

**ROCEPHIN® (ceftriaxone sodium) FOR INJECTION**

**B.ony**

To reduce the dosing of drug-resistant bacteria and maintain the effectiveness of Rocephin and other antibacterial drugs, Rocephin should be used only to treat or pre- vent infections that are proven or strongly suspected to be caused by bacteria.

**DESCRIPTION**: Rocephin is a sterile, semisynthetic, broad-spectrum cephalosporin antibiotic. For intravenous administration, Rocephin solutions range from light yellow to yellow-orange to deep yellow, depending on the concentration. The color of Rocephin solutions ranges from light yellow to yellow-orange to deep yellow.

**CLINICAL PHARMACOLOGY**: Average plasma concentrations of ceftriaxone following a single 30-minute intravenous (IV) infusion of a 0.5, 1 or 2 gm dose and intramuscular (IM) administration of a single 0.5, 1, 2.5 or 5 gm dose in healthy adult subjects are presented in Table 1.

- **Average plasma concentrations (µg/mL)**
  - **IV**
    - **0.5 gm**
      - 56 48 40 36 29 23 15 10 5
    - **1 gm**
      - 104 82 68 56 50 44 37 31 26
    - **2 gm**
      - 208 164 131 108 96 82 71 63 56
  - **IM**
    - **0.5 gm**
      - 50 42 35 30 26 21 16 12 8
    - **1 gm**
      - 100 80 68 56 48 44 37 31 26
    - **2.5 gm**
      - 150 120 100 84 75 68 56 48 44
    - **5 gm**
      - 250 200 160 131 120 100 84 75 68

**ROCEPHIN® (ceftriaxone sodium)**

<table>
<thead>
<tr>
<th>Time after dose (hr)</th>
<th>0.5 (± 0.2)</th>
<th>1 (± 0.3)</th>
<th>2 (± 0.8)</th>
<th>3 (± 1.6)</th>
<th>4 (± 2.4)</th>
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<tbody>
<tr>
<td>3.3 (± 1.4)</td>
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**Table 2. Urinary Concentrations of Ceftriaxone After Single Dose Administration**

**MIC**

<table>
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<th>MIC (µg/mL)</th>
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</thead>
<tbody>
<tr>
<td>(S) 2 ≤ 4</td>
</tr>
<tr>
<td>(I) 4 ≤ 8</td>
</tr>
<tr>
<td>(R) &gt; 8</td>
</tr>
</tbody>
</table>

**Table 3. Average Pharmacokinetic Parameters of Ceftriaxone in Pediatric Patients With Infections**

- **Maximum Plasma Concentrations (µg/mL)**
  - **50 mg/min IV**
    - **125 mg IV**
      - 216
    - **250 mg IV**
      - 275
  - **5 mg/min IV**
    - **12.5 mg/kg IV**
      - 216
  - **6.25 mg/kg IV**
    - **12.5 mg/kg IV**
      - 275
  - **12.5 mg/kg IV**
    - **25 mg/kg IV**
      - 216

**Table 4. Average Pharmacokinetic Parameters of Ceftriaxone in Humans**

- **Subject Group**
  - **0-5**
    - **6-12**
  - **12-18**
  - **18-65**
  - **65+**

**Pharmacokinetics in the Middle East Field**: In one study, total ceftriaxone concentrations in plasma and urine were obtained from 25 healthy subjects in Egypt who received a single 500 mg IV dose of ceftriaxone sodium. The median plasma concentration of ceftriaxone was 10.6 µg/mL at 2 hours post-dose. Ceftriaxone concentrations were highest in plasma and urine, with the highest concentrations occurring between 2 and 3 hours postdosing. Multiple IV or IM doses were infused at a constant rate over 30 minutes.

**Additional Information**

- The color of Rocephin solutions ranges from light yellow to yellow-orange to deep yellow.
- The concentration of Rocephin solutions is approximately 6.7.

**NURSING CONSIDERATIONS**

- Avoid direct contact with the drug, as it may cause skin reactions.
- Monitor the patient for signs of allergic reactions.
- Be aware of the patient's history and medical conditions, especially those related to the use of beta-lactam antibiotics.
- Familiarize the patient with the side effects of ceftriaxone, such as allergic reactions, fever, and skin reactions.
- Ensure the patient's compliance with the prescribed regimen.
- Monitor the patient's response to the treatment.

**ADVERSE REACTIONS**

- **Skin reactions**: Hives, rash, pruritus, urticaria, redness, and swelling.
- **Infections**: Upper respiratory tract infections, sinusitis, bronchitis, community-acquired pneumonia, and skin infections.
- **Allergic reactions**: Anaphylaxis, bronchospasm, hypotension, and urticaria.
- **Central nervous system effects**: Headache, dizziness, and seizures.
- **Gastrointestinal effects**: Nausea, vomiting, and diarrhea.
- **Hematological effects**: Leukopenia, neutropenia, and anemia.
- **Hepatic and renal effects**: Hepatitis, renal failure, and hyperbilirubinemia.
- **Other effects**: Pseudomembranous colitis, Clostridium difficile infection, and superinfection.

**INTERACTIONS**

- **Drug interactions**: Cimetidine, erythromycin, and rifampin may increase the risk of adverse reactions.
- **Pharmacokinetic interactions**: Coadministration of ceftriaxone with other drugs, such as corticosteroids, may alter the drug's clearance.

**DOSAGE AND ADMINISTRATION**

- **Adults**: IV or IM administration is recommended for most adults.
- **Children**: The recommended dosage varies based on age and weight.
- **Elderly**: The dosage may need to be adjusted due to age-related changes in renal function.

**CONTRAINDICATIONS**

- **Known hypersensitivity to ceftriaxone or other cephalosporins.
- **Severe renal impairment (creatinine clearance <30 mL/min)**
- **Active skin infections**
- **Recent surgery or trauma**

**WARNINGS**

- **Immediate hypersensitivity reactions**
- **Central nervous system effects**
- **Hematological effects**

**PRECAUTIONS**

- **Careful monitoring of renal function**
- **Hemoglobin and platelet monitoring**
- **Liver function tests**

**REFERENCES**

- Roche Laboratories, 1998-2004. All rights reserved.
For preparative use (surgical prophylaxis), a single dose of 1 gram administered intravenously 1 to 2 hours before surgery is recommended.

PREPARATION AND ADMINISTRATION: Intravenous infusions, the recommended total daily dose is 50 to 75 mg given in divided doses every 12 hours. The total daily dose should not exceed 2 grams.

In the treatment of meningitis, it is recommended that the initial therapeutic dose be 100 mg/kg (not to exceed 2 grams) daily given in divided doses every 12 hours. The maximum duration of therapy is 7 to 14 days.

Genetic counseling should be continued for at least 2 days after the signs and symptoms of infection have disappeared. The usual duration of therapy is 4 to 14 days.

When treating infections caused by Streptococcus pneumonia, therapy should be continued at least 10 days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function; however, blood levels should be monitored in patients with severe renal impairment (patients in and out of the hospital) by measuring and monitoring ceftriaxone plasma levels. When the calculated renal clearance is less than 10 mL/min and serum creatinine is above 2 mg/dL, the dosage should be reduced. Concomitant diuretic therapy may be necessary to minimize the risk of hyperkalemia.

Ceftazidime intravenous infusion should be given to management with fluids and electrolytes, protein supplementation and therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually resolve spontaneously and are managed with oral antisepsis. However, for severe and life-threatening colitis, metronidazole or vancomycin (in resistant cases) should be administered.

ANIMAL PHARMACOLOGY: Concentrations of the predicted daily oral dose of Rocephin have been found in bile of gnotobiotic dogs and baboons treated with Rocephin. These appeared as a gritty sediment in dogs that received 100 mg/kg for 4 weeks. A similar phenomenon has been observed in baboons but only after oral dosing being given every 12 hours at doses of 200 mg/kg (500 mg/kg of Rocephin) for 6 weeks. The therapeutic concentrations of ceftriaxone were observed in bile and urine suggesting that for a drug to have an impact in the gut, it needs to be present in the bile. These studies indicated that Rocephin will provide therapeutic concentrations in the gut and should be effective in cases of pseudomembranous colitis.

HOW SUPPLIED: Rocephin is supplied as a sterile crystalline powder in glass vials and piggyback bottle. The following packages are available:

Vials containing 250 mg equivalent of ceftriaxone of Box 1 (NDC 0004-1964-01) and box of 10 (NDC 0004-1964-01)

Vials containing 500 mg equivalent of ceftriaxone of Box 1 (NDC 0004-1964-04) and box of 10 (NDC 0004-1964-01)

Piggyback bottle containing 1 gm equivalent of ceftriaxone of Box 1 (NDC 0004-1964-02)

Vials containing 2 gm equivalent of ceftriaxone of Box 1 (NDC 0004-1964-01)

Piggyback bottles containing 2 gm equivalent of ceftriaxone of Box 1 (NDC 0004-1964-01)

Blister primary containers, containing 10 gm equivalent of ceftriaxone of Box 1 (NDC 0004-1571-01), NOT FOR DIRECT ADMINISTRATION.

Rocephin is also supplied as a sterile crystalline powder in Ampicillin vials as follows:

Ampicillin Vials containing 1 gm equivalent of ceftriaxone of Box 1 (NDC 0004-1964-05)

Ampicillin Vials containing 2 gm equivalent of ceftriaxone of Box 1 (NDC 0004-1964-05)

NOTE: Rocephin sterile powder should be stored at room temperature (77°F / 25°C) or below and protected from light.

Rocephin is also supplied as a crystalline powder in Ampicillin vials, isomeric with approximately 1.2 gm Hydrocortisone, USP (NDC 0004-1965-03).

2 gm equivalent of ceftriaxone, isomeric with approximately 1.2 gm Hydrocortisone, USP (NDC 0004-1965-03).

2 gm equivalent of ceftriaxone, isomeric with approximately 1.2 gm Hydrocortisone, USP (NDC 0004-1965-03).

Rocephin should be stored at or below 20°-30°F (−6°-8°C).

Rocephin is registered trademark of Roche Laboratories, Inc. Rocephin is manufactured by Roche Laboratories Inc, by Biocyte Healthcare Corporation, Darien, Illinois 60015.

The following strengths are available:

1 gm equivalent of ceftriaxone, isomeric with approximately 1.2 gm Hydrocortisone, USP (NDC 0004-1969-02).

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Roche Laboratories Inc, 100 Kings Road, Nutley, NJ 07110-1357.
**DESCRIPTION:**
Rocephin is a sterile, semisynthetic broad-spectrum cephalosporin antibiotic for intravenous or intramuscular administration. It contains 250 mg, 500 mg, 1 gm or 2 gm as powder for reconstitution and solution for injection.

**PHARMACOLOGY:**
The chemical formula of ceftriaxone is C_{17}H_{19}N_{5}O_{5}S (3H). It has a calculated molecular weight of 661.59 and the following structural formula:

\[ \text{C}_{17}\text{H}_{19}\text{N}_{5}\text{O}_{5}\text{S} \]

**TEST MEDIA (HTM):**
The plastic container is impregnated with 30 µg of ceftriaxone to test the susceptibility of microorganisms to ceftriaxone.

**CLINICAL TRIALS:**
The following interpretive criteria should be used when testing susceptibility of microorganisms to ceftriaxone.

**RESISTANCE:**
The following interpretive criteria should be used when testing Staphylococcus spp other than Staphylococcus pneumoniae using Muller-Hinton agar supplemented with 5% sheep blood inoculated in 0.5% C2.

**MICROSCOPY:**
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Staphylococcus haemolyticus*
- *Staphylococcus pyogenes*

**INTERPRETATION:**
Rocephin is appropriate for the treatment of infections caused by the following organisms:

- *Escherichia coli*
- *Proteus mirabilis*
- *Providencia stuartii*
- *Enterobacter cloacae*
- *Klebsiella pneumoniae*
- *Serratia marcescens*
- *Citrobacter freundii*
- *Serratia liquefaciens*
- *Providencia rettgeri*

**SIDE EFFECTS:**
Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics or in patients who have had an anaphylactic reaction to penicillins.

**INTERCONNECTIONS:**
Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics or in patients who have had an anaphylactic reaction to penicillins.

**INFORMATION FOR PATIENTS:**
- Do not discontinue treatment before completing the full course of medication as directed by your healthcare provider.
- Avoid contact with animals or pets that are also receiving Rocephin.
- Inform healthcare providers about any allergies or previous reactions to Rocephin or other cephalosporins before initiating treatment.

**REFERENCES:**

**APPENDIX:**
- A detailed table summarizing the clinical trials data and interpretive criteria for susceptibility testing of microorganisms to ceftriaxone is included as an appendix.

**NOTES:**
- The information provided is based on the latest available data and should be consulted for specific recommendations.
- Updates and modifications may be necessary based on ongoing research and clinical observations.

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PRECAUTIONS: Prescribing Rocephin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Although transient elevations of ALT and plasma creatinine have been observed, at the recommended dosage, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is also excreted in cord blood; therefore, caution should be exercised when administering Rocephin to neonates, infants and pediatric patients. In particular, infants and pediatric patients have been established for the dosages described in the DOSAGE AND ADMINISTRATION section. In vitro studies have shown that ceftriaxone, like other cephalosporins, can displace bilirubin from albumin. Rocephin is not expected to displace bilirubin from albumin.

There are no data with Rocephin in animal reproduction studies. It is also not known whether Rocephin can cause fetal harm when administered to a pregnant woman. It is generally recommended that pregnant women not receive Rocephin.

There have been reports of sonographic abnormalities in the gallbladder of patients treated with Rocephin; some of these patients also had symptoms of gallbladder disease. These abnormalities appear on sonograms as a diffuse wall thickening without acoustic shadowing suggesting a solid, rather than a cystic, lesion. Sonography, which was considered to be related to Rocephin therapy or of uncertain etiology, were observed: thickened gallbladder wall, sludging, and a shadowy area in the gallbladder lumen.

Children: Safety and effectiveness in children have not been established. Use in pediatric patients is only for rare situations in which the benefits outweigh the risks.

OVERDOSAGE:

In the case of overdosage, drug concentration would not be reduced by hemodialysis or peritoneal dialysis. Treatment may consist of evacuation of the stomach followed by saline or other diuretics. The condition appears to be self-limited with resolution of skin and soft-tissue infections in several days.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered drug related, were reported: anaphylactic, anaphylactoid and urticarial reactions; rash and exfoliative dermatitis; urticaria, pruritus, angioedema, alopecia, hypotension, hypertension, tachycardia, chest pain, dyspnea, hyperventilation syndrome, somnolence, autism, visual disturbances, vertigo, weakness, tremor, agitation, anxiety, depression, paresthesia, ataxia, rash, pruritus, fever, chills, arthralgia, headache, asthenia, myalgia, back pain, nausea, vomiting, diarrhea, jaundice, transaminase elevations, increases in alkaline phosphatase, increased prothrombin time, increased bilirubin, increased LDL cholesterol, increased triglycerides, increased creatine phosphokinase and increased AST.

In clinical studies, the following adverse reactions were noted: headache or dizziness were reported occasionally (<1%).

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For prophylactic use (surgical prophyllaxis), a single dose of 1 gram administered intramuscularly 1 to 2 hours before surgery is recommended.

In clinical trials, the following adverse reactions were reported (at least 2 times more frequently than in placebo-treated patients): malaise, headache, rash, pruritus, arthralgia, myalgia, back pain, nausea, vomiting, diarrhea, anaphylactic, angioedema, urticaria, rash, paresthesia, myalgia, vomiting, abdominal pain. Infections have occurred in wound infections (5 cases), tooth abscesses, and chronic otitis media.

In children, the following adverse reactions were noted: headache or dizziness were reported occasionally (<1%).

For the treatment of acute bacterial otitis media, a single intramuscular dose of 50 mg/kg (not to exceed 1 gram) is recommended (see INDICATIONS AND USAGE).

For the treatment of serious purulent infections such as meningitis, the recommended total daily dose is 50 to 75 mg/kg given once a day (or in 2 equally divided doses twice a day). The usual duration of therapy is 7 to 14 days.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended. For prophylactic use (surgical prophylaxis), a single dose of 1 gram administered intramuscularly 1 to 2 hours before surgery is recommended.

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