



August 2007

## **IMPORTANT CLARIFICATION OF PRESCRIBING INFORMATION**

Dear Healthcare Professional:

In a letter dated June 2007, Roche advised you of a recent update to the Rocephin® (ceftriaxone sodium) for Injection Prescribing Information that provided new information in the CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections describing the potential risk associated with concomitant use of Rocephin with calcium or calcium-containing solutions or products.

Since then, additional changes have been made to the Prescribing Information to further clarify the subject of that update.

Although there are no reports to date of intravascular or pulmonary precipitations in patients, other than neonates, treated with ceftriaxone and calcium-containing IV solutions, the theoretical possibility exists for an interaction between ceftriaxone and IV calcium-containing solutions in patients other than neonates. Therefore, Rocephin and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites. As a further theoretical consideration and based on 5 half-lives of ceftriaxone, Rocephin and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient.

No data are available on potential interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and calcium-containing products (IV or oral).

Accordingly, we wish to advise you that we have updated the Rocephin Prescribing Information to provide clarity regarding this subject. **The sections of the Prescribing Information affected by this new update now read as follows (please refer to the enclosed Prescribing Information for the full text of all information contained within these sections):**

### **CONTRAINDICATIONS**

#### **Neonates ( $\leq 28$ days)**

**Rocephin must not be co-administered with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition, in neonates because of the risk of precipitation of ceftriaxone-calcium salt.** Cases of fatal reactions with ceftriaxone-calcium precipitates in lung and kidneys in neonates have been described. In some cases the infusion lines and the times of administration of ceftriaxone and calcium-containing solutions differed.

For information regarding all other patients, see **WARNINGS**.

## **WARNINGS**

### **Interaction with Calcium-Containing Products**

There are no reports to date of intravascular or pulmonary precipitations in patients, other than neonates, treated with ceftriaxone and calcium-containing IV solutions. However, the theoretical possibility exists for an interaction between ceftriaxone and IV calcium-containing solutions in patients other than neonates. Therefore, Rocephin and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites. As a further theoretical consideration and based on 5 half-lives of ceftriaxone, Rocephin and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient (see **CONTRAINDICATIONS** and **DOSAGE AND ADMINISTRATION**).

No data are available on potential interaction between ceftriaxone and oral calcium-containing products or interaction between intramuscular ceftriaxone and calcium-containing products (IV or oral).

## **DOSAGE AND ADMINISTRATION**

Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute Rocephin. Particulate formation can result. Rocephin and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites (see **CONTRAINDICATIONS** and **WARNINGS**).

*NEONATES*: Hyperbilirubinemic neonates, especially prematures, should not be treated with Rocephin (see **CONTRAINDICATIONS**).

Note: A new subsection entitled "*NEONATES*" has been added to the **DOSAGE AND ADMINISTRATION** section of the Prescribing Information and the subsections have been reordered beginning with the presentation of information for neonates followed by the information for pediatric patients and adults. In addition, information within the subsection entitled "*COMPATIBILITY AND STABILITY*" has been reordered beginning with the presentation of information about compatibility followed by the information about stability.

Updated Prescribing Information is enclosed for your information. In addition, healthcare professionals can access the revised Rocephin Prescribing Information at <http://www.rocheusa.com/products/rocephin>.

We encourage you to become familiar with these changes in the Prescribing Information. If you have any questions or require additional information concerning Rocephin, please contact the Roche Pharmaceuticals Service Center at 1-800-526-6367.

Roche will continue to monitor the safety of Rocephin through established reporting mechanisms and notify regulatory authorities of any serious adverse events for evaluation. We will continue to provide you with the most current Prescribing Information for Rocephin moving forward. You can assist us in monitoring the safety of Rocephin by reporting adverse reactions to us at 1-800-526-6367 or by FAX at 1-800-532-3931; or to the FDA at [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or by mail to MedWatch, HF-2, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20851.

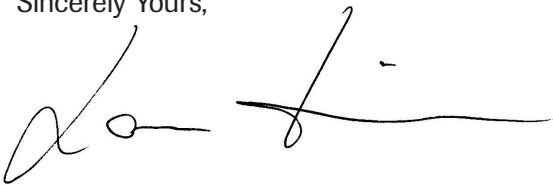
**Safety Information**

Rocephin is indicated for the treatment of lower respiratory tract infections, urinary tract infections, bacterial septicemia, skin/skin structure infections, bone and joint infections, pelvic inflammatory disease, uncomplicated gonorrhea, intra-abdominal infections, acute bacterial otitis media and meningitis when caused by susceptible organisms (please see the Prescribing Information for a list of susceptible organisms). Rocephin is also indicated for surgical prophylaxis in patients undergoing certain surgical procedures (please see the Prescribing Information for a description of these surgical procedures).

Adverse clinical effects in adults occur at levels similar to those of other cephalosporins: diarrhea (2.7%), rash (1.7%) and local reactions ( $\leq 1\%$ ). Rocephin is contraindicated in patients with a known allergy to cephalosporins and should be used cautiously in penicillin-sensitive patients.

Hyperbilirubinemic neonates, especially prematures, should not be treated with Rocephin. Rocephin must not be co-administered with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition, in neonates because of the risk of precipitation of ceftriaxone-calcium salt. Rocephin and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites. Rocephin and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient.

Sincerely Yours,

A handwritten signature in black ink, appearing to read 'Lars Birgerson', with a long horizontal flourish extending to the right.

Lars Birgerson, M.D., Ph.D.  
Vice President  
Medical Affairs

Enclosure: Prescribing Information for Rocephin<sup>®</sup> (ceftriaxone sodium) for Injection