

## IMPORTANT MEDICINE SAFETY INFORMATION

30 June 2008

Dear Healthcare Professional

### **New information regarding the potential risk associated with concomitant use of ceftriaxone with calcium-containing solutions or products.**

Cases of neonatal deaths associated with calcium-ceftriaxone precipitates in the lungs and kidneys have been described worldwide. In some of these cases ceftriaxone and the calcium-containing solutions or medications were administered by different routes and at different times.

The prescribing information of ceftriaxone-containing products listed below has been amended to include new safety information under the sections **Contra-indications, Warnings, Side-effects and special precautions and Dosage and directions for use**, describing the potential risk associated with concomitant use of ceftriaxone with calcium-containing solutions or products.

New information has been added to the prescribing information for ceftriaxone-containing products under the **Contra-indications** section as follows:

Hyperbilirubinemic neonates, especially prematures, should not be treated with the ceftriaxone-containing products listed below. In vitro studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin and bilirubin encephalopathy can possibly develop in these patients.

Ceftriaxone-containing products should not be administered concurrently with calcium-containing solutions or products in newborns because of the risk of precipitation of ceftriaxone-calcium salt (see **Warnings**).

New information has been added to the prescribing information under the **Warnings** section as follows:

**Ceftriaxone (TRADE NAMES listed below) must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines. Calcium-containing solutions or products must not be administered within 48 hours of last administration of ceftriaxone (TRADE NAMES listed below).**

**Cases of fatal reactions with calcium-ceftriaxone precipitates in lung and kidneys in both term and premature neonates have been described. In some cases the infusion lines and times of administration of ceftriaxone and calcium-containing solutions differed (see Contra-indications and Side-effects).**

**Do not use diluents containing calcium, such as Ringer's solution or Hartman's solution to reconstitute the below-mentioned ceftriaxone-containing products. Particulate formation can result.**

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, the below-mentioned ceftriaxone-containing products 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, the below-mentioned ceftriaxone-containing products and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient (see **Contra-indications** and **Dosage and directions for use**).

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).

New information has been added to the prescribing information under **Dosage and directions for use** as follows:

See **Incompatibilities** and sections on how ceftriaxone should be reconstituted. Calcium-containing solutions are not among the appropriate solutions described for reconstitution, due to possible incompatibility.

Do not use diluents containing calcium, such as Ringer's solution or Hartman's solution to reconstitute the below-mentioned ceftriaxone-containing products. Particulate formation can result. Ceftriaxone-containing products and 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 **Contra-indications** and **Warnings**).

The sections on **Side-effects** and **Special precautions** will reflect the changes as described above.

The updated package inserts for these ceftriaxone-containing products are available on request. If you would like to receive copies, please contact the Medical Information Department at the contact numbers given below.

Healthcare professionals should report all adverse events associated with the use of the below-mentioned ceftriaxone-containing products to the relevant companies by telephone or fax or alternatively to the National Adverse Drug Event Monitoring Centre (NADEMC) at Tel: (021) 4471618 or Fax: (021) 448 6181.

TRADE NAMES (Products)	Company	Contact number	Company Contact Person
Oframax 250 & 1 g	Ranbaxy (SA) (Pty) Ltd	012-643 2000	Susan Heritage
Triaxiphin 250 & 500 mg & 1 g	Be-Tabs Pharmaceuticals (Pty)Ltd	011-495 0100	Grace Job
Adco-Ceftriaxone 500 mg, 1 g & 2 g	Adcock Ingram Critical Care	011-494 8000	Viral Desai
Sabax-Ceftriaxone 250 & 500 mg, 1 & 2 g	Adcock Ingram Critical Care	011-494 8000	Viral Desai
Aspen Ceftriaxone 0,5 g, 1 g & 2 g	Aspen Pharmacare	011-239 6524	Michelle Singleton
Rociject 0,5 g, 1 g & 2 g	Aspen Pharmacare	011-239 6524	Michelle Singleton
Arrow Ceftriaxone Sodium 500 mg & 1 g	Arrow Pharma South Africa (Pty) Ltd	011-656 1726	Avanthi Govender
Austell-Ceftriaxone 1 g (powder for injection)	Austell Laboratories (Pty) Ltd	011-210 4100	Naeema Khan
CPL Alliance Ceftriaxone 250 & 500 mg & 1 g	Alliance Pharma	011-334 3600	Firoz Abram

Yours sincerely



Susan Heritage  
Ranbaxy (SA) (Pty) Ltd



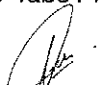
Grace Job  
Be-Tabs Pharmaceuticals (Pty) Ltd



Viral Desai  
Adcock Ingram Critical Care



Michelle Singleton  
Aspen Pharmacare



Avanthi Govender  
Arrow Pharma South Africa (Pty) Ltd



Naeema Khan  
Austell Laboratories (Pty) Ltd



Firoz Abram  
Alliance Pharma