# MACFRAN

250mg
500mg
1g

(Cefotaxime Sodium U.S.P.)

*For Intravenous or Intramuscular Injection*

# میکفران

(سیفوٹیکسم سوڈیم یو۔ایس۔پی)

وریدی یا عضلاتی انجکشن کے لئے

**COMPOSITION:**

***MACFRAN*** 250mg injection for IM/IV use.
Each vial contains Cefotaxime sodium equivalent to Cefotaxime 250mg.
***MACFRAN*** 500mg injection for IM/IV use.
Each vial contains Cefotaxime sodium equivalent to Cefotaxime 500mg.
***MACFRAN*** 1g injection for IM/IV use.
Each vial contains Cefotaxime sodium equivalent to Cefotaxime 1g.

**DESCRIPTION:**

***MACFRAN*** (cefotaxime sodium) is a semisynthetic, broad spectrum cephalosporin antibiotic for intramuscular/intravenous administration. Sterile, white or pale yellow powder for injection.

**MICROBIOLOGY:**

The bactericidal activity of cefotaxime sodium results from inhibition of cell wall synthesis. Cefotaxime sodium has in vitro activity against a wide range of gram-positive and gram-negative organisms. Cefotaxime sodium has a high degree of stability in the presence of ß-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria. Cefotaxime sodium has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections.

**Aerobes, Gram-positive:**
Enterococcus spp.
Staphylococcus aureus*, including ß-lactamase-positive and negative strains Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus pyogenes (Group A beta-hemolytic streptococci)
Streptococcus spp.
*Staphylococci which are resistant to methicillin/oxacillin must be considered resistant to Cefotaxime sodium.

**Aerobes, Gram-negative:**
Acinetobacter spp.
Citrobacter spp.
Enterobacter spp.
Escherichia coli
Haemophilus influenzae (including ampicillin-resistant strains)
Haemophilus parainfluenzae
Klebsiella spp. (including Klebsiella pneumoniae)
Morganella morganii
Neisseria gonorrhoeae (including ß-lactamase-positive and negative strains)
Neisseria meningitidis
Proteus mirabilis
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Serratia marcescens

**NOTE:** Many strains of the above organisms that are multiply resistant to other antibiotics, e.g. penicillins, cephalosporins, and aminoglycosides, are susceptible to cefotaxime sodium. Cefotaxime sodium is active against some strains of Pseudomonas aeruginosa.

**Anaerobes:**
Bacteroides spp., including some strains of Bacteroides fragilis
Clostridium spp. (Note: Most strains of Clostridium difficile are resistant.)
Fusobacterium spp. (Including Fusobacterium nucleatum)
Peptococcus spp.
Peptostreptococcus spp.
Aerobes, Gram-negative:
Providencia spp.
Salmonella spp. (including Salmonella typhi)
Shigella spp.

Cefotaxime sodium and aminoglycosides have been shown to be synergistic in vitro against some strains of pseudomonas aeruginosa but the clinical significance is unknown.

**TREATMENT:**

***MACFRAN*** is indicated for the treatment of patients with serious infections caused by susceptible strains of the designated microorganisms (as mentioned in the Microbiology section of this leaflet).

Lower respiratory tract infections, including pneumonia.
Genitourinary infections and Urinary tract infections. Also, uncomplicated gonorrhea (cervical/urethral and rectal).
Gynecologic infections, including pelvic inflammatory disease, endometritis and pelvic cellulitis.
Bacteremia/Septicemia.
Skin and skin structure infections.
Intra-abdominal infections.
Bone and/or joint infections.
Central nervous system infections, e.g., meningitis and ventriculitis.

***MACFRAN*** may be used concomitantly with an aminoglycoside. Renal function should be carefully monitored, especially if higher dosages of the aminoglycosides are to be administered or if therapy is prolonged, because of the potential nephrotoxicity and ototoxicity of aminoglycoside antibiotics.

**PREVENTION:**

The administration of ***MACFRAN*** preoperatively reduces the incidence of certain infections in patients undergoing surgical procedures (e.g., abdominal or vaginal hysterectomy, gastrointestinal and genitourinary tract surgery) that may be classified as contaminated or potentially contaminated. In patients undergoing cesarean section, intraoperative (after clamping the umbilical cord) and postoperative use of ***MACFRAN*** may also reduce the incidence of certain postoperative infections.

**CONTRAINDICATIONS:**

***MACFRAN*** is contraindicated in patients who have shown hypersensitivity to cefotaxime sodium or the cephalosporin group of antibiotics.

**WARNINGS:**

BEFORE THERAPY WITH CEFOTAXIME SODIUM IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFOTAXIME SODIUM, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN WITH CAUTION TO PATIENTS WITH TYPE I HYPERSENSITIVITY REACTIONS TO PENICILLIN. SERIOUS HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

**PRECAUTIONS:**

**General**

As with other antibiotics, prolonged use of ***MACFRAN*** may result in overgrowth of nonsusceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.
For courses of treatment lasting longer than 10 days, blood counts should therefore be monitored. ***MACFRAN***, like other parenteral anti-infective drugs, may be locally irritating to tissues. In most cases, perivascular extravasation of ***MACFRAN*** responds to changing of the infusion site. In rare instances, extensive perivascular extravasation of ***MACFRAN*** may result in tissue damage and require surgical treatment. To minimize the potential for tissue inflammation, infusion sites should be monitored regularly and changed when appropriate.

**DRUG INTERACTIONS:**

Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics.

**DRUG/LABORATORY TEST INTERACTIONS:**

Cephalosporins, including cefotaxime sodium, are known to occasionally induce a positive direct Coombs' test.

**Carcinogenesis, Mutagenesis:**

***MACFRAN*** was not mutagenic in the mouse micronucleus test or in the Ames test.
***MACFRAN*** did not impair fertility to rats when administered subcutaneously at doses up to 250 mg/kg/day or in mice when administered intravenously at doses up to 2000 mg/kg/day

**Pregnancy: Pregnancy Category B:**

No evidence of embryotoxicity or teratogenicity was seen in animal studies. There are no well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing Mothers**

***MACFRAN*** is excreted in human milk in low concentrations. Caution should be exercised when ***MACFRAN*** is administered to a nursing woman.

**Geriatric Use**

No overall differences in safety or effectiveness were observed. This drug 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 it may be useful to monitor renal function.

**ADVERSE REACTIONS:**

***MACFRAN*** is generally well tolerated. The most common adverse reactions have been local reactions following IM or IV injection. Hypersensitivity - Rash, pruritus, fever, eosinophilia and less frequently urticaria and anaphylaxis. Gastrointestinal - Colitis, diarrhea, nausea, and vomiting. Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

**Less frequent adverse reactions are:**

Cardiovascular System - Potentially life-threatening arrhythmias following rapid (less than 60 seconds) bolus administration via central venous catheter have been observed.

Hematologic System - Neutropenia, transient leukopenia, eosinophilia, thrombocytopenia and agranulocytosis have been reported. Some individuals have developed positive direct Coombs Tests during treatment with Cefotaxime sodium and other cephalosporin antibiotics. Rare cases of hemolytic anemia have been reported.

Genitourinary System - Moniliasis, vaginitis.

Central Nervous System - Headache.

Liver - Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase levels have been reported.

Kidney - As with some other cephalosporins, interstitial nephritis and transient elevations of BUN and creatinine have been occasionally observed.

Cutaneous-As with other cephalosporins, isolated cases of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported.

**OVERDOSAGE:**

The most frequent reactions were elevations of BUN and creatinine. Patients who receive an acute overdosage should be carefully observed and given supportive treatment.

**DOSAGE AND ADMINISTRATION**

**Adults**

Dosage and route of administration should be determined by susceptibility of the causative organisms, severity of the infection, and the condition of the patient). ***MACFRAN*** may be administered IM or IV after reconstitution. The maximum daily dosage should not exceed 12 grams.

**GUIDELINES FOR DOSAGE OF *MACFRAN*:**

| Type of Infection | Daily Dose | Frequency and Route |
|---|---|---|
| Gonococcal urethritis/ cervicitis in males and females | 500mg | 500mg IM (single dose) |
| Rectal gonorrhea in females | 500mg | 500mg IM (single dose) |
| Rectal gonorrhea in males | 1g | 1g IM (single dose) |
| Uncomplicated infections | 2g | 1g every 12 hours IM or IV |
| Moderate to severe infections | 3-6g | 1-2g every 8 hours IM or IV |
| Infections commonly needing antibiotics in higher dosage (e.g., septicemia) Life-threatening infections | 6-8g up to 12g | 2g every 6-8 hours IV 2g every 4 hours IV |

If C. trachomatis is a suspected pathogen, appropriate anti-chlamydial coverage should be added, because cefotaxime sodium has no activity against this organism.

To prevent postoperative infection in contaminated or potentially contaminated surgery, the recommended dose is a single 1 gram IM or IV administered 30 to 90 minutes prior to start of surgery.

**Cesarean Section Patients**

The first dose of 1 gram is administered intravenously as soon as the umbilical cord is clamped. The second and third doses should be given as 1 gram intravenously or intramuscularly at 6 and 12 hours after the first dose.

**Neonates, Infants and Children**

The following dosage schedule is recommended:

Neonates (birth to 1 month):

0-1 week of age 50 mg/kg per dose every 12 hours IV

1-4 weeks of age 50 mg/kg per dose every 8 hours IV

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

Infants and Children (1 month to 12 years):

For body weights less than 50 kg, the recommended daily dose is 50 to 180 mg/kg IM or IV body weight divided into four to six equal doses. The higher dosages should be used for more severe or serious infections, including meningitis. For body weights 50 kg or more, the usual adult dosage should be used; the maximum daily dosage should not exceed 12 grams.

**Geriatric Use**

This drug 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 it may be useful to monitor renal function.

**NOTE:** As with antibiotic therapy in general, administration of ***MACFRAN*** should be continued for a minimum of 48 to 72 hours after the patient defervesces or after evidence of bacterial eradication has been obtained; a minimum of 10 days of treatment is recommended for infections caused by Group A beta-hemolytic streptococci in order to guard against the risk of rheumatic fever or glomerulonephritis; frequent bacteriologic and clinical appraisal is necessary during therapy of chronic urinary tract infection and may be required for several months after therapy has been completed; persistent infections may require treatment of several weeks and doses smaller than those indicated above should not be used.

**ADMINISTRATION:**

*Intravenous administration*

The solution containing 250mg and 500mg in 2ml and 1g in 4ml of water for injection can be injected over a period of 3 to 5 minutes.

With an infusion system, a solution containing 2g in 100 ml saline or 5% glucose solution can be administered over a period of 50 minutes. For the shorter period infusion, a solution containing 2g in 40 ml saline or 5% glucose solution can be administered over a period of 20 minutes.

After reconstitution in water for injection, solution is chemically stable up to 12 hours at room temperature (not exceeding 25°C) and up to 24 hours at 2-8°C (in refrigerator). A pale yellowish color of the solution does not indicate impairment of the antibiotic activity.

*Intramuscular administration*

Cefotaxime 250mg to be diluted in 2ml water for injection or 1% lidocaine solution.

Cefotaxime 500mg to be diluted in 2ml water for injection or 1% lidocaine solution.

Cefotaxime 1g to be diluted in 4ml water for injection or 1% lidocaine solution.

1% lidocaine solution should only be used for intramuscular administration.

Solution should be injected well with in the body of a relatively large muscles such as the upper outer quadrant of the buttock (i.e., gluteus maximus); aspiration is necessary to avoid inadvertent injection into a blood vessel.

Individual IM doses of 2 grams may be given if the dose is divided and is administered in different intramuscular sites.

After reconstitution in water for injection, solution is chemically stable up to 8 hours at room temperature (not exceeding 25°C) and up to 24 hours at 2-8°C (in refrigerator).

**HOW SUPPLIED:**

***MACFRAN*** 250mg IM/IV Injection
Cefotaxime 250mg powder in a vial and 1 ampoule of 5ml water for injection.

***MACFRAN*** 500mg IM/IV Injection
Cefotaxime 500mg powder in a vial and 1 ampoule of 5ml water for injection.

***MACFRAN*** 1g IM/IV Injection
Cefotaxime 1g powder in a vial and 1 ampoule of 5ml water for injection.

خوراک وہدایات:

ڈاکٹر کے مشورے کے مطابق استعمال کریں۔ مزید تفصیلات کے لئے معلوماتی پرچہ کا مطالعہ کریں۔

روشنی سے محفوظ، 25°C سے کم درجہ حرارت پر رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور، ٹھنڈی اور خشک جگہ پر رکھیں۔

انجکشن کے لئے تازہ تیار کردہ محلول استعمال کریں۔ استعمال کی میعاد ختم ہونے پر دوا استعمال نہ کریں۔

وریدی انجکشن کے لئے وقت ۳ سے ۵ منٹ ہے۔

ISO 9001 : 2000 Certified Company

Manufactured by:

Macquin's

MACQUIN'S INTERNATIONAL
F-2/H, P.T.C. Industrial Complex,
S.I.T.E., KARACHI.

Marketed by:

CENRJY Pharmaceuticals
Karachi