Mefoxin is a broad-spectrum, semi-synthetic antibiotic for parenteral administration.

The new class of beta-lactam antibiotics, the cephemycins, is characterized by a 7 alpha-methoxy-beta-lactam. The methoxy group is responsible for the property of resistance to degradation by bacterial beta-lactamases (penicillinases and cephalosporinases). Side chains, attached by chemical modification of the basic cephemycin nucleus, determine some of the specific antibacterial actions and other properties.

**Indications**

**Treatment**

Mefoxin is indicated for the treatment of the following infections when due to susceptible organisms:
- Peritonitis and other intra-abdominal and intrapelvic infections
- Gynecological infections
- Septicemia
- Endocarditis
- Urinary tract infections, including uncomplicated gonorrhea
- Respiratory tract infections
- Bone and joint infections
- Skin and soft tissue infections

Mefoxin is a broad-spectrum bactericidal antibiotic indicated for the treatment of infections caused by susceptible strains of gram-positive and gram-negative pathogens both aerobic and anaerobic (see Microbiology). Mefoxin has been clinically effective not only in infections due to antibiotic-sensitive organisms, but also in infections due to organisms resistant to one or more of the following antibacterial agents: penicillin, ampicillin, carbenicillin, tetracyclines, erythromycin, chloramphenicol, cephalosporins, kanamycin, gentamicin, tobramycin, and sulfamethoxazole-trimethoprim.

Many gram-negative pathogens are resistant to penicillins and cephalosporins through the action of the beta-lactamases which are produced by these pathogens. Mefoxin is remarkably stable in the presence of these bacterial beta-lactamases, both penicillinases and cephalosporinases. Hence, the clinical efficacy of Mefoxin extents to many infections caused by such pathogens, of which the following are of particular clinical importance: *E. coli*; *Klebsiella*; *Proteus mirabilis*; *Proteus*, indole-positive (which include the organisms now called *Morganelli morganii* and *Proteus vulgaris*); *Serratia marcescens*; *Providencia* including *Providencia rettgeri*; and the anaerobic *Bacteroides fragilis*.

Mefoxin is indicated for the treatment of mixed infections caused by susceptible strains of aerobic and anaerobic bacteria. The majority of these mixed infections are associated with contamination by fecal flora as well as flora originating from the vagina, skin and mouth.

In these mixed infections, *Bacteroides fragilis* is the most commonly encountered anaerobic pathogen and is usually resistant to aminoglycosides, cephalosporins, and virtually all penicillins. However, *Bacteroides fragilis* is usually susceptible to Mefoxin.

Mefoxin is indicated for adjunctive therapy in the surgical treatment of infections, including abscesses, infection complicating hollow viscous perforations, cutaneous infections and infections of serous...
surfaces, whether caused by aerobes, mixed aerobes and anaerobes, or anaerobes. Clinical experience has demonstrated that Mefoxin can be administered to patients who are also receiving carbenicillin, kanamycin, gentamicin, tobramycin or amikacin (see Precautions and administration).

**Prophylaxis**

Mefoxin is indicated for the prevention of certain postoperative infections in patients undergoing surgical procedures that are classified as contaminated, potentially contaminated or where the occurrence of post-operative infection could be specially serious.

**Dosage and administration**

Mefoxin may be administered intravenously or intramuscularly (see reconstitution directions for each route below). Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organisms and conditions of the patient. Therapy may be started while awaiting the results of susceptibility testing.

**Treatment dosage**

**Adults**

The usual dosage is 1 g or 2 g of Mefoxin every 8 hours.

### Usual adult dosage

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>Dose</th>
<th>Frequency</th>
<th>Total daily dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated</td>
<td>1 g</td>
<td>every 8 hours</td>
<td>3 g (4 g)</td>
</tr>
<tr>
<td>Moderate severe or severe</td>
<td>2 g</td>
<td>every 8 hours (occasionally every 6 hrs)</td>
<td>6 g (8 g)</td>
</tr>
<tr>
<td>Infections generally needing antibiotics in higher dosage</td>
<td>3 g</td>
<td>(every 4 hours)</td>
<td>12 g (2 g)</td>
</tr>
</tbody>
</table>

In adults with renal insufficiency, an initial loading dose of 1 g to 2 g may be given. After a loading dose, the recommendations for maintenance dosage may be used as a guide. In patients undergoing hemodialysis, the loading dose of 1-2 g should be given after each hemodialysis and the maintenance dose should be given as indicated in the table below.

<table>
<thead>
<tr>
<th>Renal function</th>
<th>Creatinine clearance (ml/min)</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild impairment</td>
<td>50-30</td>
<td>1-2 g</td>
<td>every 8-12 hrs</td>
</tr>
<tr>
<td>Moderate impairment</td>
<td>29-10</td>
<td>1-2 g</td>
<td>every 12-24 hrs</td>
</tr>
<tr>
<td>Severe impairment</td>
<td>9-5</td>
<td>0.5-1 g</td>
<td>every 12-24 hrs</td>
</tr>
<tr>
<td>Essentially no function</td>
<td>15</td>
<td>0.5-1 g</td>
<td>every 24-48 hrs</td>
</tr>
</tbody>
</table>

**Uncomplicated urinary tract infections**

In uncomplicated urinary tract infections due to susceptible organisms, 1 g intramuscularly twice a day has been shown to be effective.

**Uncomplicated gonorrhea**

For single dose therapy of uncomplicated gonorrhea, including that caused by penicillinase-producing strains, the recommended dose is 2 g of Mefoxin intramuscularly given with 1 g of probenecid by mouth (at the same time or up to 1 hour before).

<table>
<thead>
<tr>
<th>Age group</th>
<th>Do not exceed 12 g per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 week of age</td>
<td>20-40 mg/kg</td>
</tr>
<tr>
<td>1-4 weeks of age</td>
<td>20-40 mg/kg</td>
</tr>
<tr>
<td>Infants</td>
<td>20-40 mg/kg</td>
</tr>
<tr>
<td>Children</td>
<td>20-40 mg/kg</td>
</tr>
</tbody>
</table>

In severe infections, the total daily dosage may be increased to 200 mg/kg, but not to exceed 12 g per day.

Mefoxin is not recommended for the therapy of meningitis. If meningitis is suspected, an appropriate antibiotic should be used.

In children with renal insufficiency the dosage frequency should be reduced as indicated for adults.

**** See warning for neonates under “Administration”.

**Prophylaxis dosage**

For prophylactic use in surgery, the following doses are recommended:
General surgery

Adults
2 grams administered intramuscularly or intravenously 1/2 to 1 hour before initial incision; then 2 grams every 6 hours. Ordinarily, prophylactic therapy does not extend beyond 24 hours.

Neonates**, infants and children
In case of infants and children, 30-40 mg/kg doses may be given at times designated above. However, in neonates 30-40 mg/kg doses may be given one-half to 1 hour before initial incision and the second and third dose may be given every 8-12 hours.

Obstetric-gynecologic
For patients undergoing caesarian section a single 2 gram dose should be administered intravenously as soon as the umbilical cord is clamped.
For prophylactic use in gynecologic surgical procedures a single 2 gram dose administered intravenously or intramuscularly one-half to one hour prior to surgery has been effective.
For prolonged or heavily contaminated procedures, additional 2 gram doses may be given at 6 hour intervals. Ordinarily, prophylactic therapy does not extend beyond 24 hours.
**See warning for neonates under “Administration”.

Administration

Warning for neonates
Solutions containing preservatives should not be used for injection or for flushing catheters in treating neonates.
Benzy alcohol as a preservative in Bacteriostatic Water for Injection and Bacteriostatic Sodium Chloride Injection has been associated with toxicity in neonates. Data are unavailable on the toxicity of other preservatives in this age group.
Therefore, any diluent used with Mefoxin in the treatment of neonates should be free of any preservative.

Intravenous administration
Reconstitute Mefoxin with Sterile Water for Injection: 1 g is soluble in 2 ml. Although Mefoxin is very soluble, for intravenous use it is preferable to add 10 ml of Sterile Water for Injection to the 1 g vial or to the 2 g vial. Shake to dissolve and then withdraw entire contents of vial into syringe. For direct intravenous injection, Mefoxin may be slowly injected into the vein over a period of 3 to 5 minutes or may be given through the tubing when the patient is receiving parenteral solutions. An intermittent intravenous infusion of Mefoxin may be employed when large amounts of fluid are to be given. However, during infusion of the solution containing Mefoxin, it may be advisable temporarily to discontinue administration of any other infusion solution at the same site (by using an appropriate IV infusion set).
A solution of Mefoxin may also be given by continuous intravenous infusion (see below for compatibility and stability).

Intramuscular administration only
Reconstitute Mefoxin 1 g with 2 ml of Sterile Water for Injection, or 0.5 percent or 1 percent lidocaine HCL (without epinephrine) solution. For the 0.5 g dosage form, one half the volume of diluent recommended for 1 g cefoxitin may be used. Mefoxin is given by deep injection into a large muscle mass. Avoid injection into a blood vessel.

Note: Some patients may be hypersensitive to lidocaine.

Preparation of solution
The following table is provided for convenience in constituting Mefoxin for both intravenous and intramuscular administration.

<table>
<thead>
<tr>
<th>Strength</th>
<th>Amount of diluent to be added (ml++)</th>
<th>Approximate average concentration (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 g vial</td>
<td>I.V. 2</td>
<td>I.M. 400</td>
</tr>
<tr>
<td>1 g vial</td>
<td>I.V. 10</td>
<td>I.M. 95</td>
</tr>
<tr>
<td>2 g vial</td>
<td>I.V. 10 or 20</td>
<td>I.M. 180 or 95</td>
</tr>
<tr>
<td>1 g Infusion Bottle</td>
<td>50 to 100</td>
<td>I.M. 20 to 40</td>
</tr>
<tr>
<td>2 g Infusion Bottle</td>
<td>50 to 100</td>
<td>I.M. 40 to 20</td>
</tr>
</tbody>
</table>

++Shake to dissolve and let stand until clear.

Compatibility and stability
The compatibility and stability of cefoxitin sodium in
solution with the following series of frequently used intravenous infusion fluids and injectable additives have been established:

- 0.9% Sodium Chloride Injection
- 5% or 10% Dextrose Injection
- 5% Dextrose and 0.9% Sodium Chloride Injection
- 5% Dextrose Injection with 0.02% sodium bicarbonate solution
- 5% Dextrose Injection with 0.2% or 0.45% saline solution
- Lactated Ringer’s Injection
- 5% dextrose in Lactated Ringer’s Injection
- 5% or 10% invert sugar in water
- 10% invert sugar in saline solution
- 5% Sodium Bicarbonate Injection
- M/6 sodium lactate solution
- Insulin in normal saline
- Insulin in 10% invert sugar
- Heparin, 100 units/ml and 0.1 unit/ml
- Mannitol 2.5% and 5%
- Mannitol 10%

Mefoxin has been shown to be chemically and visually compatible with aminoglycosides such as amikacin, gentamicin, kanamycin, and tobramycin when admixed in 200 ml of 0.9% sodium chloride or 5% dextrose in water.

Mefoxin, as constituted with Sterile Water for Injection, Bacteriostatic Water for Injection** preserved with parabens or benzyl alcohol, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, or 0.5% and 1.0% lidocaine HCL (preserve paraben), maintains satisfactory potency for 24 hours at room temperature, for one week under refrigeration (below 5°C) and for at least 30 weeks in the frozen state and will maintain potency immediately after thawing and for at least 24 hours at room temperature thereafter. After constitution with Sterile Water for Injection and subsequent storage in disposable plastic syringes, Mefoxin is stable for 24 hours at room temperature and 48 hours under refrigeration. After the periods mentioned above, any unused solutions or frozen material should be discarded. Do not refreeze.

Note: Mefoxin in the dry state should be stored below 30°C. Avoid exposure to temperature above 50°C. The dry material as well as solutions tends to darken, depending on storage conditions; product potency, however, is not adversely affected.

**Contraindications**

Mefoxin is contraindicated in persons who have shown hypersensitivity to cefoxitin. In the absence of clinical experience, Mefoxin should not be administered to patients who have shown hypersensitivity to cephalosporins.

**Precautions**

There is some clinical and laboratory evidence of partial cross-allergenicity between cephemycins and the other beta-lactam antibiotics, penicillins and cephalosporins. Severe reactions (including anaphylaxis) have been reported with most beta-lactam antibiotics.

Before therapy with Mefoxin, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. Mefoxin should be given cautiously to penicillin allergic patients. Any patient who has demonstrated some form of allergy, particularly to drugs, should be given antibiotics cautiously. If an allergic reaction to Mefoxin occurs, the drug should be discontinued. Pseudomembranous colitis has been reported with virtually all antibiotics. This colitis can range from mild to life threatening in severity. Antibiotics should therefore be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. It is important to consider a diagnosis of pseudomembranous colitis in patients who develop diarrhea in association with antibiotic use. While studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis, other causes should also be considered.

The total daily dosage should be reduced when Mefoxin is administered to patients with transient or persistent reduction of urinary output due to renal insufficiency (see Dosage and Administration) because high and prolonged serum antibiotic concentrations can occur from usual doses.
Interference with laboratory tests
A false-positive reaction to glucose in the urine may occur with reducing substances but not with the use of specific glucose oxidase methods. Using the Jaffe Technique, falsely high creatinine values in serum may occur if Mefoxin serum concentrations exceed 100 mcg/ml. Serum samples from patients treated with Mefoxin should not be analysed for creatinine if withdrawn within two hours of drug administration. High concentrations of cefoxitin in the urine may interfere with measurement of urinary 17-hydroxy-corticosteroids by the Porter-Silber reaction, and produce false increases of modest degree in the levels reported.

Use in pregnancy
There are no controlled studies in pregnant women. Use of the drug during pregnancy requires that the anticipated benefits be weighed against possible hazards.

Nursing mothers
Mefoxin is excreted in human milk. Caution should be exercised if use is indicated.

Side effects
Mefoxin is generally well tolerated. Side effects rarely required cessation of treatment and usually have been mild and transient. The most common side effects have been local reactions following intravenous or intramuscular injection.

Local reactions
Thrombophlebitis has occurred with intravenous administration. Pain, induration, and tenderness after intramuscular injections have been reported.

Allergic
Rash (including exfoliative dermatitis), urticaria, pruritus, fever and other allergic reactions (including anaphylaxis) have been noted.

Cardiovascular
Hypotension.

Gastrointestinal
Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Hematologic
Eosinophilia, leukopenia, including granulocytopenia, neutropenia, anemia (including hemolytic anemia), thrombocytopenia and bone marrow depression have been reported. Some individuals, particularly those with azotemia, may develop positive direct Coombs tests during therapy with Mefoxin.

Hepatic function
Transient elevations in SGOT, SGPT, serum LDH, serum alkaline phosphatase, and jaundice have been reported.

Renal function
Elevations in serum creatinine and/or blood urea nitrogen levels have been observed. As with the cephalosporins, acute renal failure has been reported rarely. The role of Mefoxin in changes in renal function tests is difficult to assess since factors predisposing to pre-renal azotemia or to impaired renal function usually have been present.

Microbiology
Mefoxin has a broad spectrum of antibacterial activity against gram-positive and gram-negative pathogens, both aerobic and anaerobic. Mefoxin inhibits bacterial cell wall synthesis and is bactericidal. The unique molecular structure of Mefoxin gives it a particularly high degree of resistance to beta-lactamases, a major mechanism of bacterial resistance to penicillins and cephalosporins. A high percentage of gram-negative rods which are beta-lactamase producing and resistant to penicillins or cephalosporins is susceptible to Mefoxin. In addition, a high percentage of penicillinase-producing penicillin-resistant gram-positive and gram-negative cocci is susceptible to Mefoxin. With respect to the clinical reliability and predictability of Mefoxin, analysis of the overall clinical experience with this antibiotic revealed a high correlation between the results of sensitivity tests with Mefoxin, the bacteriological efficacy of the antibiotic in man, and the clinical efficacy of the antibiotic.
Mefoxin is active against the following microorganisms *in vitro*:
Mefoxin is not active against *Pseudomonas* spp., most strains of enterococci, many strains of *Enterobacter cloacae*, methicillin-resistant staphylococci and *Listeria monocytogenes*.
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