PATIENT INFORMATION LEAFLET

Please read the following patient information leaflet carefully because it contains important information to note about the use of this medicine. If you have any questions, please speak to your doctor or pharmacist.

Megion®250 mg – vials

powder for preparing an injection solution

SANDOZ

Composition

What does Megion 250 mg contain?
One vial contains 250 mg ceftriaxone as a sterile powder comprising 298.3 mg hydrated ceftriaxone sodium. One solvent ampoule contains 5 ml water for Injections

Pharmaceutical form: white to yellowish crystalline powder for preparing an injection solution.

Presentations: single packs of 1 vial + solvent,
hospital packs of 10, 25 and 50 vials.

Pharmaceutical and therapeutic category and mode of action

How does Megion 250 mg act?
Ceftriaxone is a bactericidal antibiotic with a broad range of activity against gram-positive and in particular gram-negative micro-organisms. The range of activity encompasses both aerobic and some anaerobic organisms. It is highly stable to most beta-lactamases.

Registered owner and manufacturer:

Sandoz GmbH, Kundl, Austria

Indications

When is Megion 250mg used?
Ceftriaxone is used

- for the treatment of pneumonia
- in blood poisoning
- in meningitis
- in infections of the bones, skin and soft tissue
- in infections affecting neutropenic patients
- in gonorrhoea
- for perioperative prophylaxis of infections in connection with surgical procedures

Therapy can be started even before the results from susceptibility tests are available.

Contraindications

When must Megion 250 mg not be used?
Ceftriaxone must not be administered to patients with a history of hypersensitivity to cephalosporin antibiotics.
Ceftriaxone must not be administered to newborn babies with jaundice or patients suffering from hypoalbuminaemia or acidosis, or in other cases, such as premature birth, in which the binding of bilirubin is likely to be restricted.

Pregnancy and breast-feeding

Animal studies have not yielded any indication of harmful effects on the development of the fetus. However, the safety of the use of ceftriaxone in pregnant women has not been established. Ceftriaxone should therefore be used during pregnancy only if indicated after thorough medical assessment.
Only small amounts of ceftriaxone pass into breast milk. Caution is nevertheless advised in breast-feeding women.

Precautions for use and special warnings

The recommended dosage should not be exceeded.
Ceftriaxone should be administered with care to patients with a history of hypersensitivity reactions (in particular anaphylactic reactions) to penicillins or other beta-lactam antibiotics (non-cephalosporins), as cross allergies between cephalosporins and these antibiotics have been reported occasionally. If anaphylactic shock occurs, immediate countermeasures must be taken.
A dose reduction will be required in cases of severely impaired kidney function, accompanied by liver function impairment (see *Dosage*).
Ceftriaxone may precipitate out in the gallbladder and become detectable as shadows on ultrasound scans (see *Side effects*). This may occur in patients of any age, but the probability of this happening is greater in infants and small children, because they are usually treated with a ceftriaxone dose which is higher in proportion to the body weight. Owing to the increasing risk of precipitations in the gallbladder, doses above 80 mg/kg must be avoided in children. There is no clear evidence that children or infants treated with ceftriaxone develop gallstones or acute inflammation of the gallbladder.
Conservative treatment of ceftriaxone precipitations in the gallbladder is recommended.
The class of cephalosporins shows a tendency to be absorbed on the surface of erythrocyte membranes, to react with the antibodies which target the medicine, and to yield a positive Coombs´ test and occasionally cause haemolytic anaemia which tends to be mild. A certain cross reactivity with penicillins may be present connection. Cases of inflammation of the pancreas were reported during treatment with ceftriaxone, which were possibly due to biliary obstruction. Most of such patients had risk factors for bile retention and bile sludge, e.g. preceding major surgery, severe illness or total parenteral feeding. It cannot be ruled out that ceftriaxone is involved, either as a trigger or a cofactor, in the precipitation process occurring in the gallbladder.
The treating physician must be informed if pregnancy occurs.

Keep out of the reach of children.

Interactions

May Megion 250 mg be taken at the same time as other medicines?
Antagonistic effects have been observed in vitro with the combination of chloramphenicol and ceftriaxone.
The Coombs´ test may in rare cases yield false-positive results during treatment with ceftriaxone. Like other antibiotics, ceftriaxone may result in false-positive tests for galactosaemia. Likewise, non-enzymatic methods for the determination of sugar levels in the urine may yield a false-positive result. Determinations of urine sugar levels during ceftriaxone therapy should therefore be done enzymatically.

Dosage

How often should Megion 250 mg be taken and in what quantity?
The product may be administered ONLY by a doctor.

After preparation of the ready-for-use solution, ceftriaxone can be administered according to the instructions given below by deep intramuscular injection, slow intravenous injection or slow intravenous infusion. Dosage and mode of administration will depend on the severity of the infection, the sensitivity of the causative agent and the patient´s condition.

Since ceftriaxone has a relatively long plasma elimination half-life of about eight hours, a single administration (for the treatment of gonorrhoea, for example) or a single daily dose will be suitable for most patients.

Adults and children from the age of 12 years
Usual therapeutic dosage: 1 g once daily
Severe infections: 2-4 g daily, usually in one dose every 24 hours
The **duration of treatment** varies according to the course of the disease. As with antibiotic therapy in general, treatment with ceftriaxone must be continued for at least 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.
Acute uncomplicated gonorrhoea:
A single intramuscular administration of 250 mg. The simultaneous administration of probenecid is not indicated.
Perioperative prophylaxis: The usual dose is 1 g, which is administered as a single intramuscular or slow intravenous injection. In colorectal surgery, the dose to be administered is 2 g by intramuscular or slow intravenous injection or infusion in conjunction with a suitable agent against anaerobic bacteria.

Elderly patients
Elderly patients require no adjustment of the ceftriaxone dose, if liver and kidney functions are satisfactory (see below).

Newborn babies, infants and children up to 12 years of age
The following dosage schemes are recommended for the once daily administration.
Newborn babies: 20-50 mg/kg once daily. Intravenous doses should be administered over a period of 60 minutes in order to reduce the displacement of bilirubin from binding sites on serum albumin, and consequently limit the potential risk of bilirubin encephalopathy.
Infants and children up to 12 years of age:
Usual therapeutic dosage:
20-50 mg/kg once daily.
In severe infections, the daily dose can be raised up to 80 mg/kg. Doses of or above 50 mg per kg body weight should be administered by slow intravenous infusion over a period of at least 30 minutes. Doses exceeding 80 mg/kg must be avoided due to the risk of precipitations in the gallbladder.

Dosage where liver and kidney function is impaired

Patients with impaired kidney function require no adjustment of the ceftriaxone dose, provided liver function is normal. In cases of preterminal impairment of kidney function (creatinine clearance < 10 ml per minute), the daily dose should be limited to 2 g or less.
Patients with liver damage require no dose reduction, provided kidney function is normal.
In patients suffering from impaired kidney function accompanied by severe liver function impairment, it is recommended that plasma ceftriaxone concentrations are checked at regular intervals and the dose adjusted appropriately.
Patients undergoing dialysis require no additional supplementary dose following the dialysis. Serum concentrations should, however, be monitored in order to determine whether a dose adjustment is required, since the elimination rate may be lowered.

Mode of administration

How do you use Megion 250 mg?
Megion 250 mg powder for preparing an injection solution is dissolved in an appropriate solvent (see section "Instructions for handling"). The solution should be used immediately after preparation.
Megion 250 mg must not be mixed in the same syringe with other medicines, except 1.06% lidocaine hydrochloride solution BP (exclusively for intramuscular injection). Ceftriaxone-containing solutions must not be mixed with or piggybacked into solutions which contain other agents. Ceftriaxone is not compatible in particular with calcium-containing solutions such as Hartmann´s and Ringer´s solutions. It is evident from the literature that ceftriaxone is incompatible with amsacrine, vancomycin, fluconazole, aminoglycosides and labetalol.

Instructions for handling

Preparation of a solution for injection or infusion
Intramuscular injection: Megion 250 mg must be dissolved in 1 ml of 1.06% lidocaine hydrochloride solution BP. The solution should be administered by deep intramuscular injection.
Intravenous administration of solutions containing lidocaine must be avoided.
Intravenous injection: Megion 250 mg must be dissolved in 5 ml of water for injections BP. The injection must be administered directly into the vein or by infusion via a venous cannula over a period of at least 2-4 minutes.
Intravenous infusion: Megion 250 mg may be dissolved in any of the following calcium-free solutions: dextrose solution for injection BP 5% or 10%, sodium chloride solution for injection BP, sodium chloride and dextrose solution for injection BP (0.45% sodium chloride and 2.5% dextrose), dextrane 6% in dextrose solution for injection BP 5%, hydroxyethyl starch solution for injection 6-10%. The infusion should be given over at least 30 minutes.

Overdosage

In the event of an overdosage, it will not be possible to reduce the drug concentration by haemodialysis or peritoneal dialysis. No specific antidote is known. Treatment should be symptomatic.

Side effects

What unwanted effects (side effects) may Megion 250 mg have, although they do not necessarily occur in all patients?
Ceftriaxone is generally well tolerated. Unwanted effects are usually mild and transient in nature.
The most common side effects are **gastrointestinal complaints**, predominantly taking the form of loose stools or diarrhoea, occasional nausea and vomiting, inflammation of the mucous membrane of the mouth and burning tongue.
Skin reactions, such as maculopapulous skin rashes or exanthemas, itching, nettle rash, swelling and allergic skin inflammation have occurred. A few cases of severe skin reactions (erythema multiforme, Stevens-Johnson syndrome and Lyell´s syndrome/toxic epidermal necrolysis) have been reported.
Haematological changes such as anaemia (all grades), destruction of red blood cells accompanied by jaundice (haemolytic anaemia), blood count abnormalities (leukopenia, neutropenia, thrombocytopenia, eosinophilia, agranulocytosis) and positive Coombs´ test. It is recommended that blood counts are checked regularly during therapy. Ceftriaxone was in rare cases associated with prolonged prothrombin time.
A few cases of headache and dizziness, drug fever, chills and transient elevations in liver function parameters have been reported. Other rare side effects include: excretion of sugar with the urine (glucosuria), reduced urine volume (oliguria), excretion of intact red blood cells with the urine (haematuria), elevation in serum creatinine, fungal diseases affecting the genital tract, and anaphylactic-type reactions such as asthma-like shortness of breath (bronchospasm).
Reversible symptomatic precipitations of the calcium salt of ceftriaxone in the urinary tract occurred very rarely after treatment with ceftriaxone. Very young, bedridden patients or patients with reduced fluid intake are at a higher risk. A few cases have been reported where this reaction was followed by complete lack of urine excretion and impaired kidney function.
Shadows have been found on ultrasound scans, and were erroneously interpreted as gallstones. These shadows are precipitations of the calcium salt of ceftriaxone. These precipitations were generally found in adults receiving a daily dose of 2 g or more and in children after the administration of an equivalent dose. With daily doses of 2 g or more, these precipitations in the gallbladder may occasionally be associated with symptoms. If symptoms occur, nonsurgical measures are recommended, and discontinuation of treatment with ceftriaxone must be taken into consideration. These precipitations in the gallbladder usually disappear on discontinuation of ceftriaxone therapy. The risk of biliary precipitations increases if treatment lasts longer than 14 days, in cases of impaired kidney function, reduced body fluid (dehydration) or total parenteral feeding. Isolated cases of inflammation of the pancreas (pancreatitis) were reported, but ceftriaxone could not be identified as the cause.
Superinfections with yeasts and fungi or other resistant organisms may occur. In connection with an infection with Clostridium difficile, pseudomembranous colitis was described as a rare side effect during treatment with ceftriaxone. It is therefore important to consider this diagnosis in patients who have diarrhoea after the administration of antibacterial agents.
Transient pain or discomfort may occur at the injection site immediately after intramuscular injection; however, tolerability is generally good. In rare cases an intravenous administration was followed by a local inflammation of the vein. This can be substantially avoided by slow injection over at least 2-4 minutes.
If you notice any side effect not mentioned in this patient information leaflet, please inform your doctor or pharmacist.

Note on expiry date and storage

Note the expiry date on the package.
Powder for preparing an injection solution: Do not store above 30°C.
Keep the container in the outer carton.
Ready-for-use solution: Must be used immediately.
From a microbiological point of view, the ready-for-use product must be used immediately. If it is not used immediately, the user will be responsible for the duration and conditions of storage prior to use. Reconstituted solutions retain their potency for 24 hours at 25°C and 48 hours at 2-8°C.
Megion must not be used after this date. You can dispose of unused medicines in any pharmacy.

Date of Information

September 2003

If you have further questions regarding Megion 250 mg, please speak to your doctor or pharmacist.

Sandoz GmbH, Kundl - Austria