

## DBL<sup>®</sup> CEFTRIAXONE SODIUM FOR INJECTION

**250 mg, 500 mg, 1 g, 2 g vials**

### Presentation

Active ingredient: ceftriaxone in the form of the disodium salt.

DBL<sup>®</sup> Ceftriaxone Sodium for Injection contains approximately 83 mg (3.6 mEq) of sodium per gram of ceftriaxone.

Appearance: Vials are colourless and contain dry substance which is a white or yellowish crystalline powder equivalent to 250 mg, 500 mg, 1g or 2g ceftriaxone.

### Uses

#### Actions

The bactericidal activity of ceftriaxone results from inhibition of bacterial cell wall synthesis. Ceftriaxone exerts in-vitro activity against a wide range of gram-negative and gram-positive micro-organisms.

Ceftriaxone is highly stable to most  $\beta$ -lactamases, both penicillinases and cephalosporinases, of gram-positive and gram-negative bacteria.

Ceftriaxone is usually active against the following micro-organisms in vitro and in clinical infections (see Indications and usage):

#### Gram-positive aerobes

*Staphylococcus aureus* (methicillin-sensitive), Staphylococci coagulase-negative, *Streptococcus pyogenes* ( $\beta$  -hemolytic, group A), *Streptococcus agalactiae* ( $\beta$  -hemolytic, group B),  $\beta$  -hemolytic Streptococci (non-group A or B), *Streptococcus viridans*, *Streptococcus pneumoniae*.

Note: Methicillin-resistant *Staphylococcus* spp. is resistant to cephalosporins, including ceftriaxone. In general, *Enterococcus faecalis*, *Enterococcus faecium* and *Listeria monocytogenes* are resistant.

#### Gram-negative aerobes

*Acinetobacter Iwoffii*, *Acinetobacter anitratus* (mostly *A. baumannii*)\*, *Aeromonas hydrophila*, *Alcaligenes faecalis*, *Alcaligenes odorans*, *Alcaligenes* -like bacteria, *Borrelia burgdorferi*, *Capnocytophaga* spp., *Citrobacter diversus* (including *C. amalonaticus*), *Citrobacter freundii*\*, *Escherichia coli*, *Enterobacter aerogenes*\*, *Enterobacter cloacae*\*, *Enterobacter* spp. (other)\*, *Haemophilus ducreyi*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Hafnia alvei*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*\*\*\*, *Moraxella catarrhalis* (former *Branhamella catarrhalis*), *Moraxella osloensis*, *Moraxella* spp. (other), *Morganella morganii*, *Neisseria gonorrhoea*, *Neisseria meningitidis*, *Pasteurella multocida*, *Plesiomonas shigelloides*, *Proteus mirabilis*, *Proteus penneri*\*, *Proteus vulgaris*\*, *Pseudomonas fluorescens*\*, *Pseudomonas* spp. (other)\*, *Providentia rettgeri*\*, *Providentia* spp. (other), *Salmonella typhi*, *Salmonella* spp. (non-typhoid), *Serratia marcescens*\*, *Serratia* spp. (Other)\*, *Shigella* spp., *Vibrio* spp., *Yersinia enterocolitica*, *Yersinia* spp. (other).

\* Some isolates of these species are resistant to ceftriaxone, mainly due to the production of the chromosomally encoded  $\beta$ -lactamase.

\*\* Some isolates of these species are resistant due to production of extended spectrum, plasmid-mediated  $\beta$ -lactamase.

Note: Many strains of the above micro-organisms that are multiple resistant to other antibiotics, e.g. amino-penicillins and ureido-penicillins, older cephalosporins and aminoglycosides, are susceptible to ceftriaxone. *Treponema pallidum* is sensitive in vitro and in animal experiments. Clinical investigations indicate that primary and secondary syphilis respond well to ceftriaxone therapy. With a few exceptions clinical *P. aeruginosa* isolates are resistant to ceftriaxone.

#### Anaerobic organisms

*Bacteroides* spp. (bile-sensitive)\*, *Clostridium* spp. (excluding *C. difficile*), *Fusobacterium nucleatum*, *Fusobacterium* spp. (other), *Gaffkia anaerobica* (formerly *Peptococcus*), *Peptostreptococcus* spp.

\* Some isolates of these species are resistant to ceftriaxone due to  $\beta$ -lactamase-production.

Note: Many strains of  $\beta$ -lactamase-producing *Bacteroides* spp. (notably *B. fragilis*) are resistant. *Clostridium difficile* is resistant.

Susceptibility to ceftriaxone can be determined by the disk diffusion test or by the agar or broth dilution test using standardised techniques for susceptibility testing such as those recommended by the National Committee for Clinical Laboratory Standards (NCCLS). The NCCLS issued the following interpretative breakpoints for ceftriaxone:

	Susceptible	Moderately susceptible	Resistant
<u>Dilution test</u> inhibitory concentrations in mg/l	=8	16-32	=64
<u>Diffusion test</u> (disk with 30 $\mu$ g ceftriaxone), inhibition zone diameter in mm	=21	20-14	=13

Micro-organisms should be tested with the ceftriaxone disk since it has been shown by in-vitro tests to be active against certain strains resistant to cephalosporin class disks.

Where NCCLS recommendations are not in daily use, alternative, well standardised, susceptibility-interpretative guidelines such as those issued by DIN, ICS and others may be substituted.

### Pharmacokinetics

*The pharmacokinetics of ceftriaxone are non-linear and all basic pharmacokinetic parameters, except the elimination half-life, are dose dependent if based on total drug concentrations.*

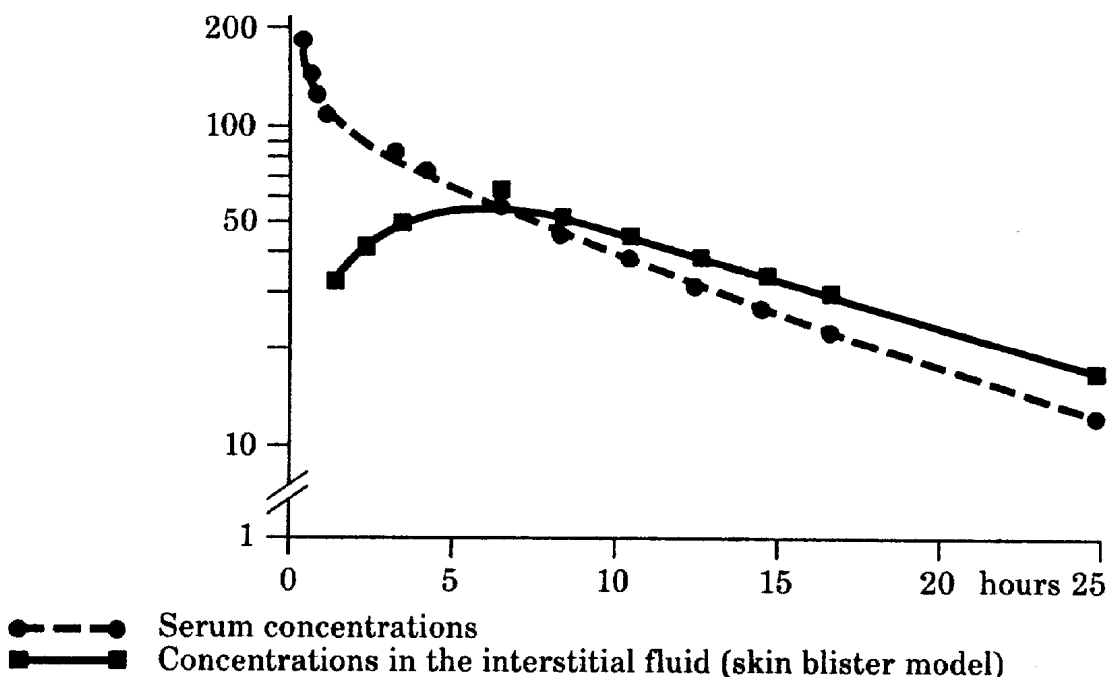
#### Absorption

The maximum plasma concentration after a single i.m. dose of 1 g is about 81 mg/l and is reached in 2-3 hours after administration. The area under the plasma concentration-time curve after i.m. administration is equivalent to that after i.v. administration of an equivalent dose, indicating 100% bioavailability of intramuscularly administered ceftriaxone.

#### Distribution

The volume of distribution of ceftriaxone is 7-12 l. Ceftriaxone has shown excellent tissue and body fluid penetration after a dose of 1-2 g; concentrations well above the minimal inhibitory concentrations of most pathogens responsible for infection are detectable for more than 24 hours in over 60 tissues or body fluids including lung, heart, biliary tract/liver, tonsil, middle ear and nasal mucosa, bone as well as cerebrospinal, pleural, prostatic and synovial fluids.

On intravenous administration, ceftriaxone diffuses rapidly into the interstitial fluid, where bactericidal concentrations against susceptible organisms are maintained for 24 hours (see figure).



### Protein binding

Ceftriaxone is reversibly bound to albumin, and the binding decreases with the increase in concentration, e.g. from 95% binding at plasma concentrations of <100 mg/l to 85% binding at 300 mg/l. Owing to the lower albumin content, the proportion of free ceftriaxone in interstitial fluid is correspondingly higher than in plasma.

### Penetration into particular tissues

Ceftriaxone penetrates the inflamed meninges of neonates, infants and children: Ceftriaxone concentrations exceed 1.4 mg/l in the Cerebrospinal Fluid (CSF) 24 hours after i.v. injection of ceftriaxone in doses of 50-100 mg/kg (neonates and infants respectively). Peak concentration in CSF is reached about 4 hours after i.v. injection and gives an average value of 18 mg/l. Mean CSF levels are 17% of plasma concentrations in patients with bacterial meningitis and 4% in patients with aseptic meningitis. In adult meningitis patients, administration of 50 mg/kg leads within 2-24 hours to CSF concentrations several times higher than the minimum inhibitory concentrations required for the most common meningitis pathogens.

Ceftriaxone crosses the placental barrier and is secreted in the breast milk at low concentrations.

### Metabolism

Ceftriaxone is not metabolised systemically; but is converted to inactive metabolites by the gut flora.

### Elimination

Total plasma clearance is 10-22 ml/min. Renal clearance is 5-12 ml/min.

50-60% of ceftriaxone is excreted unchanged in the urine, while 40-50% is excreted unchanged in the bile. The elimination half-life in adults is about 8 hours.

### Pharmacokinetics in special clinical situations

In neonates, urinary recovery accounts for about 70% of the dose. In infants aged less than 8 days and in elderly persons aged over 75 years the average elimination half-life is usually two to three times that in young adults.

In patients with *renal or hepatic dysfunction*, the pharmacokinetics of ceftriaxone are only minimally altered and the elimination half-life is only slightly increased. If kidney function alone is impaired, biliary elimination of ceftriaxone is increased; if liver function alone is impaired, renal elimination is increased.

## Indications

Infections caused by pathogens sensitive to ceftriaxone, e.g.:

- sepsis;
- meningitis;
- abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts);
- infections of the bones, joints, soft tissue, skin and of wounds;
- infections in patients with impaired defence mechanisms;
- renal and urinary tract infections;
- respiratory tract infections, particularly pneumonia, and ear, nose and throat infections;
- genital infections, including gonorrhoea.

Perioperative prophylaxis of infections.

## Dosage and administration

### Standard dosage

Adults and children over 12 years. The usual dosage is 1-2 g of DBL<sup>®</sup> Ceftriaxone Sodium for Injection *once daily* (every 24 hours). In severe cases or in infections caused by moderately sensitive organisms, the dosage may be raised to 4 g, once daily.

Neonates, infants and children up to 12 years. The following dosage schedules are recommended for *once daily* administration:

Neonates (up to 14 days): 20-50 mg/kg bodyweight once daily. The daily dose should not exceed 50 mg/kg. It is not necessary to differentiate between premature and term infants.

Infants and children (15 days to 12 years): 20-80 mg/kg once daily.

For children with bodyweights of 50 kg or more, the usual adult dosage should be used.

Intravenous doses of  $\geq 50$  mg/kg bodyweight should be given by infusion over at least 30 minutes.

Elderly patients. The dosages recommended for adults require no modification in geriatric patients.

### Duration of therapy

The duration of therapy varies according to the course of the disease. As with antibiotic therapy in general, administration of DBL<sup>®</sup> Ceftriaxone Sodium for Injection should be continued for a minimum of 48-72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.

### Combination therapy

Synergy between ceftriaxone and aminoglycosides has been demonstrated with many gram-negative Bacteria under experimental conditions. Although enhanced activity of such combinations is not always predictable, it should be considered in severe, life threatening infections due to micro-organisms such as *Pseudomonas aeruginosa*. Because of physical incompatibility the two medicines must be administered separately at the recommended dosages.

### Special dosage instructions

Meningitis: In bacterial meningitis in *infants and children*, treatment begins with doses of 100 mg/kg (up to a maximum of 4 g) once daily. As soon as the causative organism has been identified and its sensitivity determined, the dosage can be reduced accordingly. The following duration of therapy has shown to be effective:

*Neisseria meningitidis* 4 days

*Haemophilus influenzae* 6 days

*Streptococcus pneumoniae* 7 days

Gonorrhoea (penicillinase-producing and nonpenicillinase-producing strains): a single i.m. dose of 250 mg.

Perioperative prophylaxis: A single dose of 1-2 g depending on the risk of infection of 30-90 minutes prior to surgery. In colorectal surgery, administration of DBL<sup>®</sup> Ceftriaxone Sodium for Injection with or without a 5-nitroimidazole, e.g. ornidazole (separate administration, see **Method of administration**) has been proven effective.

Impaired renal and hepatic function: In patients with *impaired renal function*, there is no need to reduce the dosage of DBL<sup>®</sup> Ceftriaxone Sodium for Injection *provided hepatic function is intact*. Only in cases of preterminal renal failure (creatinine clearance <10 ml/min) should the DBL<sup>®</sup> Ceftriaxone Sodium for Injection dosage not exceed 2 g daily. In patients with *liver damage*, there is no need for the dosage to be reduced *provided renal function is intact*.

In *patients with both severe renal and hepatic dysfunction*, the plasma concentrations of ceftriaxone should be determined at regular intervals and if necessary the dose should be adjusted.

In patients undergoing *dialysis* no additional supplementary dosing is required following the dialysis. Plasma concentrations should, *however*, be monitored, to determine whether dosage adjustments are necessary, since the elimination rate in these patients may be altered.

### Method of administration

As a *general rule* the solutions should be used immediately after preparation .

Reconstituted solutions retain their physical and chemical stability for 6 hours at room temperature (or 24 hours in the refrigerator at 2 - 8°C). The solutions range in colour from pale yellow to amber, depending on the concentration and length of storage. The coloration of the solutions is of no significance for the efficacy or tolerance of the drug.

DBL<sup>®</sup> Ceftriaxone Sodium for Injection should not be added to solutions containing calcium such as Hartmann's solution and Ringer's solution (see **WARNINGS and PRECAUTIONS: Calcium-containing Solutions**).

**Intramuscular injection.** For IM injection, DBL<sup>®</sup> Ceftriaxone Sodium for Injection 1 g is dissolved in 3.5 ml of 1% lidocaine hydrochloride solution and injected well within the body of a relatively large muscle. It is recommended that not more than 1 g be injected at one site.

The lidocaine solution should never be administered intravenously.

**Intravenous injection.** For IV injection, DBL<sup>®</sup> Ceftriaxone Sodium for Injection 250 mg or 500 mg is dissolved in 5 ml, and DBL<sup>®</sup> Ceftriaxone Sodium for Injection 1 g in 10 ml sterile water for injections. The intravenous administration should be given over 2-4 minutes.

**Intravenous infusion.** The infusion should be given over at least 30 minutes. For IV infusion, 2 g DBL<sup>®</sup> Ceftriaxone Sodium for Injection is dissolved in 40 ml of one of the following calcium-free infusion solutions: sodium chloride 0.9%, sodium chloride 0.45% + dextrose 2.5%, dextrose 5%, dextrose 10%, dextran 6% in dextrose 5%, hydroxy ethyl starch 6-10%, water for injections. DBL<sup>®</sup> Ceftriaxone Sodium for Injection solutions should *not* be mixed with or piggybacked into solutions containing other antimicrobial medicines or into diluent solutions other than those listed above, owing to possible incompatibility.

### Contraindications

Ceftriaxone is contraindicated in patients with known hypersensitivity to cephalosporin antibiotics. In patients hypersensitive to penicillin, the possibility of allergic cross-reactions should be borne in mind. Lignocaine should not be used as a diluent for intramuscular injection in patients who are hypersensitive to lignocaine.

DBL<sup>®</sup> Ceftriaxone Sodium for Injection must not be administered with calcium-containing solutions in newborns because of the risk of precipitation of ceftriaxone-calcium salt (see **WARNINGS and PRECAUTIONS: Calcium-containing Solutions and ADVERSE EFFECTS**). Cases of fatal reactions with calcium-ceftriaxone precipitates in lung and kidneys in newborns have been described. In some cases the infusion lines and the times of administration of ceftriaxone and calcium-containing solutions differed. Therefore, DBL<sup>®</sup> Ceftriaxone Sodium for Injection and IV calcium-containing solutions must not be administered within 48 hours of each other in newborns.

Hyperbilirubinaemic newborns and preterm newborns should not be treated with ceftriaxone. *In vitro* studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin, leading to a possible risk of bilirubin encephalopathy in these patients.

## Warnings and Precautions

BEFORE THERAPY WITH CEFTRIAXONE IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS ADRENALINE AND OTHER EMERGENCY MEASURES. IF AN ALLERGIC REACTION OCCURS CEFTRIAXONE SHOULD BE DISCONTINUED.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including ceftriaxone. A toxin produced by *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *C. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Drugs which delay peristalsis eg opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used. Other causes of colitis should also be considered.

Ceftriaxone should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

Superinfections with non-susceptible micro-organisms may occur as with other antibacterial agents. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Immune mediated haemolytic anaemia has been observed in patients receiving cephalosporin class antibacterials. Severe cases of haemolytic anaemia, including fatalities, have been reported during treatment in both adults and children. If a patient develops anaemia while on ceftriaxone, the diagnosis of a cephalosporin associated anaemia should be considered and ceftriaxone discontinued until the etiology is determined.

There have been reports of sonographic abnormalities in the gall bladder of patients treated with ceftriaxone sodium; some of these patients also had symptoms of gall bladder disease. These abnormalities appear on sonography as an echo without acoustical shadowing suggesting sludge, or as an echo with acoustical shadowing which may be misinterpreted as gallstones. The chemical nature of the sonographically detected material has been determined to be predominantly a ceftriaxone calcium salt. The condition appears to be transient and reversible upon discontinuation of ceftriaxone and institution of conservative management. Therefore DBL<sup>®</sup> Ceftriaxone Sodium for Injection should be discontinued in patients who develop signs and symptoms suggestive of gall bladder disease and/or the sonographic finding described above.

Cases of pancreatitis, possibly of biliary obstruction aetiology, have been rarely reported in patients treated with ceftriaxone. Most patients presented with risk factors for biliary stasis and biliary sludge, e.g. preceding major therapy, severe illness and total parenteral nutrition. A trigger or cofactor role of ceftriaxone- related biliary precipitation cannot be ruled out.

Ceftriaxone has shown some evidence of renal toxicity in animals. Clinical studies have shown only transient elevations of serum urea and serum creatinine at the recommended dosages. Ceftriaxone is excreted via both biliary and renal excretion (see **Pharmacokinetics**). The half life of ceftriaxone may be prolonged in some patients with renal failure, adjustment in dosage may be required. Concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly. Dosage adjustments should not be necessary in patients with hepatic dysfunction. In patients with both hepatic dysfunction and significant renal disease, DBL<sup>®</sup> Ceftriaxone Sodium for Injection dosage requires close monitoring of serum concentrations.

Repeated use of lignocaine hydrochloride should be avoided in patients with severe liver disease or decreased hepatic blood flow due to the possibility of lignocaine toxicity (resulting from decreased metabolism and accumulation).

Alterations in prothrombin times have occurred rarely in patients treated with ceftriaxone. Patients with impaired vitamin K synthesis or low vitamin K stores (eg chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during ceftriaxone treatment. Vitamin K administration (10 milligram weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Safety and effectiveness of ceftriaxone in neonates, infants and children have been established for the dosages described under Dosage and administration. Studies have shown that ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Ceftriaxone should not be used in neonates (especially prematures) at risk of developing bilirubin encephalopathy (see **CONTRAINDICATIONS**).

During prolonged treatment the blood should be checked at regular intervals.

There are no data to indicate any effect on a person's ability to drive or use machines.

### **Calcium-containing Solutions:**

In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites. However, in patients older than 28 days of age ceftriaxone and calcium-containing solutions may be administered sequentially one after another if infusion lines at different sites are used, or if the infusion lines are replaced or thoroughly flushed between infusions with physiological salt-solution to avoid precipitation. In patients requiring continuous infusion with calcium-containing TPN solutions, healthcare professionals may wish to consider the use of alternative antibacterial treatments which do not carry a similar risk of precipitation. If use of ceftriaxone is considered necessary in patients requiring continuous nutrition, TPN solutions and ceftriaxone can be administered simultaneously, albeit via different infusion lines at different sites. Alternatively, infusion of TPN solution could be stopped for the period of ceftriaxone infusion, considering the advice to flush infusion lines between solutions. See **CONTRAINDICATIONS** for information regarding newborns.

### **Pregnancy, nursing mothers**

Category B1

Ceftriaxone crosses the placental barrier. Safety in human pregnancy has not been established. Reproductive studies in animals have shown no evidence of embryotoxicity, fetotoxicity, teratogenicity or adverse effects on male or female fertility, birth or perinatal and postnatal development. In primates, no embryotoxicity or teratogenicity has been observed.

*Australian categorisation definition of Category B1: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage.*

Low concentrations of ceftriaxone are secreted in human milk. Caution should be exercised when ceftriaxone is administered to a nursing woman.

### **Adverse Effects**

During the use of ceftriaxone, the following side effects, which were reversible either spontaneously or after withdrawal of the medicine, have been observed:

#### **Systemic side effects**

Gastrointestinal complaints: loose stools or diarrhoea, nausea, vomiting, stomatitis glossitis, dysgeusia, abdominal pain, flatulence, dyspepsia,

Hematological changes: occasional eosinophilia, thrombocytosis and leukopenia. Less frequently reported were haemolytic anaemia, neutropenia, lymphopenia, granulocytopenia, leukocytosis, lymphocytosis, monocytosis, basophilia, thrombocytopenia and prolongation of the prothrombin time and bleeding. In very rare cases agranulocytosis has been reported.

Skin reactions: rash, exanthema, allergic dermatitis, pruritus, urticaria, oedema. Isolated cases of severe cutaneous adverse reactions (erythema multiforme, Stevens Johnson syndrome or Lyell's Syndrome/toxic epidermal necrolysis) have been reported.

Other, rare side effects: headache and dizziness, symptomatic precipitation of ceftriaxone calcium salt in the gallbladder, increase in liver enzymes, jaundice, genital mycosis, vaginitis, fever, flushing, shivering,

diaphoresis and anaphylactic or anaphylactoid reactions, bronchospasm, oedema, serum sickness, palpitations and epistaxis.

Pseudomembranous enterocolitis and coagulation disorders have been reported as very rare side effects. Renal: infrequent elevations of the serum urea. Less frequently reported were elevations of creatinine and the presence of casts in the urine. Glycosuria, haematuria, crystalluria and oliguria have been reported very rarely. Renal adverse effects were somewhat more frequent in the elderly. Very rare cases of renal precipitation have been reported, mostly in children older than 3 years and who have been treated with either high daily doses (e.g.  $\geq 80$  mg/kg/day) or total doses exceeding 10 grams and presenting other risk factors (e.g. fluid restrictions, confinement to bed, etc.). This event may be symptomatic or asymptomatic, may lead to renal insufficiency, and is reversible upon discontinuation of ceftriaxone.

Cases of fatal reactions with calcium-ceftriaxone precipitates in lung and kidney in neonates and premature infants have been described. In some cases the infusion lines and times of administration of ceftriaxone and calcium-containing solutions differed. Ceftriaxone must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines.

### Local side effects

Infrequent pain, induration or tenderness at the site of injection. In rare cases, phlebitic reactions occurred after IV administration. These may be minimized by slow (2-4 minutes) injection. Intramuscular injection *without* lidocaine solution is painful.

### Interactions

No impairment of renal function has so far been observed after concurrent administration of large doses of ceftriaxone and potent diuretics (e.g. frusemide). There is no evidence that ceftriaxone increases renal toxicity of aminoglycosides. No effect similar to that of disulfiram has been demonstrated after ingestion of alcohol subsequent to the administration of ceftriaxone. Ceftriaxone does not contain an N-methylthiotetrazole moiety associated with possible ethanol intolerance and bleeding problems of certain other cephalosporins. The elimination of ceftriaxone is not altered by probenecid.

In an in-vitro study antagonistic effects have been observed with the combination of chloramphenicol and ceftriaxone.

DBL<sup>®</sup> Ceftriaxone Sodium for Injection must not be administered with calcium-containing solutions in newborns because of the risk of precipitation of ceftriaxone-calcium salt (see **CONTRAINDICATIONS**). In patients of any age ceftriaxone must not be mixed or administered simultaneously with any calcium-containing IV solutions, even via different infusion lines or at different infusion sites (see **WARNINGS and PRECAUTIONS: Calcium-containing Solutions**).

### Laboratory Tests

In patients treated with ceftriaxone the Coombs' test may rarely become false-positive. Ceftriaxone, like other antibiotics, may result in false-positive tests for galactosemia.

Likewise, nonenzymatic methods for the glucose determination in urine may give false-positive results. For this reason, urine-glucose determination during therapy with ceftriaxone should be done enzymatically.

### Overdosage

In the case of overdosage, ceftriaxone concentration would not be reduced by hemodialysis or peritoneal dialysis. There is no specific antidote. Treatment of overdosage should be symptomatic.

In case of overdose, immediately contact the Poisons Information Centre for advice (in New Zealand call 0800 764 766).

## Pharmaceutical Precautions

### Incompatibilities

DBL<sup>®</sup> Ceftriaxone Sodium for Injection should not be added to solutions containing calcium such as Hartmann's solution and Ringer's solution.

Based on literature reports ceftriaxone is incompatible with amsacrine, vancomycin and fluconazole and aminoglycosides.

### Stability

Store below 25°C.

Reconstituted solutions retain their physical and chemical stability for 6 hours at room temperature (or 24 hours in the refrigerator at 2 - 8°C).

This medicine should not be used after the expiry date shown on the pack.

### Medicine Classification

Prescription Medicine.

### Package Quantities

*For intramuscular or intravenous injection:*

Vials containing powder equivalent to 1 g ceftriaxone, single packs and packs of 5 vials.

0.25 g (not marketed), 0.5 g (not marketed).

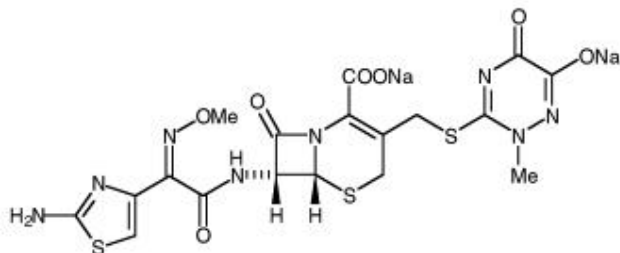
*For intravenous infusion:*

Vial containing powder equivalent to 2 g ceftriaxone, single pack.

### Further Information

Ceftriaxone sodium is sodium (Z)-(6R,7R)-7-[2-(2-amino-1,3-thiazol-4-yl)-2-(methoxy-imino)acetamido]-8-oxo-3-[(2,5-dihydro-2-methyl-6-oxido-5-oxo-1,2,4-triazin-3-yl)thiomethyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, hydrate (2:7).

The chemical formula of ceftriaxone sodium is  $C_{18}H_{16}N_8Na_2O_7S_3 \cdot 3.5H_2O$ . It has a calculated molecular weight of 661.59 (CAS registry number: 104376-79-6). The chemical structure for ceftriaxone sodium is shown below.



Ceftriaxone sodium is a white or yellowish crystalline powder, which is readily soluble in water, sparingly soluble in methanol and very slightly soluble in ethanol. The pH of a 5% aqueous solution is approximately 6 to 8. The colour of ceftriaxone sodium solutions ranges from light yellow to amber, depending on the length of storage, concentration and diluent used.

### Name and Address

Hospira NZ Limited  
23 Haining Street  
Te Aro  
Wellington  
New Zealand

### Date of Preparation

20 January 2012