,5 g:** Elke flessie bevat droë, steriele natriumkeftriaksoon gelykstaande aan 0,5 g keftriaksoon.
**SEFTRY 1,0 g:** Elke flessie bevat droë, steriele natriumkeftriaksoon gelykstaande aan 1,0 g keftriaksoon.
**SEFTRY 2,0 g:** Elke flessie bevat droë, steriele natriumkeftriaksoon gelykstaande aan 2,0 g keftriaksoon.

Suikervry.

**FARMAKOLOGIESE KLASSIFIKASIE**

A. 20.1.1 Breë- en mediumspektrumantibiotika

**FARMAKOLOGIESE WERKING:**

Keftriaksoon is 'n derdegenerasie kefalosporien. Die bakterisidiese aktiwiteit van keftriaksoon is vanweë remming van bakteriële selwandsintese.

***Farmakokinetiese eienskappe***

*Absorpsie*

Die maksimum konsentrasie na 'n enkele intramuskulêre (IM) dosis van 1,0 g is ongeveer 81 mg/liter en word binne 2 tot 3 uur na toediening bereik.

Die oppervlak (area) onder die kurwe van plasmakonsentrasie teenoor tyd (AOK) na intramuskulêre (IM) toediening is gelykstaande aan dié na intraveneuse (IV) toediening van dieselfde dosis wat 100% biobeskikbaarheid van die intramuskulêr toegediende keftriaksoon aantoon.

*Verspreiding*

Die oënskynlike volume van verdeling van keftriaksoon is 0,13 tot 0,19 l/kg. Keftriaksoon vertoon na 'n dosis van 1 tot 2 g goeie penetrasie in weefsel en verdeling in liggaamsvloeistof; konsentrasies heelwat bo die minimum inhibisiekonsentrasie van die meeste patogene verantwoordelik vir infeksie is vir meer as 24 uur waarneembaar in liggaamsvloeistof of weefsel waaronder die longe, hart, galweg/lewer, mangels, middeloor en neusmukosa, been asook serebrospinale, pleurale, prostaat- en sinoviale vloeistof.

*Proteïenbinding*

Keftriaksoon bind omkeerbaar aan albumien. Daar is 'n proporsionele afname in binding aan albumien soos wat die plasmakonsentrasie van keftriaksoon toeneem.

*Penetrasie in spesifieke weefsel*

Kinders

Keftriaksoon penetreer die ontsteekte meninges van pasgeborenes, babas en kinders. Konsentrasies van keftriaksoon oorskry 1,4 mg/l in die serebrospinale vloeistof (SSV) 24 uur na intraveneuse inspuiting van dosisse van 50 mg/kg in pasgeborenes tot 100 mg/kg in babas. Piekkonsentrasie in SSV met 'n gemiddeld van 18 mg/l word ongeveer 4 uur na intraveneuse inspuiting bereik.

Gemiddelde konsentrasies in die SSV is 17% van die plasmakonsentrasies in pasiënte met bakteriële meningitis en 4% in pasiënte met aseptiese meningitis.

Die gemiddelde waardes van maksimum konsentrasie in die plasma, eliminasiehalfleeftyd, plasma-opruiming en volume van verdeling na 'n intraveneuse dosis van 50 mg/kg en na 'n intraveneuse dosis van 75 mg/kg aan pediatriese pasiënte wat aan bakteriële meningitis ly, word in die tabel hieronder gegee.

*Gemiddelde farmakokinetiese parameters van keftriaksoon in pediatriese pasiënte met meningitis*

| | ***50 mg/kg IV*** | ***75 mg/kg IV*** |
|---|---|---|
| Maksimum plasmakonsentrasies (μg/ml) | 216 | 275 |
| Eliminasiehalfleeftyd (h) | 4,6 | 4,3 |
| Plasma-opruiming (ml/h/kg) | 49 | 60 |
| Volume van verdeling (ml/kg) | 338 | 373 |
| SSV-konsentrasie – ontsteekte breinvlies (μg/ml) | 5,6 | 6,4 |
| Gebied (μg/ml) | 1,3 to 18,5 | 1,3 to 44 |
| Tyd na dosering (h) | 3,7 (± 1,6) | 3,3 (± 1,4) |

Volwassenes

Tydens meningitis in volwassenes lei toediening van 50 mg/kg binne 2 tot 24 uur tot konsentrasies in die SSV van etlike kere hoër is as die minimum in vitro inhibisiekonsentrasie nodig vir die meeste algemene patogene wat meningitis veroorsaak.

Keftriaksoon kruis die plasentale skans en word in lae konsentrasies in borsmelk uitgeskei.

In gesonde jong volwasse vrywilligers is die totale opruiming uit die plasma 10 tot 22 ml/min.

Die opruiming deur die niere is 5-12 ml/min. 50 tot 60% van die keftriaksoon word onveranderd in die urien uitgeskei terwyl 40 – 50% onveranderd in die gal uitgeskei word. Die eliminasiehalfleeftyd in volwassenes is ongeveer 8 uur.

***Farmakokinetika in spesiale kliniese situasies***

*Pasgeborenes:*

Herwinning uit die urien bedra ongeveer 70% van die dosis.

*Babas jonger as agt dae en bejaarde persone ouer as 75 jaar:*

Die eliminasiehalfleeftyd is gewoonlik 2 tot 3 keer dié van jong volwassenes.

*Pasiënte met nier- of lewerdisfunksie:*

Die farmakokinetika van keftriaksoon verskil slegs minimaal en die eliminasiehalfleeftyd slegs effens langer.

*Slegs swak nierfunksie:*

Uitskeiding van keftriaksoon in die gal is hoër.

*Slegs swak lewerfunksie:*

Uitskeiding van keftriaksoon deur die niere is hoër.

***Mikro-organismes wat weerstandig teenoor keftriaksoon is***

Metisillienweerstandige *Staphylococcus*-spesies; *Enterococcus faecum; Listeria monocytogenes, Pseudomonas aeruginosa; Ureaplasma urealyticum; Mycoplasma-spesies; Mycobacterium-spesies;* sommige isolate van Bacteriodes-spesies (galsensitief); en die meeste stamme van Clostridium difficile

**INDIKASIES**

***SEFTRY is aangedui vir die behandeling van die volgende infeksies:***

Bakteriële septisemie veroorsaak deur:
Metisilliensensitiewe *Staphylococcus aureus* (MSSA), *Streptococcus pneumoniae, Haemophilus influenzae, Escherichia coli of Klebsiella pneumoniae.*

*Meningitis veroorsaak deur:*
*Haemophilus influenzae, Neisseria meningitides of Streptococcus pneumoniae.*

*Infeksies van die vel en velstrukture veroorsaak deur:*
*Escherichia coli, Klebsiella pneumoniae of Peptostreptococcus*-spesies.

*Infeksies van skeletbene en gewrigte veroorsaak deur:*
Metisilliensensitiewe *Staphylococcus aureus* (MSSA), *Streptococcus pyogenes, Streptococcus viridans-groep, Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii, Serratia marcescens of Peptostreptococcus*-spesies.

*Infeksies van skeletbene en gewrigte veroorsaak deur:*
Metisilliensensitiewe *Staphylococcus aureus (MSSA), Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae of Enterobacter-spesies.*
*Nier- en urienweginfeksies (gekompliseer en ongekompliseerd) veroorsaak deur:*
*Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii of Klebsiella pneumoniae.*

*Lugweginfeksies veroorsaak deur:*
*Streptococcus pneumoniae, metisilliensensitiewe Staphylococcus aureus* (MSSA), *Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis of Serratia marcescens.*

*Infeksies van die oor, neus en keel (akute bakteriële otitis media) veroorsaak deur:*
*Streptococcus pneumoniae, Haemophilus influenzae,* (waaronder stamme wat beta-laktamase produseer) *of Moraxella catarrhalis (waaronder stamme wat beta-laktamase produseer).*

*Ongekompliseerde gonorree (servikaal/uretraal en rektaal) veroorsaak deur:*
*Neisseria gonorrhoeae, waaronder stamme wat beta-laktamase produseer en die wat dit nie doen nie en faringeale gonorree veroorsaak deur stamme van Neisseria gonorrhoeae wat nie beta-laktamase produseer nie.*

*Peri-operatiewe profilakse van infeksie*

**KONTRA-INDIKASIES**

SEFTRY is teenaangedui vir pasiënte met bekende hipersensitiwiteit teenoor betalaktaamantibiotika. Vir pasiënte wat hipersensitief teenoor penisillien is, moet die moontlikheid van kruisreaksies in gedagte gehou word.

Pasgeborenes met hiperbilirubinemie, en veral vroeggeborenes, moet nie met SEFTRY behandel word nie. In vitro-studies het getoon dat keftriaksoon bilirubien uit serumalbumien verplaas en enkefalopatie vanweë bilirubien kan in pasiënte ontwikkel.

SEFTRY is teenaangedui vir:

- premature pasgeborenes tot 'n gekorrigeerde ouderdom van 41 weke (weke swangerskap + weke na geboorte)
- Pasgeborenes na volle termyn (tot 28 dae oud) met geelsug of hipoalbuminie of asidose omdat dit toestande is waartydens bilirubienbinding waarskynlik swak is
- Pasgeborenes na volle termyn (tot 28 dae oud) as hulle intraveneuse kalsium of kalsiumbevattende infusies nodig het (of vermoedelik nodig het) vanweë die risiko vir neerslag van kalsiumkeftriaksoon.

Teenaanduidings van lignokaïen moet voor intramuskulêre inspuiting van SEFTRY uitgesluit word as lignokaïen in die oplossing gebruik word.

**WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**

**SEFTRY moet nie vir pasiënte van enige ouderdom met enige kalsiumbevattende IV-oplossing gemeng of saam daarmee toegedien word nie en selfs nie deur ander infusielyne of op ander infusieplekke nie. SEFTRY en kalsiumbevattende IV-oplossings kan egter na mekaar aan pasiënte van enige ouderdom gegee word as die infusielyne by verskillende plekke gebruik word of as die infusielyne tussen infusies vervang of deeglik met fisiologiese soutoplossing gespoel word om neerslag te voorkom. Vir pasiënte wat kontinue infusie met oplossings met kalsium vir volle parenterale voeding (VPV) nodig het, kan die gesondheidskundige alternatiewe antibakteriële middels oorweeg wat nie 'n risiko vir neerslag het nie. As die gebruik van SEFTRY as nodig beskou word vir pasiënte wat kontinue voeding nodig het, kan oplossings vir VPV en SEFTRY saam gegee word, hoewel met verskillende infusielyne en op verskillende plekke. As alternatief kan infusie van die VPV tydens infusie van SEFTRY gestaak en die lyne tussen die infusietye deeglik gespoel word. Gevalle van dodelike reaksies met neerslag van kalsiumkeftriaksoon in die longe en niere van sowel premature as voltermyn-babas jonger as een maand is beskryf. In party gevalle het die infusielyne en toedieningstye van keftriaksoon en oplossings wat kalsium bevat, verskil. Daar is geen verslae in die beskikbare wetenskaplike data van bevestigde intravaskulêre neerslag in pasiënte, behalwe pasgeborenes, wat met SEFTRY en oplossings of enige ander produk wat kalsium bevat, behandel is nie. In vitro-studies het getoon dat pasgeborenes 'n hoër risiko vir die neerslag van kalsiumkeftriaksoon as ander ouderdomsgroepe het (kyk "Kontra-indikasies" en "Newe-effekte").**

**Moenie oplosmiddels wat kalsium bevat, soos Ringer of Hartman se oplossings, gebruik om SEFTRY aan te maak of om 'n aangemaakte flessie vir IV-infusie te verdun nie omdat 'n neerslag kan vorm. 'n Neerslag van kalsiumkeftriaksoon kan ook vorm as keftriaksoon in dieselfde IV-lyn as kalsiumbevattende oplossings gemeng word. Daarom moet keftriaksoon en oplossings wat kalsium bevat nie gemeng of saam toegedien word nie.**

***Interaksie met produkte wat kalsium bevat***

Daar is tot op datum geen verslae van intravaskulêre of pulmonêre neerslag in pasiënte, behalwe neonate, wat behandel is met keftriaksoon en intraveneuse oplossings wat kalsium bevat nie. Die teoretiese moontlikheid bestaan egter vir 'n interaksie tussen keftriaksoon en intraveneuse oplossings wat kalsium bevat in ander pasiënte as pasgeborenes. Daarom moet SEFTRY en oplossings wat kalsium bevat, waaronder kontinue kalsiumbevattende infusies soos aarvoeding, nie gemeng of saam aan enige pasiënt onafgesien van ouderdom toegedien word nie en selfs nie deur verskillende infusielyne by verskillende plekke nie. As 'n verdere teoretiese oorweging en gebaseer op 5 halfleeftye van keftriaksoon, moet SEFTRY en IV-oplossings wat kalsium bevat, nie binne 48 uur van mekaar aan enige pasiënt gegee word nie (sien "KONTRA-INDIKASIES" en "DOSIS EN GEBRUIKSAANWYSINGS").

Geen data oor die moontlike interaksie tussen keftriaksoon en orale produkte wat kalsium bevat of interaksie tussen intramuskulêre keftriaksoon en produkte wat kalsium bevat (IV of oraal), is beskikbaar nie.

***Spesiale voorsorgmaatreëls***

Pseudomembraanenterokolitis en versteurings in koagulasie is tydens gebruik van SEFTRY aangemeld. Dit is belangrik om pseudomembraanenterokolitis te oorweeg in pasiënte wat na toediening van SEFTRY diarree ontwikkel. Superinfeksies met nie-vatbare mikro-organismes kan voorkom.

Skadu's wat vir galstene aangesien is, is in sonogramme van die galblaas waargeneem en gewoonlik na dosisse hoër as die standaard aanbevole dosis.

Hierdie skaduwees is egter neerslag van kalsiumkeftriaksoon wat verdwyn na voltooiing of staking van SEFTRY. In simptomatiese gevalle word konserwatiewe nie-chirurgiese behandeling aanbeveel.

Gevalle van pankreatitis, moontlik vanweë obstruksie van die gal, is aangemeld in pasiënte wat met SEFTRY behandel is. Die meeste pasiënte wat pankreatitis ontwikkel het, het risikofaktore vanweë stase en neerslag in die gal, byvoorbeeld ernstige siekte en totale parenterale voeding gehad.

Keftriaksoon verplaas bilirubien uit serumalbumien.

**SEFTRY word nie aanbeveel vir gebruik in pasgeborenes (veral premature babas) wat 'n risiko het om enkefalopatie vanweë bilirubien te ontwikkel nie** (sien "KONTRA-INDIKASIES").

**Invloed op vermoë om motor te bestuur of masjinerie te gebruik**

Omdat SEFTRY soms duiseligheid veroorsaak kan dit die vermoë om 'n voertuig te bestuur of masjinerie te gebruik belemmer.

**INTERAKSIES**

Interaksies van SEFTRY met produkte wat kalsium bevat (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS and DOSIS EN GEBRUIKSAANWYSINGS)

Geen agteruitgang in nierfunksie is na gelyktydige toediening van groot dosisse SEFTRYen kragtige diuretika (bv. furosemied) waargeneem nie. Daar is geen getuienis dat SEFTRY die toksisiteit van aminoglikosiede op die nier vererger nie.

Geen effek soortgelyk aan dié van disulfiraam is na inname van alkohol na toediening van SEFTRY waargeneem nie.

Keftriaksoon bevat nie 'n N-metieltiotetrasooleenheid wat moontlik onverdraagbaarheid teenoor alkohol of bloedingsprobleme van sekere ander kefalosporiene kan veroorsaak nie.

In 'n in *vitro*-studie is antagonistiese effekte met die kombinasie van chlooramfenikol en SEFTRY waargeneem.

Die uitskeiding van SEFTRY word nie deur probenesied beïnvloed nie.

SEFTRY kan die effektiwiteit van hormonale voorbehoedmiddels negatief beïnvloed. voorbehoedmiddels.

Dit is gevolglik raadsaam om tydens behandeling en in die maand daarna bykomende (nie-hormonale) voorbehoedmiddels te gebruik.

***Interaksies met laboratoriumtoetse***

Die Coombstoets en toetse vir galaktosemie kan in enkele gevalle vals-positief wees vir pasiënte wat met SEFTRY behandel word.

Nie-ensimatiese metodes vir die bepaling van glukose in die urien kan vals positiewe resultate gee.

**MENSLIKE VOORTPLANTING**

SEFTRY kruis die plasentale skans en word in borsmelk uitgeskei.

Die veiligheid tydens swangerskap en borsvoeding is nie bepaal nie.

**DOSIS EN GEBRUIKSAANWYSINGS**

Moenie oplosmiddels wat kalsium bevat, soos Ringer of Hartman se oplossings, gebruik om SEFTRY aan te maak of om 'n aangemaakte flessie vir IV-infusie te verdun nie omdat 'n neerslag kan vorm.

'n Neerslag van kalsiumkeftriaksoon kan ook vorm as keftriaksoon in dieselfde IV-lyn as kalsiumbevattende oplossings gemeng word. Daarom moet keftriaksoon en oplossings wat kalsium bevat nie gemeng of saam toegedien word nie.

SEFTRY en oplossings wat kalsium bevat soos aarvoeding moet nie gemeng of saam aan enige pasiënt onafgesien van ouderdom toegedien word nie en selfs nie op verskillende infusietye by verskillende plekke nie (sien"KONTRA-INDIKASIES" en"WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS").

***Standaarddosis***

*Volwassenes en kinders ouer as 12 jaar*

Die gewone dosis is 1 tot 2 g SEFTRY een keer per dag. Vir ernstige gevalle of vir infeksies veroorsaak deur organismes wat net gedeeltelik sensitief is kan die dosis tot 4 g een keer per dag verhoog word.

*Pasgeborenes, babas en kinders tot 12 jaar*

Die volgende doseerskedules word aanbeveel vir toediening een keer per dag:

*Pasgeborenes (tot 14 dae)*

20 tot 50 mg/kg liggaamsmassa een keer per dag. Die daaglikse dosis moet nie 50 mg/kg oorskry nie. Dit is nie nodig om onderskeid te tref tussen premature en voltydbabas nie.

*Babas en kinders (15 dae tot 12 jaar)*

20 tot 80 mg/kg een keer per dag. Vir kinders met liggaamsmassa van 50 kg of meer moet die gewone volwasse dosis gebruik word. Intraveneuse dosisse van > 50 mg/kg liggaamsmassa moet per infusie oor ten minste 30 minute gegee word.

*Bejaarde pasiënte*

Geen aanpassing in die dosis vir bejaardes is nodig nie.

***Duur van behandeling***

Die duur van behandeling wissel afhangende van die verloop van die siekte. Toediening van SEFTRY moet vir 'n minimum van 48 tot 72 uur volgehou word nadat die pasiënt nie meer koorsig is nie of getuienis van bakteriële uitwissing verkry is.

***Spesiale doseerinstruksies***

*Meningitis*

Vir bakteriële meningitis in babas en kinders moet die behandeling met dosisse van 100 mg/kg een keer per dag begin (dit moet nie 4 g oorskry nie). Sodra die oorsakende organisme geïdentifiseer en die sensitiwiteit daarvan bepaal is, kan die dosis dienooreenkomstig aangepas word. Vir bakteriële meningitis in volwassenes is die aanbevole dosis 4 g een keer per dag.

*Gonorree*

Vir die behandeling van ongekompliseerde gonorree (deur sowel stamme wat beta-laktamase produseer as dié wat dit nie doen nie) word 'n enkele intramuskulêre dosis van 250 mg SEFTRY aanbeveel.

*Peri-operatiewe profilakse van infeksie*

'n Enkele dosis van 1 tot 2 g SEFTRY 30 tot 90 minute voor die operasie toegedien.
Vir kolorektale operasies is getoon dat toediening van SEFTRYmet of sonder 'n 5-nitro-imidasool, bv. metronidasool, effektief is (afsonderlike toediening: sien "Metode van Toediening").

*Swak nier- of lewerfunksie*

Dit is nie nodig om die dosis van SEFTRY te verminder vir pasiënte met swak nierfunksie nie op voorwaarde dat lewerfunksie ongeskonde is.

In gevalle van erge nierversaking (kreatinienopruiming < 10 ml/min) moet die dosis van SEFTRY nie 2 g per dag oorskry nie.

Dit is nie nodig om die dosis te verminder vir pasiënte met lewerskade nie op voorwaarde dat nierfunksie ongeskonde is.

***Metode van toediening***

SEFTRY moet voor gebruik aangemaak word. Aangemaakte oplossings behou hulle fisiese en chemiese stabiliteit vir 24 uur indien teen of benede 25°C gehou of 48 uur in die yskas by 2 tot 8 °C. As 'n algemene reël moet die oplossings egter onmiddellik na voorbereiding gebruik word. Die oplossings wissel in kleur van liggeel tot donkergeel afhangende van die konsentrasie en van hoe lank dit gestoor is. Die kleur van die oplossings is van geen betekenis vir die effektiwiteit of verdraagbaarheid van die medisyne nie.

*Intramuskulêre inspuiting:*

Vir IM-inspuiting word 1g SEFTRY in 3,5ml water vir inspuiting opgelos.
Intramuskulêre toediening van sekere kefalosporiene kan pyn by die plek van die inspuiting veroorsaak. Dit kan aansienlik verminder word deur toediening in kombinasie met 'n plaaslike verdower.

SEFTRY opgelos in 3,5 ml van 'n 1% lignokaïenoplossing in plaas van water vir inspuiting kan die pyn by die plek van die inspuiting verminder. Dit word aanbeveel dat nie meer as 1 g by een plek ingespuit word nie.

Aanmaak met 1% lignokaïen (sonder adrenalien) het geen effek op die absorpsie of die eliminasie van SEFTRY nie.

As lignokaïen as oplosmiddel gebruik word, moet SEFTRY-oplossings slegs intramuskulêr toegedien word.

**Die lignokaïenoplossing moet nooit intraveneus toegedien word nie.**

*Intraveneuse inspuiting*

Vir IV-inspuiting word 0,5 g SEFTRY in 5 ml en 1 g SEFTRY in 10 ml water vir inspuiting opgelos. Die intraveneuse toediening moet oor 2 tot 4 minute gegee word.

*Intraveneuse infusie*

Die infusie moet oor 'n periode van ten minste 30 minute gegee word. Vir IV-infusie word 2 g SEFTRY in ongeveer 40 ml van een van die volgende kalsiumvrye oplossings vir infusie opgelos:

- 0,9% natriumchloried
- 0,45% natriumchloried + 2,5% dekstrose
- 5% dekstrose
- 10 % dekstrose
- 6% dekstraan in 5% dekstrose
- 6 – 10% hidroksi-etielstysel vir infusie

Steriele water vir inspuiting

Vanweë moontlike onverenigbaarheid moet SEFTRY nie gemeng of toegedien word saam met oplossings wat ander antimikrobiese middels bevat of in oplossings anders as dié wat hier bo gelys is nie.

***Onverenigbaarhede***

SEFTRY moet nie gevoeg word by oplossings wat kalsium bevat, soos Hartman of Ringer se oplossings, nie en hierdie oplossings moet nie gebruik word om 'n aangemaakte flessie vir IV-infusie te verdun nie omdat 'n neerslag kan vorm. 'n Neerslag van kalsiumkeftriaksoon kan ook vorm as SEFTRY in dieselfde IV-lyn as kalsiumbevattende oplossings gemeng word.

SEFTRY moet nie toegedien word saam met IV-oplossings wat kalsium bevat nie, waaronder kontinue kalsiumbevattende infusies soos aarvoeding deur 'n Y-stuk nie. Vir pasiënte anders as pasgeborenes kan SEFTRY en kalsiumbevattende IV-oplossings egter na mekaar toegedien word as die infusielyne tussen infusies deeglik met 'n verenigbare vloeistof gespoel word. In vitro-studies met plasma van bloed uit die naelstring van die volwassene en die pasgeborene het getoon dat pasgeborenes 'n hoë risiko vir neerslag van kalsiumkeftriaksoon het.

SEFTRY is onverenigbaar met amsakrien, vankomisien, flukonasool en aminoglikosiede.

**NEWE-EFFEKTE**

*Gastro-intestinale stelsel*

Minder dikwels: Los stoelgang/diarree, naarheid, braking, stomatitis, glossitis en neerslag van kalsiumsoute van keftriaksoon in die galblaas is waargeneem en meesal in pasiënte wat met hoër dosisse as die aanbevole standaarddosis behandel is. In verkennende studies met kinders is 'n wisselende voorkoms van neerslag met intraveneuse toediening waargeneem en in party studies tot meer as 20%.
Dit lyk asof die voorkoms tydens stadige infusie (20 – 30 min) laer is. Hierdie effek is gewoonlik asimptomaties, maar in enkele gevalle het die neerslag met kliniese simptome soos pyn, naarheid en braking gepaardgegaan.
Simptomatiese behandeling word vir hierdie gevalle aanbeveel. Die neerslag klaar gewoonlik na staking van SEFTRY op.
Hoër vlakke lewerensieme, pseudomembraankolitis

*Hematologiese stelsel*

Minder dikwels: Eosinofilie, leukopenie, granulositopenie, hemolitiese anemie, trombositopenie. Enkele gevalle van agranulositose (< 500 mm3) is aangemeld en die meeste daarvan na totale dosisse van 20 g of meer.
Hematome of bloeding, limfopenie, verlenging van protrombientyd.

*Vel en aanhangsels*

Urtikarie, eksanteem, allergiese dermatitis, pruritus, edeem. Onbekende frekwensie: Geïsoleerde gevalle van ernstige nadelige reaksies op die vel (multivorme eriteem, Stevens-Johnsonsindroom of Lyell se sindroom/toksiese epidermale nekrolise) is aangemeld.

*Sentrale senustelsel*

Selde: Hoofpyn en duiseligheid.

*Urogenitale stelsel*

Selde: Oligurie, genitale mikose.
Gevalle van neerslag van die middel in die niere is aangemeld en meestal in kinders ouer as 3 jaar wat of met hoë daaglikse dosisse (bv. ≥ 80 mg/kg/dag) of totale dosisse meer as 10 g behandel is en wat met ander risiko faktore gepresenteer het (bv. beperkte vloeistofinname, kluistering aan die bed, ens.). Die risiko vir die vorming van 'n neerslag is hoër in immobiele of ontwaterde pasiënte. Dit kan simptomaties of asimptomaties wees, kan tot swak nierfunksie lei en is gewoonlik omkeerbaar na staking van SEFTRY.

*Hipersensitiwiteitsreaksies*

Selde: Anafilaktiese skok en anafilaktoïede reaksies, bv. brongospasma.

*Lokale reaksies*

Flebitiese reaksies kan na IV toediening voorkom. Dit kan deur stadige inspuiting (2 tot 4 minute) van die medisyne geminimaliseer word. Intramuskulêre inspuitings sonder lignokaïen is pynlik (sien "DOSIS EN GEBRUIKSAANWYSINGS").

*Ander*

Selde: Koors, vertigo, toename in serumkreatinien, bewerasie.
SEFTRY moet nie met oplossings of produkte wat kalsium bevat gemeng of saam toegedien word nie – selfs nie deur verskillende infusielyne nie.
Gevalle van erge en soms dodelike nadelige reaksies is beskryf in premature en voltermyn-babas (jonger as 28 dae) wat met intraveneuse SEFTRY en kalsium behandel is. Nadoodse ondersoeke het neerslag van die kalsiumsout van keftriaksoon in die longe en niere aangetoon.
Die hoë risiko vir neerslag in pasgeborenes is vanweë hulle klein bloedvolume en langer halfleeftyd van SEFTRY vergeleke met volwassenes.

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

Naarheid, braking en diarree kan in geval van oordosering voorkom. Die konsentrasie van SEFTRY in die serum kan nie deur hemodialise of peritoneale dialise verlaag word nie. Daar is geen spesifieke teenmiddel nie. Behandeling is simptomaties.

**IDENTIFIKASIE**

SEFTRY 0,5 g poeier vir oplossing vir inspuiting:
Wit tot gelerige poeier in 'n inspuitflessie van 10 of 15 ml van kleurlose glas met 'n grys rubberprop en aluminiumdoppie met 'n grys afwipseël
SEFTRY 1,0 g poeier vir oplossing vir inspuiting:
Wit tot gelerige poeier in 'n inspuitflessie van 15 ml van kleurlose glas met 'n grys rubberprop en aluminiumdoppie met 'n liglou afwipseël
SEFTRY 2,0 g poeier vir oplossing vir inspuiting:
Wit tot gelerige poeier in 'n inspuitflessie van 30 ml van kleurlose glas met 'n grys rubberprop en aluminiumdoppie met 'n oranje afwipseël
Na aanmaak word 'n geel tot bruin-geel helder oplossing verkry.

**AANBIEDING**

Pakke vir IM-, IV-inspuiting of vir IV-infusie wat die volgende bevat:
SEFTRY 0,5 g, 1,0 g en 2,0 g poeier vir oplossing vir inspuiting word in kartonne verpak wat 1 of 10 glasflessie met 'n enkele dosis bevat met 'n grys rubberprop en aluminiumdoppie met 'n afwipseël.

**BEWARINGSINSTRUKSIES**

Berg in die oorspronklike verpakking (in die karton) teen of benede 25 °C en beskerm die flessies teen lig.

Die aangemaakte oplossing moet onmiddellik gebruik word, maar die oplossing kan vir 48 uur in die oorspronklike flessies in die yskas teen 2 tot 8 °C of vir 24 uur teen of benede 25 °C gebêre word.

Gooi alle oorblywende oplossing na gebruik weg.

HOU BUITE DIE BEREIK VAN KINDERS.

**Registrasienommers**

SEFTRY 0,5 g: 41/20.1.1/0869
SEFTRY 1,0 g: 41/20.1.1/0870
SEFTRY 2,0 g: 41/20.1.1/0871

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

Oethmaan Biosims (Pty) Ltd
14 Komatie Road, Emmarentia
Johannesburg 2195

**DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET**

25 November 2011

1220707-V1