MACXONE

(C e f t r i a x o n e)

250mg I.V & I.M
500mg I.V & I.M
1gm Injection I.V

میکزون

(سیفٹریاکزون)

COMPOSITION

MACXONE 250mg IV/IM Injection contains:
Ceftriaxone sodium USP equivalent to Ceftriaxone 250mg

MACXONE 500mg IV/IM Injection contains:
Ceftriaxone sodium USP equivalent to Ceftriaxone 500mg

MACXONE 1g IV Injection contains:
Ceftriaxone sodium USP equivalent to Ceftriaxone 1g

DESCRIPTION

MACXONE (Ceftriaxone sodium) is a sterile, semi-synthetic, broad-spectrum cephalosporin antibiotic for intravenous or intramuscular administration. ***MACXONE*** (Ceftriaxone sodium) is (6R,7R)-7-[2-(2-Amino-4-thiazolyl)glyoxylamido]-8-oxo-3-[[(1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-as-triazin-3-yl)thio]methyl]-5-thia-1-azabicyclo [4.2.0]-oct-2-ene-2-carboxylic acid, 7^2-(Z)(O-methyloxime), disodium salt, sesquaterhydrate. ***MACXONE*** (Ceftriaxone sodium) contains approximately 83mg (3.6 mEq) of sodium per gram of Ceftriaxone activity.

CLINICAL PHARMACOLOGY

Pharmacodynamics Properties

Mechanism of Action

MACXONE (Ceftriaxone sodium) is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis through inhibition of transpeptidase or penicillin binding protein. ***MACXONE*** (Ceftriaxone sodium) has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Ceftriaxone has been shown to be active against most strains of the following microorganisms:

Gram-negative Bacteria: *Acinetobacter calcoaceticus, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Moraxella catarrhalis, Morganella morganii, Neisseria gonorrhoeae, Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens, Citrobacter diversus, Citrobacter freundii, Providencia species* (including *Providencia rettgeri), Salmonella species* (including *Salmonella typhi*) & *Shigella species*

Gram-positive Bacteria: *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes, Viridans group streptococci, Streptococcus agalactiae*

Anaerobic Bacteria: *Bacteroides fragilis, Clostridium species, Peptostreptococcus species, Porphyromonas (Bacteroides) melaninogenicus, Prevotella (Bacteroides) bivius.*

Pharmacokinetic Properties

The pharmacokinetics of ***MACXONE*** (Ceftriaxone sodium) is nonlinear and all basic pharmacokinetic parameters, except the elimination half-life, are dose dependent if based on total drug concentrations.

Absorption: The maximum plasma concentration after a single IM dose of 1g is about 81mg/l and is reached in 2-3 hours after administration. The area under the plasma concentration-time curve after IM administration is equivalent to that after IV administration of an equivalent dose, indicating 100% bioavailability of intramuscularly administered ceftriaxone.

Distribution: Ceftriaxone has shown excellent tissue and body fluid penetration after a dose of 1-2g; concentrations well above the minimal inhibitory concentrations of most pathogens responsible for infection are detectable for more than 24 hours in over 60 tissues or body fluids including lung, heart, biliary tract/liver, tonsil, middle ear and nasal mucosa, bone as well as cerebrospinal, pleural, prostatic and synovial fluids.

On intravenous administration, ceftriaxone diffuses rapidly into the interstitial fluid, where bactericidal concentrations against susceptible organisms are maintained for 24 hours.

Protein binding: Ceftriaxone is reversibly bound to albumin, plasma protein binding is about 95% at plasma concentrations below 100mg/l. Binding is saturable and the bound portion decreases with rising concentration (up to 85% at a plasma concentration of 300mg/l).

Penetration into particular tissues: Penetration is greatest when the meninges are inflamed. Mean peak ceftriaxone concentrations in CSF in patients with bacterial meningitis are reported to be up to 25% of plasma levels compared to 2% of plasma levels in patients with un-inflamed meninges. Peak ceftriaxone concentrations in CSF are reached approximately 4-6 hours after intravenous injection.

Metabolism: ***MACXONE*** (Ceftriaxone sodium) is not metabolised systemically; but is converted to inactive metabolites by the gut flora.

Elimination: Total plasma clearance is 10-22 ml/min. Renal clearance is 5-12 ml/min. 50-60% of ceftriaxone is excreted unchanged in the urine, while 40-50% is excreted unchanged in the bile. The elimination half-life in adults is about 8 hours.

INDICATIONS

MACXONE (Ceftriaxone sodium) is indicated for the treatment of the following infections when caused by susceptible organisms:

Lower Respiratory Tract Infections caused by *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis or Serratia marcescens.*

Acute Bacterial Otitis Media caused by *Streptococcus pneumoniae, Haemophilus influenzae (including beta-lactamase producing strains) or Moraxella catarrhalis* (including beta-lactamase producing strains).

Skin and Skin Structure Infections caused by *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Viridans group streptococci, Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii, Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter calcoaceticus, Bacteroides fragilis or Peptostreptococcus species*.

Urinary Tract Infections (complicated and uncomplicated) caused by Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii or Klebsiella pneumoniae.

Uncomplicated Gonorrhoea (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae, including both penicillinase-and nonpenicillinase -producing strains, and pharyngeal gonorrhea caused by nonpenicillinase -producing strains of Neisseria gonorrhoeae.*

Pelvic Inflammatory Disease caused by Neisseria gonorrhoeae. Ceftriaxone like other cephalosporins, has no activity against Chlamydia trachomatis. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and Chlamydia trachomatis is one of the suspected pathogens, appropriate antichlamydial coverage should be added.

Bacterial Septicemia caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae or Klebsiella pneumoniae.

Bone and Joint Infections caused by *Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae or Enterobacter species*.

Intra-Abdominal Infections caused by *Escherichia coli, Klebsiella pneumoniae, Bacteroides fragilis, Clostridium species (Note: most strains of Clostridium difficile are resistant) or Peptostreptococcus species*.

Meningitis caused by **Haemophilus influenzae, Neisseria meningitidis or Streptococcus pneumoniae**. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infection caused by *Staphylococcus epidermidis and Escherichia coli*.

Surgical Prophylaxis: For preoperative administration of a single 1gm dose of Ceftriaxone may reduce the incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated (eg, vaginal or abdominal hysterectomy or cholecystectomy for chronic calculous cholecystitis in high-risk patients.

CONTRAINDICATION:

Ceftriaxone is contraindicated in patients with known hypersensitivity to ceftriaxone, any of its excipients or to any other cephalosporin. Patients with previous hypersensitivity reactions to penicillin and other beta lactam agents may be at greater risk of hypersensitivity to Ceftriaxone.

WARNING & PRECAUTIONS:

1- Before therapy with Ceftriaxone is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. This drug should be given cautiously to pencillin-sensitive patients. If an allergic reaction to Ceftriaxone occurs, discontinue the drug.

2- Pregnancy: Ceftriaxone crosses the placental barrier. Safety in human pregnancy has not been established.

3- Nursing mothers: Low concentrations of Ceftriaxone are excreted in

human milk. Caution should be exercised when Ceftriaxone is administered to a nursing woman.

ADVERSE REACTIONS:
Ceftriaxone is generally well tolerated, the following adverse reactions which were considered to be related to Ceftriaxone.
1- Gastrointestinal: nausea, vomiting, diarrhoea, stomatitis and glossitis.
2- Central nervous system: headache and dizziness.
3- Skin reactions: rash, pruritis, allergic dermatitis, urticaria, edema, erythema and anaphylactic reactions.

DRUG INTERACTIONS
In vitro, chloramphenicol has been shown to be antagonistic with respect to ceftriaxone and other cephalosporins. Caution is advised if concurrent administration of ceftriaxone with chloramphenicol is proposed.
Ceftriaxone 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.

DOSAGE & ADMINISTRATION
Standard dosage
Adults and children over 12 years
The usual dosage is 1-2g of ***MACXONE*** (ceftriaxone) once daily (every 24 hours). In severe cases or in infections caused by moderately sensitive organisms, the dosage may be raised to 4g, once daily.
Patients with hepatic impairment
In patients with liver damage, there is no need for the dosage to be reduced provided renal function is not impaired.
Patients with renal impairment
In patients with impaired renal function, there is no need to reduce the dosage of ceftriaxone provided hepatic function is not impaired. Only in cases of preterminal renal failure (creatinine clearance <10ml/min) should the ceftriaxone dosage not exceed 2g daily.
In patients with both severe renal and hepatic dysfunction, the plasma concentrations of ceftriaxone should be determined at regular intervals and if necessary the dose should be adjusted.
In patients undergoing dialysis no additional supplementary dosing is required following the dialysis. Plasma concentrations should, however, be monitored, to determine whether dosage adjustments are necessary, since the elimination rate in these patients may be altered.
Elderly
The dosages recommended for adults require no modification in geriatric patients.
Children
Neonates, *infants and children* up to 12 years
The following dosage schedules are recommended for once daily administration:
Neonates (up to 14 days): 20-50mg/kg bodyweight once daily. The daily dose should not exceed 50mg/kg. It is not necessary to differentiate between premature and term infants.
For neonates, infants, and children (15 days to 12 years): 20–80 mg/kg once daily.
For children with bodyweights of 50kg or more, the usual adult dosage should be used.
Intravenous doses of ≥ 50mg/kg bodyweight should be given by infusion over at least 30 minutes.
Meningitis
In bacterial meningitis in infants and children, treatment begins with doses of 100mg/kg (up to a maximum of 4 g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly.
The following duration of therapy has shown to be effective:
Neisseria meningitides 4 days
Haemophilus influenzae 6 days
Streptococcus pneumoniae 7 days

Duration of therapy
The duration of therapy varies according to the course of the disease. As with antibiotic therapy in general, administration of ceftriaxone (***MACXONE***) should be continued for a minimum of 48-72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

Combination therapy
Synergy between Ceftriaxone and aminoglycosides has been demonstrated with many gram-negative bacteria under experimental conditions. Although enhanced activity of such combinations is not always predictable, it should be considered in severe, life threatening infections due to microorganisms such as Pseudomonas aeruginosa. Due to chemical incompatibility between Ceftriaxone and aminoglycosides, the two drugs must be administered separately at the recommended dosages.

Method of administration
As a general rule the solutions should be used immediately after preparation. Reconstituted solutions retain their physical and chemical stability for 6 hours at room temperature (or 24 hours in the refrigerator at 2 - 8°C).

Intramuscular injection
For IM injection, ***MACXONE*** (ceftriaxone sodium) 250mg or 500mg is dissolved in 2ml of 1% lidocaine hydrochloride solution and injected well within the body of a relatively large muscle. The lidocaine solution should never be administered intravenously.
Intravenous injection
For i.v. injection, ***MACXONE*** (ceftriaxone sodium) 250mg or 500mg is dissolved in 5ml, and ceftriaxone 1g in 10ml, sterile water for injections. The intravenous administration should be given over 2-4 minutes.

HOW SUPPLIED
MACXONE (Ceftriaxone) IV Injection 250mg is available in unit pack size of 1 vial alongwith a 5ml ampoule of sterile water for Injection.

MACXONE (Ceftriaxone) IM Injection 250mg is available in unit pack size of 1 vial alongwith a 2ml ampoule of 1% Lidocaine solution.

MACXONE (Ceftriaxone) IV Injection 500mg is available in unit pack size of 1 vial alongwith a 5ml ampoule of sterile water for Injection.

MACXONE (Ceftriaxone) IM Injection 500mg is available in unit pack size of 1 vial alongwith a 2ml ampoule of 1% Lidocaine solution.

MACXONE (Ceftriaxone) IV Injection 1g is available in unit pack size of 1 vial alongwith a 10ml ampoule of sterile water for Injection.

خوراک وہدایات:

- ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
- انٹرامسکیولر/انٹراوینس استعمال کے لئے۔
- 30°C سے کم درجہ حرارت پر محفوظ رکھیں۔
- تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
- نمی اور روشنی سے بچائیں۔

Manufactured by:
Macquin's
MACQUIN'S INTERNATIONAL
F-2/H, S.I.T.E., Karachi

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ISO 9001 : 2000 Certified Company