APPROVED PROFFESSIONAL INFORMATION

SCHEDULING STATUS: **S4**

PROPRIETARY NAME AND DOSAGE FORM:

1. AURO CEFOTAXIME 250 mg (Powder For Injection)
2. AURO CEFOTAXIME 500 mg (Powder For Injection)
3. AURO CEFOTAXIME 1000 mg (Powder For Injection)
4. AURO CEFOTAXIME 2000 mg (Powder For Injection)

COMPOSITION:

1. Each vial contains Cefotaxime Sodium equivalent to **Cefotaxime 250 mg**.
2. Each vial contains Cefotaxime Sodium equivalent to **Cefotaxime 500 mg**.
3. Each vial contains Cefotaxime Sodium equivalent to **Cefotaxime 1000 mg**.
4. Each vial contains Cefotaxime Sodium equivalent to **Cefotaxime 2000 mg**.

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 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 metabolised 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 1g doses. The peak plasma attained is dose-dependant – approximately 24 µg/ml after the 1g 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-lives 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 metabolised 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 0.5g, 1g or 2g administered over 15 minutes followed by sustaining infusions of 0.5, 1 or 2g per hour produces mean peak serum levels of 41µg/ml, 93 µg/ml or 160 µg/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:

AURO CEFOTAXIME 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 sensitivities are recommended.

AURO CEFOTAXIME is indicated perioperatively to reduce the incidence of 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 **AURO CEFOTAXIME**. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhoea (which may be blood) and fever should be investigated for this diagnosis. If the diagnosis of pseudomembranous colitis is suspected **AURO CEFOTAXIME** should be stopped immediately and the appropriate therapy initiated.

AURO CEFOTAXIME 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 **AURO CEFOTAXIME** 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 **AURO CEFOTAXIME**. Haemolysis is not usually associated with the phenomenon but it may interfere with cross-matching of blood.

AURO CEFOTAXIME may give false-negative test 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 **AURO CEFOTAXIME**.

Adults:

2 g daily administered as two injections of 1 g.

In severe injections, the dose may be increased to 3 g or 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 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 intervals.

Directions for preparation of injections:

IV and IM injections:

Dissolve **AURO CEFOTAXIME** in Water For Injection (WFI) BP (0.5 g vial in 2 ml WFI: 1g vial in 4 ml WFI). Shake vial until dissolved. Withdraw the entire contents of the vial into the syringe and use immediately.

Intravenous infusions:

Dissolve **AURO CEFOTAXIME** 1 g or 2 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 administered over 20 to 60 minutes.

Note: Use freshly prepared solution. **AURO CEFOTAXIME** IV infusion solution in a concentration of 1 g per 250 ml is stable for 24 hours in a refrigerator or for 12 hours at a temperature not exceeding 23 °C.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side Effects

Blood and lymphatic system disorders

Frequent: eosinophilia,

Less frequent: haemolytic anaemia, neutropenia, thrombocytopenia (reversible)

The following side effects have been reported and frequencies are unknown:

Agranulocytosis

Cardiovascular disorders

The following side effects have been reported and frequencies are unknown:

Arrhythmias following rapid bolus infusion through a central venous catheter

Nervous system disorders

Frequent: headache

The following side effects have been reported and frequencies are unknown:

confusion, encephalopathy

Gastrointestinal disorders

Frequent: diarrhoea, nausea, vomiting, abdominal pain

Renal and urinary disorders

Less frequent: decrease in renal function (especially when co-prescribed with aminoglycosides),

The following side effects have been reported and frequencies are unknown: interstitial nephritis

Hepato-biliary disorders

The following side effects have been reported and 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

Less frequent: rash, pruritus, urticaria, erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis

General disorders and administration site conditions

Less frequent: local inflammatory reactions at the injection site

Immune system disorders

Less frequent*:* Hypersensitivity reactions including skin rashes, urticaria, pruritus, bronchospasm, drug fever, serum sickness, shock, anaphylaxis

Special Precautions:

Stop treatment with **AURO CEFOTAXIME** in the event of an allergic reaction.

Prolonged use of **AURO CEFOTAXIME** 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 the 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, **AURO CEFOTAXIME** should be stopped immediately and appropriate therapy initiated.

A Jarisch-Herxheimer reaction may develop during the first few days of treatment with **AURO CEFOTAXIME**.

After several weeks of treatment with **AURO CEFOTAXIME**, skin rash, itching, fever, Leucopenia, increase in liver enzymes, dyspnoea and arthralgia has been reported.

KNOWN SYMPTOMS OF OVER-DOSAGE AND PARTICULARS OF IT'S 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:

1. **AURO CEFOTAXIME 250 mg** – A white or slightly yellow powder filled in Type-I 15 ml moulded clear glass vial fitted with 20 mm bromo butyl rubber stopper and sealed with 20 mm light brown flip off aluminium seal.
2. **AURO CEFOTAXIME 500 mg** – A white or slightly yellow powder filled in Type-I 15 ml moulded clear glass vial fitted with 20 mm bromo butyl rubber stopper and sealed with 20 mm light green flip off aluminium seal.
3. **AURO CEFOTAXIME 1000 mg** – A white or slightly yellow powder filled in Type-I 15 ml moulded clear glass vial fitted with 20 mm bromo butyl rubber stopper and sealed with 20 mm lime green flip off aluminium seal.
4. **AURO CEFOTAXIME 2000 mg** – A white or slightly yellow powder filled in Type-I 15 ml moulded clear glass vial fitted with 20 mm bromo butyl rubber stopper and sealed with 20 mm pink flip off aluminium seal.

PRESENTATION:

1. **AURO CEFOTAXIME 250 mg** – Single clear glass vial packed in printed carton with a package insert.
2. **AURO CEFOTAXIME 500 mg** – Single clear glass vial packed in printed carton with a package insert.
3. **AURO CEFOTAXIME 1000 mg** – Single clear glass vial packed in printed carton with a package insert.
4. **AURO CEFOTAXIME 2000 mg** – Single clear glass vial packed in printed carton with a package insert.

STORAGE INSTRUCTIONS:

Store below 25 °C. Protect from light.

Keep the vials in the carton until required for use.

Discard any unused portion of the re-constituted solution in the vial.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

AURO CEFOTAXIME 250 mg: 42/20.1.1/0601.

AURO CEFOTAXIME 500 mg: 42/20.1.1/0602.

AURO CEFOTAXIME 1000 mg: 42/20.1.1/0603.

AURO CEFOTAXIME 2000 mg: 42/20.1.1/0604.

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

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