APPROVED PACKAGE INSERT

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

AUSTELL CEFOTAXIME 0,5 g (POWDER FOR INJECTION) [VIAL]

AUSTELL CEFOTAXIME 1 g (POWDER FOR INJECTION) [VIAL]

COMPOSITION

AUSTELL CEFOTAXIME 0,5 g:

Each vial contains sterile cefotaxime sodium equivalent to cefotaxime 0,5 g.

AUSTELL CEFOTAXIME 1 g:

Each vial contains sterile cefotaxime sodium equivalent to cefotaxime 1 g.

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 stains.

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-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 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, 1 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 monocytogenes.

INDICATIONS

AUSTELL CEFOTAXIME is indicated for the treatment of infections caused by suspeptible strains of organisms in the following infections: -

Upper Respiratory Tract Infections:

- Pneumococcal infections – Pneumonia, bronchitis, cellulitus, otitis media.
- *Heamophilus influenzae* infections – Otitis media, laryngotracheobronchitis, meningitis (in children).

Urinary tract infections:

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

Gastro-intestinal 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 determine causative organisms and sensitivities are recommended. **AUSTELL CEFOTAXIME** is indicated peri-operatively 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 restrictions.

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 **AUSTELL CEFOTAXIME**. 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, **AUSTELL CEFOTAXIME** should be stopped immediately and appropriate therapy initiated.

AUSTELL CEFOTAXIME should be used with caution in patients with: -

- A history of gastro-intestinal 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 **AUSTELL 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 **AUSTELL CEFOTAXIME**. Haemolysis is not usually associated with the phenomenon but it may interfere with cross-matching of blood.

AUSTELL 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 **AUSTELL CEFOTAXIME**.

Adults:

2 g daily administered as two injections of 1 g.

In severe infections, the dose may be increased to 3 - 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 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 **AUSTELL-CEFOTAXIME** 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.

Intravenous infusions:

Dissolve **AUSTELL-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. **AUSTELL-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 ºC.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side-effects:

Haematological

Neutropenia, agranulocytosis, eosinophilia, thrombocytopenia (reversible), haemolytic anaemia.

Cardiovascular

Arrhythmias following rapid bolus infusion through a central venous catheter.

Neurological

Headache, confusion, encephalopathy.

Gastro-intestinal

Diarrhoea, nausea, vomiting, abdominal pain.

Kidney/Genito-urinary

Decrease in renal function (especially when co-prescribed with aminoglycosides), interstitial nephritis.

Liver

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

Local inflammatory reactions at the injection site, rash, pruritis, urticaria, erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis.

Other

Hypersensitivity reactions including skin rashes, urticaria, pruritus, bronchospasm, drug fever, serum sickness, shock, anaphylaxis.

Special precautions:

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

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

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

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTIULARS 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

AUSTELL CEFOTAXIME 0,5 g:

Off-white to pale yellow crystalline powder.

AUSTELL CEFOTAXIME 1 g:

Off-white to pale yellow crystalline powder.

PRESENTATION

AUSTELL CEFOTAXIME 0,5 g: Colourless glass vials of 10 ml.

AUSTELL CEFOTAXIME 1 g: Colourless glass vials of 10 ml.

STORAGE INSTRUCTIONS

Store at or below 25 ºC. Protect from light.

Reconstituted product should be stored in original vials. These maintain potency for at least 6 hours at or below 25 ºC in daylight, or 24 hours at 2-8 ºC.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

AUSTELL CEFOTAXIME 0,5 g: 37/20.1.1/0364

AUSTELL CEFOTAXIME 1 g: 37/20.1.1/0365

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

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