Approved Professional Information (Clean copy)

SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

AURO CEFEPIME INJECTION 500 mg (Powder for injection)

AURO CEFEPIME INJECTION 1 000 mg (Powder for injection)

AURO CEFEPIME INJECTION 2 000 mg (Powder for injection)

COMPOSITION:

AURO CEFEPIME INJECTION 500 mg:

Each vial contains cefepime dihydrochloride monohydrate equivalent to 500 mg cefepime, L-Arginine added as buffer.

AURO CEFEPIME INJECTION 1 000 mg:

Each vial contains cefepime dihydrochloride monohydrate equivalent to 1 000 mg cefepime, L-Arginine added as buffer.

AURO CEFEPIME INJECTION 2 000 mg:

Each vial contains cefepime dihydrochloride monohydrate equivalent to 2 000 mg cefepime, L-Arginine added as buffer.

CATEGORY AND CLASS:

A 20.1.1 Broad and Medium Spectrum Antibiotics.

PHARMACOLOGICAL ACTION:

Microbiology:

Cefepime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis, and it has a spectrum of activity against a range of Gram-positive and Gram-negative bacteria. Cefepime is highly resistant to hydrolysis by a number of beta-lactamases, has a low affinity for chromosomally encoded beta-lactamases, and exhibits rapid penetration into Gram-negative bacterial cells.

Cefepime minimum bactericidal concentrations were ≤ 2 times the minimum inhibitory concentration for the majority of organisms tested.

Gram-positive aerobes:

Note: Enterococci like *Enterococcus faecalis* and methicillin-resistant staphylococci, are resistant to cefepime.

Gram-negative aerobes:

Note: Cefepime is inactive against most strains of *Xanthomonas maltophilia (Pseudomonas maltophilia)*. Not all pseudomonas strains are susceptible.

Anaerobes:

Note: Cefepime is inactive against *Bacteroides fragilis* and *Clostridium difficile.*

Pharmacokinetics:

Adults:

Following intramuscular injection, cefepime is completely absorbed. Therapeutic concentrations are found in various body fluids such as urine, bile, blister fluid, peritoneal fluid and sputum, and tissues such as bronchial mucosa, appendix, prostate, and gallbladder, following intravenous administration of a single dose of cefepime.

The average elimination half-life of cefepime is approximately two hours.

There is no evidence of accumulation in healthy subjects receiving doses up to 2 g intravenously every 8 hours for a period of 9 days. Total body clearance averages 120 ml/min.

The average renal clearance of cefepime is 110 ml/min, demonstrating that cefepime is eliminated almost exclusively by renal mechanisms, primarily glomerular filtration.

Urinary recovery of unchanged cefepime represents approximately 85 % of dose, resulting in high concentrations of cefepime in the urine.

The serum protein binding of cefepime averages 16,4 % and is independent of concentration in the serum.

Healthy volunteers 65 years old or older, who received a single 1 g intravenous dose of cefepime had higher area under the concentration-time curve and lower renal clearance values compared to younger healthy adults. Dosage adjustments in the elderly are recommended if renal function is compromised (see "**WARNINGS AND SPECIAL PRECAUTIONS"** and "**DOSAGE AND DIRECTIONS FOR USE"**).

The pharmacokinetics of cefepime were unaltered in patients with impaired hepatic function who received a single 1 g dose.

Elimination half-life is prolonged in patients with various degrees of renal insufficiency with a linear relationship between total body clearance and creatinine clearance. This serves as the basis for dosage adjustment recommendations in this group of patients (see "**DOSAGE AND DIRECTIONS FOR USE"**).

Average half-life in severely impaired patients requiring dialysis therapy is 13 hours for haemodialysis and 19 hours for continuous ambulatory peritoneal dialysis.

Paediatrics:

Single and multiple-dose pharmacokinetics of cefepime were evaluated in patients ranging in age from 2 months to 16 years who received 50 mg/kg doses administered by IV infusion or IM injection: multiple doses were administered every 8 or 12 hours for at least 48 hours.

Mean plasma concentrations of cefepime after the first dose were similar to those at steady state, with only slight accumulation seen upon repeated dosing.

Following IM injection under steady state conditions, mean peak cefepime plasma concentrations of 68 mcg/ml were achieved at a median time of 0,75 hours, compared to 185,6 mcg/ml after IV. The mean trough concentration after IM injection at steady state was 6,0 mcg/ml at 8 hours. Bioavailability averaged 82 % after IM injection.

Other pharmacokinetic parameters in infants and children were not different between first-dose and steady-state determinations, regardless of dosing schedule (q12h or q8h). There were also no differences in pharmacokinetics among various patient ages or between males and female patients.

Following a single IV dose, total body clearance (in children over 6 months) averaged 3,4 ml/min/kg and average volume of distribution was 0,3 L/kg. The overall mean elimination half-life was 1,6 hours**.**

The urinary recovery of unchanged cefepime was 60,4 % of the administered dose, and renal clearance was the primary pathway of elimination, averaging 2,0 ml/min/kg. Elimination was slower in children 2 - 6 months (t½ 1,89 hours, clearance 2,97 ml/min/kg).

Concentrations of cefepime in cerebrospinal fluid relative to those in plasma are shown in Table 1.

TABLE 1

Mean (SD) Plasma (PL) and CSF Concentrations, and CSF/PL Ratios of Cefepime in Infants and Children*

Sampling Time (hr)	N	Plasma concentration (mcg/ml)	CSF concentration (mcg/ml)	Ratio

				CSF/PL
0,5	6	70,4 (55,4)	5,7 (8)	0,12 (0,14)
1	4	44,1 (7,8)	4,3 (1,5)	0,10 (0,04)
2	5	23,9 (12,9)	3,6 (2,0)	0,17 (0,09)
4	5	11,7 (15,7)	4,2 (1,1)	0,87 (0,56)
8	5	4,9 (5,9)	3,3 (2,8)	1,02 (0,64)

* Patients ranged in ages from 3,1 months to 14,7 years, with a mean (SD) age of 2,9 (3,9) years.

Patients with suspected central nervous system infection were treated with cefepime at a dose of 50 mg/kg administered as an IV infusion over 5 to 20 minutes every 8 hours. Single plasma and CSF samples were collected from selected patients at the sampling times shown relative to the end of infusion on day 2 or 3 of cefepime treatment.

INDICATIONS:

Adults:

AURO CEFEPIME INJECTION is indicated in the treatment of the infections listed below when caused by susceptible bacteria. Culture and susceptibility studies should be performed to determine susceptibility of the causative organism(s) to cefepime.

LOWER RESPIRATORY TRACT INFECTIONS:

Nosocomial and Community-Acquired Pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible strains), *Pseudomonas aeruginosa,* Klebsiella species (including *Klebsiella pneumoniae),* Enterobacter species, *Escherichia coli, Proteus mirabilis, Streptococcus pneumoniae* (including intermediate penicillin resistant strains), *Haemophilus influenzae* (including beta-lactamase producing strains), *Haemophilus parainfluenzae* and *Moraxella (Branhamella) catarrhalis* (including beta-lactamase producing strains), including cases associated with bacteraemia. When *P. aeruginosa* is isolated or suspected, combination therapy with an aminoglycoside should be used.

Acute Bacterial Exacerbation of Chronic Bronchitis and Acute Bronchitis due to *Streptococcus pneumoniae* (including intermediate penicillin resistant strains), *Haemophilus influenzae* (including beta-lactamase producing strains), *Moraxella (Branhamella) catarrhalis* (including beta-lactamase producing strains).

URINARY TRACT INFECTIONS:

Complicated Urinary Tract Infections caused by *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus mirabilis* and Enterobacter species, including cases associated with bacteraemia. When *P. aeruginosa* is isolated or suspected, combination therapy with an aminoglycoside should be used.

Uncomplicated Urinary Tract Infections due to *Escherichia coli, Proteus mirabilis,* Klebsiella species and Enterobacter species.

SKIN AND SKIN STRUCTURE INFECTIONS:

Skin and Skin Structure Infections caused by *Staphylococcus aureus* (methicillin-susceptible strains), *Streptococcus pyogenes* (Group A streptococci), *Streptococcus agalactiae* (Group B streptococci), other beta-haemolytic Streptococcus species, Enterobacter species, Klebsiella species, *Proteus mirabilis, Morganella morganii, Escherichia coli, Serratia marcescens* and *Acinetobacter calcoaceticus.*

INTRA-ABDOMINAL INFECTIONS:

Complicated Intra-abdominal Infections Including Peritonitis and Biliary Tract Infections caused by *Escherichia coli,* sensitive *Pseudomonas aeruginosa.* Peritonitis is often polymicrobial and may include anaerobic micro-organisms such as bacteroides species which are resistant to cefepime. When resistant anaerobes are suspected, cefepime should be combined with an antibiotic effective against these micro-organisms, including cases associated with bacteraemia.

In patients who are at risk of mixed aerobic-anaerobic infection, including infections in which *Bacteroides fragilis* may be present, concurrent therapy with an anti-anaerobic agent is recommended.

EMPIRIC TREATMENT IN FEBRILE NEUTROPENIA:

AURO CEFEPIME INJECTION is indicated for empiric monotherapy of febrile neutropenia.

Combination of **AURO CEFEPIME INJECTION** with other appropriate antimicrobial agents should be considered in patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, hypotension at presentation, an underlying haematologic malignancy, or severe or prolonged neutropenia) or when called for by host; or local epidemiological factors.

Children:

AURO CEFEPIME INJECTION is indicated in children (2 months and older) for the treatment of the infections listed below when caused by susceptible bacteria, (when *P. aeruginosa* is isolated or suspected, combination therapy with an aminoglycoside should be used):

LOWER RESPIRATORY TRACT INFECTION:

Pneumonia caused by *S. aureus, S. pneumoniae, H. influenzae.*

URINARY TRACT INFECTIONS: caused by *E. coli.*

SKIN AND SKIN STRUCTURE:

Infections caused by *Staphylococcus epidermidis,* streptococcus, S. *aureus, S. pyogenes.*

EMPIRIC TREATMENT IN FEBRILE NEUTROPENIA:

AURO CEFEPIME INJECTION is indicated for empiric monotherapy of febrile neutropenia.

Combination of **AURO CEFEPIME INJECTION** with other appropriate antimicrobial agents should be considered in patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, hypotension at presentation, an underlying haematologic malignancy, or severe or prolonged neutropenia) or when called for by host or local epidemiological factors.

CONTRA-INDICATIONS:

AURO CEFEPIME INJECTION is contraindicated in patients who have had previous hypersensitivity reactions to any component of the formulation, the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics.

Pregnancy and lactation.

WARNINGS AND SPECIAL PRECAUTIONS:

In patients with impaired renal function, such as reduction of urinary output because of renal insufficiency (creatinine clearance ≤ 50 ml/min) or other conditions that may compromise renal function, the dosage of **AURO CEFEPIME INJECTION** should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal insufficiency or other conditions that may compromise renal function, the maintenance dosage should be reduced when **AURO CEFEPIME INJECTION** is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms (see "**DOSAGE AND DIRECTIONS FOR USE"** and "**Pharmacokinetics"**).

Special Precautions:

Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to medicines. If an allergic reaction to **AURO CEFEPIME INJECTION** occurs, discontinue the medicine and treat the patient appropriately. Serious immediate hypersensitivity reactions may require epinephrine and other supportive therapy. Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics including **AURO CEFEPIME INJECTION**; therefore, it is important to consider this diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Mild cases of colitis may respond to drug discontinuation alone; moderate to severe cases may require more elaborate management.

Use of **AURO CEFEPIME INJECTION** may result in overgrowth of non-susceptible organisms. Should super-infection occur during therapy, appropriate measures should be taken.

Renal Impairment:

Renal function should be monitored carefully if medicines with nephrotoxic potential, such as aminoglycosides and potent diuretics, are administered with **AURO CEFEPIME INJECTION.**

Geriatric Use:

AURO CEFEPIME INJECTION is known to be substantially excreted by the kidney and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and renal function should be monitored (see "**SIDE-EFFECTS"** and "**PHARMACOLOGICAL ACTION"**). Serious adverse events, including reversible encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma) myoclonus, seizures (including non-convulsive status epilepticus), and/or renal failure have occurred in geriatric patients with renal insufficiency given the usual dose of **AURO CEFEPIME INJECTION**.

INTERACTIONS:

AURO CEFEPIME INJECTION exhibits physical or chemical incompatibility when admixed with vancomycin hydrochloride, gentamycin sulphate and aminophylline. In patients treated with **AURO CEFEPIME INJECTION**, false positive urinary tests for glucose may result when reducing agents are employed. False positives are not seen with glucose-oxidase methods.

PREGNANCY AND LACTATION:

The safe use of **AURO CEFEPIME INJECTION** in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

AURO CEFEPIME INJECTION can be administered either intravenously or intramuscularly. The dosage and route vary according to the susceptibility of the causative organisms, the severity of the infection, and the overall condition and renal function of the patient.

Adults:

Guidelines for dosage of **AURO CEFEPIME INJECTION** for adults with normal renal function are provided in Table 2.

TABLE 2: Recommended dosage schedule for adults with normal renal function (aged 12 years and older)*

SITE AND TYPE OF INFECTION	DOSE	FREQUENCY
Mild to moderate urinary tract infections (uncomplicated and complicated)	0.5 g – 1 g IV or IM	12 hourly
Mild to moderate infections including bronchitis, skin and skin-structure infections	1 g IV or IM	12 hourly
Severe infections including pneumonia, urinary tract infections, complicated intra-abdominal infections, including cases with an associated bacteraemia	2 g IV	12 hourly
Empiric treatment of fever in neutropenic patients	2 g IV	8 hourly

*Usual duration of therapy is 7 - 10 days; more severe infections may require longer treatment.
In the treatment of beta-haemolytic streptococcal infections a therapeutic dose must be administered for at least 10 days. For empirical treatment of febrile neutropenia, usual duration of therapy is 7 days or until resolution of neutropenia.

Paediatrics (aged 1 month up to 12 years with normal renal function):

Usual recommended dosages:

Pneumonia, urinary tract infections, and skin structure infections: Patients 2 months of age with body weight ≤ 40 kg: 50 mg/kg q12h for 10 days. For more severe infections, a dosage schedule of q8h can

be used.

Empiric treatment of febrile neutropenia: Patients > 2 months of age with body weight ≤ 40 kg: 50 mg/kg q8h for 7 - 10 days. Experience with the use of **AURO CEFEPIME INJECTION** in paediatric patients < 2 months of age is limited. While this experience has been attained using the 50 mg/kg dose, modelling of pharmacokinetic data obtained in patients > 2 months of age suggests that a dosage of 30 mg/kg q12h or q8h may be considered for patients aged 1 month up to 2 months. Administration of **AURO CEFEPIME INJECTION** in these patients should be carefully monitored.

For paediatric patients with body weights > 40 kg, adult dosing recommendations apply (see Table 2).

For patients older than 12 years who are ≤ 40 kg, the dosage recommendations for younger patients ≤ 40 kg should be used. Dosage in paediatric patients should not exceed the maximum recommended dosage in adults (2 g q8h). Experience with intramuscular administration in paediatric patients is limited.

Elderly:

Dose adjustment is not required, unless there is concurrent renal impairment.

Impaired hepatic function:

No adjustment is necessary for patients with impaired hepatic function.

Impaired renal function:

The initial dose of **AURO CEFEPIME INJECTION** is the same as in patients with normal renal function. The recommended maintenance doses of **AURO CEFEPIME INJECTION** in patients with renal insufficiency are presented in Table 3.

TABLE 3: Maintenance dosing schedule in adult patients with renal impairment *

Creatinine clearance (ml/min)	**Recommended Maintenance Dosage**			
> 50	Usual dose, no adjustment necessary			
	2 g 8 hourly	2 g 12 hourly	1 g 12 hourly	0.5 g 12 hourly
30 - 50	1 g 8 hourly	2 g daily**	1 g daily**	0.5 g daily**
11 - 29	1 g 12 hourly	1 g daily**	0.5 g daily**	0.5 g daily**
≤ 10	1 g daily**	500 mg daily**	0.25 g daily**	0.25 g daily**

* The initial dose is the same as in patients with normal renal function.

**Daily is calculated per 24 hours.

When only a serum creatinine measurement is available, the following formula (Cockcroft and Gault

equation) may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

Males:

Creatinine clearance (ml/min) = $\frac{\text{Weight (kg) x (140 - age)}}{\text{0,82 x serum creatinine (micromol/l)}}$

Females:

0,85 x value calculated using the formula for males.

Dialysis Patients:

In patients undergoing haemodialysis, approximately 68 % of the total amount of **AURO CEFEPIME INJECTION** present in the body at the start of dialysis will be removed during a 3 hour dialysis period. A repeat dose, equivalent to the initial dose, should be given at the completion of each dialysis session. In patients undergoing continuous ambulatory peritoneal dialysis, **AURO CEFEPIME INJECTION** may be administered at the same doses recommended for patients with normal renal function, i.e., 0,5 g; 1,0 g or 2,0 g depending on infection severity, but at a dosage interval of every 48 hours.

Children with Impaired Renal Function:

Since urinary excretion is the primary route of elimination of **AURO CEFEPIME INJECTION** in paediatric patients (see "**Pharmacokinetics"**), an adjustment of the dosage of **AURO CEFEPIME INJECTION** should also be considered in patients < 12 years of age with renal impairment.

Preparation of solution and administration:

AURO CEFEPIME INJECTION powder is to be constituted using the volumes of diluent shown in Table 4; the diluents to be used are identified following this table.

TABLE 4: Preparations of solutions of AURO CEFEPIME INJECTION

	Amount of diluent to be added (ml)	Approx. available volume (ml)	Approx. cefepime concentration (mg/ml)
Intravenous			
0,5 g vial	5	5,7	90
1,0 g vial	10	11,4	90
2,0 g vial	10	12,8	160
Intra-muscular			

0,5 g vial	1,5	2,2	230
1,0 g vial	3,0	4,4	230

Intravenous (IV) administration:

The IV route of administration is preferable for patients with severe or life-threatening infections, particularly if the possibility of shock is present.

For direct IV administration, constitute **AURO CEFEPIME INJECTION** with Sterile Water for Injection, 5 % Dextrose Injection or 0,9 % Sodium Chloride, using the diluent volumes shown in Table 4. The resulting solution should be injected directly into the vein over a period of three to five minutes or injected into the tubing of an administration set while the patient is receiving a compatible IV fluid (see "**Compatibility and Stability"**). For intravenous infusion, constitute the 0,5 g;1,0 g, or 2,0 g vial, as noted above for direct IV administration then, add the appropriate quantity of the resulting solution to an IV container with one of the compatible IV fluids identified under "**Compatibility and Stability"**. IV infusions of a volume between 50 ml and 100 ml should be administered over a period of approximately 30 minutes.

Intramuscular (IM) administration:

AURO CEFEPIME INJECTION should be constituted with one of the following diluents using the volumes shown in Table 4: Sterile Water for Injection, 0,9 % Sodium Chloride Injection, 5 % Dextrose Injection, or Bacteriostatic Water for Injection with Parabens or benzyl alcohol then administered by deep IM injection into a large muscle mass (such as the upper outer quadrant of the gluteus maximus). Although **AURO CEFEPIME INJECTION** can be constituted with 0,5 % or 1,0 % lidocaine hydrochloride, it is usually not necessary because **AURO CEFEPIME INJECTION** causes little or no pain upon IM administration.

Compatibility and Stability:

Intravenous:

AURO CEFEPIME INJECTION is compatible at concentrations between 1 and 40 mg/ml with one of the following IV infusion fluids: 0,9 % Sodium Chloride Injection, 5 % and 10 % Dextrose Injection, M/6 Sodium Lactate Injection, 5 % Dextrose and 0,9 % Sodium Chloride Injection, Lactated Ringers and 5 % Dextrose Injection. These solutions are stable for 24 hours at room temperature below 25 °C or 7 days under refrigeration (2 °C to 8 °C). **AURO CEFEPIME INJECTION** admixture compatibility and

stability information is summarised in the following table:

TABLE 5: Cefepime admixture stability

AURO CEFEPIME INJECTION concentration	**Admixture and concentration**	**IV infusion solutions**	**Stability time for**	
			RT/L (below 25 °C)	**Refrigeration (2 °C to 8 °C)**
40 mg/ml	amikacin 6 mg/ml	NS or D5W	24 hours	7 days
4 - 40 mg/ml	clindamycin 0,25 - 6 mg/ml	NS or D5W	24 hours	7 days
4 mg/ml	heparin 10 - 50 units/ml	NS or D5W	24 hours	7 days
4 mg/ml	potassium chloride 10 - 40 mEq/l	NS or D5W	24 hours	7 days
4 mg/ml	theophylline 0,8 mg/ml	D5W	24 hours	24 hours

NS = 0,9 % Sodium Chloride Injection; D5W = 5 % Dextrose Injection; RTL = Room temperature and light

Solutions of **AURO CEFEPIME INJECTION** like those of most beta-lactam antibiotics should not be added to solutions of metronidazole, vancomycin, gentamycin or tobramycin sulphate because of physical or chemical incompatibility. However, if concurrent therapy with **AURO CEFEPIME INJECTION** is indicated, each of these antibiotics can be administered separately.

Intramuscular:

AURO CEFEPIME INJECTION constituted as directed (in Table 4) is stable for 24 hours at room temperature below 25 °C or for 7 days under refrigeration (2 °C to 8 °C) when using the following diluents: Sterile Water for Injection, 0,9 % Sodium Chloride, 5 % Dextrose Injection, Bacteriostatic Water for Injection with Parabens or benzyl alcohol, or 0,5 % or 1 % lidocaine hydrochloride.

NOTE: Parenteral medicines should be inspected visually for particulate matter before administration, and not used if particulate matter is present. As with other cephalosporin's, the colour of **AURO CEFEPIME INJECTION** powder and solution may darken on storage, however, product potency is not adversely affected.

SIDE-EFFECTS:

Haematological disorders:

Less frequent:

Haemolytic anaemia, transient leukopenia, neutropenia, and thrombocytopenia.

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

Agranulocytosis, aplastic anaemia, haemorrhage.

Immune system disorders:

Frequent:

Eosinophilia.

Less frequent:

Anaphylaxis.

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

Fever.

Nervous system disorders:

Frequent:

Headache.

Less frequent:

Dizziness, seizures.

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

Paraesthesia.

Vascular disorders:

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

Vasodilation

Respiratory, thoracic and mediastinal disorders:

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

Dyspnoea, fever, chills.

Gastrointestinal disorders:

Frequent:

Diarrhoea, nausea, vomiting, oral moniliasis.

Less frequent:

Pseudomembranous colitis, dyspepsia.

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

Colitis, taste perversion, constipation, abdominal pain.

Hepato-biliary disorders:

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

Hepatitis and cholestatic jaundice.

Skin and subcutaneous tissue disorders:

Less frequent:

Rash, pruritus, urticaria, erythema, toxic epidermal necrolysis, erythema multiforme, Stevens-Johnson syndrome.

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

Unspecified moniliasis.

Reproductive system and breast disorders:

Less frequent:

Vaginitis.

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

Genital pruritus.

General disorders and administration site conditions:

Less frequent:

Local reactions such as phlebitis and inflammation at the site of IV injection and inflammation or pain at the site of intramuscular injection.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(See **"SIDE-EFFECTS"**.)

Treatment should be symptomatic and supportive. In case of severe overdosage, especially in patients with compromised renal function, haemodialysis will aid in the removal of **AURO CEFEPIME INJECTION** from the body; peritoneal dialysis is of no value. Accidental overdosing has occurred when large doses were given to patients with impaired renal function (see "**DOSAGE AND DIRECTIONS FOR USE"**, "**SIDE-EFFECTS"**).

IDENTIFICATION:

AURO CEFEPIME INJECTION 500 mg:

White to pale yellow powder. When reconstituted, it is a clear colourless to pale yellow solution.

AURO CEFEPIME INJECTION 1 000 mg:

White to pale yellow powder. When reconstituted, it is a clear colourless to pale yellow solution.

AURO CEFEPIME INJECTION 2 000 mg:

White to pale yellow powder. When reconstituted, it is a clear colourless to pale yellow solution.

PRESENTATION:

AURO CEFEPIME INJECTION 500 mg:

20 ml Type-1 moulded clear colourless transparent glass vials fitted with 20 mm grey bromo butyl rubber stoppers and sealed with 20 mm Mapra beige colour aluminium flip off seal.

Pack size: Single vial packed in printed carton with a package insert.

AURO CEFEPIME INJECTION 1000 mg:

20 ml Type-1 moulded clear colourless transparent glass vials fitted with 20 mm grey bromo butyl rubber stoppers and sealed with 20mm dark green colour aluminium flip off seal.

Pack size: Single vial packed in printed carton with a package insert.

AURO CEFEPIME INJECTION 2000 mg:

50 ml Type-1 moulded clear colourless transparent glass vials fitted with 32 mm grey bromo butyl rubber stoppers and sealed with 33 mm light orange colour aluminium flip off seal.

Pack size: Single vial packed in printed carton with a package insert.

STORAGE INSTRUCTIONS:

Store at or below 30 °C. Keep the vial in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

AURO CEFEPIME INJECTION 500 mg: 41/20.1.1/0689

AURO CEFEPIME INJECTION 1 000 mg: 41/20.1.1/0690

AURO CEFEPIME INJECTION 2 000 mg: 41/20.1.1/0691

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

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DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION:

05 March 2009

Date of revision:

23 August 2022