PACKAGE INSERT

SCHEDULING STATUS: **S4**

PROPRIETARY NAME AND DOSAGE FORM:

Cefotaxime 0,5 g Oethmaan (powder for solution for injection)

Cefotaxime 1,0 g Oethmaan (powder for solution for injection)

(IM, IV injection or for IV infusion)

COMPOSITION:

Cefotaxime 0,5 g Oethmaan: Each vial contains dry, sterile cefotaxime sodium equivalent to 0,5 g Cefotaxime.

Cefotaxime 1,0 g Oethmaan: Each vial contains dry, sterile cefotaxime sodium equivalent to 1,0 g Cefotaxime.

Sugar free**.**

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.1 Broad spectrum antibiotics

PHARMACOLOGICAL ACTION:

Cefotaxime is a bactericidal semi-synthetic third-generation cephalosporin. The antibacterial action results from inhibition of bacterial cell wall synthesis by binding to essential target proteins in bacterial cytoplasmic membranes. Cefotaxime has activity against a wide range of bacterial organisms (Gram positive and Gram-negative), including beta-lactamase producing strains.

Pharmacokinetics:

Cefotaxime is metabolized in the liver to both active and inactive metabolites, and is approximately 90 % excreted in the urine. Approximately 30 % of the dose of cefotaxime is excreted unchanged, while 15 %-25 % is excreted as the desacetyl derivative, the major active metabolite. The mean terminal half-life is about 80 minutes.

IM injection:

Peak plasma levels are reached 30 minutes after IM injection of 0,25 g; 0,5 g and 1 g doses. The peak plasma level attained is dose-dependent-approximately 24 ug/ml after the 1 g injection Urinary excretion is 50 % to 60 % of the administered dose within 24 hours after injection (44 % to 55 % within the first six hours). Cefotaxime crosses the blood-brain barrier.

IV injection:

Initial phase half-life for whole blood and plasma are 4,5 and 8 minutes respectively. Terminal phase half-lives for whole blood and plasma are 1,3 and 2,2 hours respectively. Most of the dose is excreted within 4 hours of dosing. The elimination half-life is prolonged with renal impairment. Between 85 % and 90 % of the administered dose is excreted in the urine and 7 % to 9,5 % is excreted in the faeces. Cefotaxime is metabolized in the liver to active and inactive metabolites. Approximately 20 % to 36 % of an IV dose is excreted as unchanged cefotaxime, while 15 % to 25 % is excreted as the desacetyl derivative, the major active metabolite. Two other inactive urinary metabolites account for 20 % to 25 % of the excreted dose.

IV infusion:

A loading dose of 0,5 g, 1 g, or 2 g, administered over 15 minutes followed by sustaining infusions of 0,5 g, 1 g, or 2 g per hour produces mean peak serum levels of 41 ug/ml, 93 ug/ml or 160 ug/ml respectively. The mean terminal half-life is 75 ± 7 minutes. Most of the administered dose (63 ± 9 %) is renally excreted within 24 hours.

Micro-organisms resistant to cefotaxime:

Most strains of enterococci are resistant.

Most strains of *Clostridium difficile* are resistant.

Pseudomonas aeroginosa, Listeria monocyogenes

INDICATIONS

Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan is indicated for the treatment of infections caused by susceptible strains of organisms in the following infections:-

Upper Respiratory Tract Infections:

- Pneumococcal infections – Pneumonia, bronchitis, cellulites, otitis media
- *Haemophilus influenzae* infections – Otitis media, Laryngotracheobronchitis, meningitis (in children)

Urinary tract Infections:

- *E. coli* infections – Pneumonia, urinary tract infections, meningitis (in children)

Gastrointestinal Infections

- Shigella infections – Bacillary dysentery

- Salmonella infections - Enteritis

Other:

- *Neisseria meningitides* – Meningitis (in children)
- Acute uncomplicated cystitis caused by *E.coli* and *Klebsiella pneumoniae.*

Note: Bacteriological tests to determine causative organisms and sensitives are recommended.

Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan is indicated perioperatively to reduce the incidence of certain post-operative infections in patients undergoing surgical procedures classified as potentially contaminated.

CONTRA-INDICATIONS

Hypersensitivity to cefotaxime, cephalosporin antibiotics or to any of the ingredients.

Hypersensitivity to penicillin and other beta-lactam antibiotics.

WARNINGS

The sodium content of cefotaxime sodium (48,2 mg/g) should be taken into consideration in patients on sodium restriction.

The white cell count should be monitored for treatment courses of more than 10 days. Treatment should be discontinued in the event of neutropenia. Pseudomembranous colitis has been reported with the use of **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan.**

Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhoea (which may be bloody) and fever, should be investigated for this diagnosis. If the diagnosis of pseudomembranous colitis is suspected, **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** should be stopped immediately and appropriate therapy initiated.

Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan should be used with caution in patients with:-

- A history of gastrointestinal disease, especially ulcerative colitis, regional enteritis or antibiotic-associated colitis.
- Renal function impairment – A reduced dose may be required (see "**Dosage and Directions for Use"**).
- Porphyria: Safety has not been established.

INTERACTIONS

Concurrent administration of potentially nephrotoxic medicines or diuretics may increase the risk of possible nephrotoxicity.

Do not mix **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** with another antibiotic in the same syringe or infusion solution.

Interaction with Laboratory Tests:

A positive Coombs reaction appears in patients who receive large doses of **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan.** Haemolysis is not usually associated with the phenomenon but it may interfere with cross-matching of blood.

Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan may give false-negative tests results with ferricyanide blood glucose test.

A false-positive reaction can occur on testing for glucose in the urine with reducing substances. This can be avoided with the use of methods specific to gluco-oxidase.

PREGNANCY AND LACTATION

Safety and efficacy in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

Dosage, route of administration and frequency of injections depends on the nature and severity of the infection, the condition of the patient and the sensitivity of the pathogens to **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan.**

Adults:

2 g daily administered as two injections of 1 g.

In severe infections, the dose may be increased to 3 g to 4 g daily given in 2 to 4 administrations. Very severe infections may require a dose of up to 12 g IV.

Children:

Neonates (0 to 1 week of age): 50 mg/kg body weight IV 12-hourly

Neonates (1 to 4 weeks of age): 50 mg/kg body weight IV 8-hourly

Note: It is not necessary to differentiate between premature and normal gestational age infants.

Infants and children: 50 mg/kg to 100 mg/kg body weight administered in 2 to 4 injections.

In exceptional cases, the dose may be increased to 200 mg/kg body weight per day.

Renal function impairment:

Reduce the dose by 50 % in patients with a creatinine clearance of less than 20 ml/minute. Do not alter the dosing interval.

Directions for preparation of injections:

IV and IM injections:

Dissolve **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** in Water for Injection (WFI) BP (0,5 g vial in 2 ml WFI; 1 g vial in 4 ml WFI). Shake vial until dissolved. Withdraw the entire contents of the vial into the syringe and use immediately.

Cefotaxime is given as deep intramuscular injection or by slow intravenous injection over 3-5 minutes.

Intravenous infusions:

Dissolve **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** 1 g or 2 x 1 g vials in 40 to 100 ml of Water For Injection, 0.9 % sodium chloride, 5 % dextrose or Ringer's solution. The prepared infusion solutions should be freshly prepared and administered over 20-60 minutes.

Stability:

The reconstituted solution should not be stored and any remaining solution should be discarded.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side Effects:

Cardiac disorders:

The following side-effects have been reported and the frequencies are unknown: Arrhythmias following rapid bolus infusion through a central venous catheter.

Nervous system disorders:

The following side-effects have been reported and the frequencies are unknown: Headache, confusion, encephalopathy.

Gastrointestinal disorders:

The following side-effects have been reported and the frequencies are unknown: Diarrhoea, nausea, vomiting,

abdominal pain.

Renal and urinary disorders:

The following side-effects have been reported and the frequencies are unknown: Decrease in renal function (especially when co-prescribed with aminoglycosides), interstitial nephritis.

Hepatobiliary disorders:

The following side-effects have been reported and the frequencies are unknown: Transient increases in hepatic enzyme levels and/or bilirubin (Values may exceed twice the upper limit of normal and lead to asymptomatic cholestatic liver injury).

Skin and subcutaneous tissue disorders:

The following side-effects have been reported and the frequencies are unknown: Local inflammatory reactions at the injection site, rash, pruritus, urticaria, erythema multiforme, Steven-Johnson syndrome, toxic epidermal necrolysis.

Immune system disorders:

The following side-effects have been reported and the frequencies are unknown: Hypersensitivity reactions including skin rashes, urticaria, pruritus, bronchospasm, drug fever, serum sickness, shock, anaphylaxis.

Special precautions:

Stop treatment with **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** in the event of an allergic reaction. Prolonged use of **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** may result in the overgrowth of non-susceptible organisms i.e. superinfection with *candida,* Enterococci or *Clostridium difficile.* Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhoea (which may be bloody) and fever, should be investigated for this diagnosis. If the diagnosis of pseudomembranous colitis is suspected, **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan** should be stopped immediately and appropriate therapy initiated.
A Jarisch-Herxheimer reaction may develop during the first few days of treatment with CE **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan.** After several weeks of treatment with **Cefotaxime 0,5 g Oethmaan and Cefotaxime 1,0 g Oethmaan,** skin rash, itching, fever, leucopenia, increase in liver enzymes, dyspnoea and arthralgia has been reported.

KNOWN SYMPTOMS OF OVER-DOSAGE AND PARTICULARS OF ITS TREATMENT.

(See "**Side Effects and Special Precautions")**

Symptoms of overdose:

Encephalopathy (impairment of consciousness, abnormal movements and seizures) has been reported.

Treatment of overdose:

Treatment is symptomatic and supportive.

IDENTIFICATION:

Cefotaxime 0,5 g Oethmaan powder for solution for injection:

White to yellowish powder.

Cefotaxime 1,0 g Oethmaan powder for solution for injection:

White to yellowish powder.

On constitution, a slightly yellow to brownish yellow clear solution is obtained.

PRESENTATIONS:

Packs for IM, IV injection or for IV infusion containing:

Cefotaxime 0,5 g Oethmaan powder for solution for injection:

15 ml single dose colourless glass vial with a grey rubber stopper and aluminium cap with a plastic flip-off seal packed in cartons.

Cefotaxime 1,0 g Oethmaan powder for solution for injection:

20 ml single dose colourless glass vial with a grey rubber stopper and aluminium cap with a plastic flip-off seal packed in cartons.

STORAGE INSTRUCTIONS:

Store in the original packaging (in the carton) below 25 °C.

The reconstituted solution is intended for immediate use and any remaining solution must be discarded after use.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER:

Cefotaxime 0,5 g Oethmaan: 41/20.1.1/1063

Cefotaxime 1,0 g Oethmaan: 41/20.1.1/1064

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