Composition
What does Megion contain?
One vial of Megion contains 1 g ceftriaxone (as disodium 3.5 hydrate).
One solvent ampoule contains 10 ml water for injections

Pharmaceutical form: powder for preparing an injection/infusion solution
The powder is white to yellowish.

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 act?
Ceftriaxone is a long-acting cephalosporin antibiotic for injection treatment, 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. This medicine derives its antibacterial effect from inhibiting the formation of the cell wall in bacteria.

Registered owner and manufacturer:
Sandoz GmbH, Kundl, Austria

Indications
When is Megion used?

Ceftriaxone is indicated for the treatment of severe infections if they are known, or very likely, to be caused by ceftriaxone-sensitive micro-organisms and when a parenteral treatment is necessary:
- bacterial meningitis
- pneumonia
- infections of the abdominal cavity: e.g. inflammation of the serous membrane (peritonitis) and infections of the bile ducts. Ceftriaxone should be combined with another antibiotic suitable for treating infections of the skin and soft tissues caused by anaerobic bacteria.
- infections of the bones and joints
- patients with late manifestation of Lyme disease (stages II and III)
- infections of the genitalia (gonorrhoea)
- Ceftriaxone can be used either alone or in combination with other antibacterial drugs to prevent infections after certain cardiovascular, urological and colorectal operations. In colorectal surgery, ceftriaxone should be combined with another antibiotic suitable for treating infections caused by anaerobic bacteria.

The official guidelines (e.g. national recommendations) regarding the appropriate use of antibacterial drugs must be taken into account.

Contraindications
When must Megion not be used?
Megion must not be used in cases of
- hypersensitivity to ceftriaxone or other cephalosporins.
- Previous immediate-type reactions and/or serious hypersensitivity reactions to a penicillin or another beta-lactam.

Ceftriaxone must not be administered to newborn babies with jaundice or hypoalbuminaemia (unduly small proportion of the protein albumin present in the blood) or excessive acidity of the blood, or in other conditions (such as premature birth) in which the binding of bilirubin is very likely to be impaired.

Administration into a muscle
If ceftriaxone and lidocaine are administered at the same time, the doctor must first ascertain whether lidocaine may be used or whether this is contraindicated.
Pregnancy and breast-feeding
The doctor will decide whether or not to use the medicine during pregnancy and breast-feeding.

Pregnancy
There is insufficient experience with the use of ceftriaxone in pregnant women in order to be

Inflammation of the colon may occur during the use of antibiotics. This diagnosis should therefore be considered if severe diarrhoea occurs during treatment with ceftriaxone, and appropriate measures must be instituted if necessary.
Ceftriaxone may be administered only with care to patients with a history of gastrointestinal disorders, especially colitis.
Please inform your doctor if you become pregnant.
Keep out of the reach of children!

Interactions
May Megion be taken at the same time as other medicines?
Since bacteriostatic antibiotics have antagonistic activity an bactericidal antibiotics such as ceftriaxone, it is inappropriate to administer them simultaneously. This applies especially in the case of acute infections which are associated with a rapid multiplication of bacteria.
Ceftriaxone/probenecid:
The simultaneous administration of probenecid (1-2 g a day) may inhibit the biliary secretion of ceftriaxone. Unlike other cephalosporins, probenecid does not inhibit tubular secretion of ceftriaxone.
Ceftriaxone/hormonal contraceptives:
Ceftriaxone may antagonize the effectiveness of hormonal contraceptives. It is therefore advised to employ additional non-hormonal contraceptive measures during and in the month after treatment with ceftriaxone.
The class of cephalosporins shows a tendency to be absorbed on the surface of erythrocyte membranes and give a positive Coombs' test with antibodies against the medicine, mild haemolytic anaemia occurs occasionally. A cross reactivity with penicillins cannot be ruled out in this connection.

Like other antibiotics, ceftriaxone can result in false-positive tests for galactosaemia. Likewise, non-enzymatic methods for the determination of glucose in the urine may yield a false-positive result. This can be avoided by using specific glucose oxidase methods.

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

Dosage
The dosage and the mode of administration must be determined according to the severity of the infection, the organs affected, the sensitivity of the micro-organism, and the age and condition of the patient. The usual duration of therapy depends on the patient´s response. As with other antibiotic therapies, the administration of ceftriaxone must be continued for at least 48 to 72 hours after the fever has ended or the micro-organisms have been killed.
Adults and adolescents older than 12 years of age weighing ≥ 50 kg:
The usual ceftriaxone dosage is 1-2 g once a day (every 24 hours). In severe infections or infections caused by micro-organisms with reduced sensitivity, the daily dose can be raised to 4 g once a day.
In cases of uncomplicated gonorrhoea in adults or adolescents from the age of 12 years and weighing ≥ 50 kg, a single dose of 250 mg ceftriaxone should be given intramuscularly.
Meningitis
For adults, adolescents from the age of 12 years and children weighing ≥ 50 kg, treatment should be started with a dose of 100 mg/kg/24 hours, however, a maximum amount of 4 g/day must not be exceeded.
In bacterial meningitis in infants and children, therapy is started with dosages between 50 and 100 mg/kg once a day. The dosage should not exceed a maximum amount of 2 g. The treatment should be continued for a period of at least 2 weeks.

Intravenous infusion: 1 g to 2 g Megion must be dissolved in 20 to 40 ml of any of the following calcium-free infusion solutions: sodium chloride 0.9%, sodium chloride 0.45% and glucose 2.5%, glucose 5% or 10%, dextran 6% in glucose 5%, hydroxyethyl starch 6-10%. The infusion should be given over a period of at least 30 minutes.

In the course of the preparation for intramuscular or intravenous administration, the white to yellowish-orange crystalline powder will dissolve to give a pale yellow to amber solution. Prepared solutions must be inspected visually. Only clear solutions without visible particles may be used. The prepared product is for single use only. Unused solution must be discarded.
Incompatibilities
Ceftriaxone-containing solutions must not be mixed with solutions or added to solutions which contain substances other than those mentioned above. Ceftriaxone is not compatible in particular with calcium-containing solutions such as Hartmann´s solution and Ringer´s solution.
It is evident from the literature that ceftriaxone is not compatible with amsacrine, vancomycin, fluconazole, aminoglycosides and labetalol.
Overdose
In the event of an overdose, a doctor must be called immediately.
Symptoms
An overdose with parenteral cephalosporins may lead to fits. Owing to the undesirable effects profile, gastrointestinal disturbances can also be expected to occur.
Treatment
There is no specific information available about the treatment of an overdose with ceftriaxone. However, if fits occur, the product must be discontinued and therapy with anticonvulsants taken into consideration.
Supportive treatment is generally indicated. Ceftriaxone is not eliminated by haemodialysis or peritoneal dialysis.

Side effects
What unwanted effects (side effects) may Megion have, although they do not necessarily occur in all patients?
Side effects are defined in this section as follows:

Common:	1% or more, but less than 10%
Uncommon:	0.1% or more, but less than 1%
Rare:	0.01% or more, but less than 0.1%
Very rare, including isolated cases:	0.01% or less

Infections and infestations
Rare
Fungal disease of the genital tract.
Blood and lymphatic system disorders
Rare
Anaemia (including haemolytic anaemia), leukocytopenia, granulocytopenia, thrombocytopenia and eosinophilia.
Very rare
Coagulation disorders.
Agranulocytosis (< 500/mm³), occurring in most cases more than 10 days after the start of therapy or following doses of 20 g or more.
Immune system disorders
Rare
Anaphylactic or anaphylactoid reactions, fever, shivering, urticaria.
Nervous system disorders
Rare
Headache, dizziness.
Gastrointestinal complaints
Common
Diarrhoea, nausea, inflammation of the mucous membrane of the mouth, burning tongue.
Very rare
Inflammation of the colon.
Inflammation of the pancreas, gastrointestinal haemorrhages.
Liver and biliary function disorders

ceftriaxone in pregnant women in order to be able to establish whether it may have any adverse effects. Animal experiments have as yet not indicated any adverse effects on the development of the fetus. Since there are only few data available, caution is advisable when prescribing ceftriaxone to pregnant women.

Breast-feeding

Ceftriaxone passes into breast milk in small concentrations. Ceftriaxone should not be used during breast-feeding unless there is clear indication for doing so.

Precautions for use and special warnings

As with other cephalosporins, cross-allergy with penicillins may occur. Before the start of cephalosporin treatment, the patient's history should be examined with respect to previous hypersensitivity reactions to penicillins or cephalosporins. As with other cephalosporins, ceftriaxone should be administered with care to patients who are known to be hypersensitive to penicillin. As with all broad-spectrum antibiotics, the possibility of superinfections due to ceftriaxone-resistant bacteria during treatment with ceftriaxone should also be considered.

In premature babies, a daily dose of 50 mg/kg should not be exceeded as their enzyme systems are not yet fully developed. In vitro studies have shown that, like several other cephalosporins, ceftriaxone can displace bilirubin from its binding site on serum albumin. Ceftriaxone should therefore be used with great care in newborn babies with hyperbilirubinaemia, especially in premature babies, owing to the risk of bilirubin encephalopathy.

The blood count must be regularly checked during long-term treatment.

As with other antibiotics, the occasional occurrence of vitamin K deficiency should be taken into account.

For patients on a low-sodium diet, the sodium content in ceftriaxone must be borne in mind: Content of sodium in ceftriaxone:

1 Megion 1 g - dry vial contains 83 mg (3.6 mEq) sodium.

The prolonged use of ceftriaxone – as with other cephalosporins - can lead to the development of resistant bacteria, such as enterococci and *Candida* species.

Shadows have been detected on ultrasound scans of the gallbladder, and were interpreted as gallstones. However, this usually happened only after administration of doses higher than the recommended standard dose. These shadows are due to the precipitation of a calcium salt of ceftriaxone and disappeared when treatment with Megion was discontinued or completed.

If symptoms appear, conservative, non-surgical measures are recommended. It is at the doctor´s discretion to discontinue treatment with Megion in such cases.

Inflammation of the pancreas has been observed very rarely. Most of the relevant patients had risk factors for bile retention/bile sludge, e.g. after surgery, parenteral feeding or severe illness. It cannot be ruled out that the use of ceftriaxone is involved in the precipitation process occurring in the gallbladder.

Aminoglycosides and ceftriaxone must not be mixed in the same syringe or in an infusion solution.

Ceftriaxone prepared with lidocaine must never be:

- administered intravenously.
- administered to infants below the age of 30 months.
- administered to patients with a heart block without pacemaker therapy.
- administered to patients with severe heart failure.

High intravenous ceftriaxone doses (> 1 g or ≥ 50 mg/kg) should be administered slowly (over a period of at least 30 minutes) in order to prevent high concentrations in the bile.

The class of cephalosporins shows a tendency to be absorbed on the surface of erythrocyte membranes and give a positive Coombs' test with antibodies against the medicine; mild haemolytic anaemia occurs occasionally. A cross reactivity with penicillins cannot be ruled out in this connection.

of at least 2 weeks.

Babies below the age of 2 weeks should be given (a maximum of) 50 mg/kg.

As soon as the microbes are identified and their sensitivities have been determined, the dose can be reduced appropriately.

The duration of treatment depends on the course of the disease. Treatment for one to two weeks is normally sufficient.

Lyme disease (stages II and III)

In adults and adolescents from the age of 12 years, the treatment dose is 50 mg/kg once a day for a period of 14 days. The maximum daily dose must not exceed 2 g ceftriaxone.

For perioperative prophylaxis, the recommended dose is 1 g, which is administered as a single intramuscular or slow intravenous injection before surgery. In colorectal surgery, a single dose of 2 g can be given in conjunction with an antibiotic against anaerobic bacteria.

Elderly patients:

The adult dose need not be adjusted if kidney and liver functions are satisfactory.

Newborn babies and children up to 12 years of age weighing < 50 kg:

The following single daily doses are recommended:

- Newborn babies: 20-50 mg/kg, administered intravenously over 60 minutes. The dose must never exceed 50 mg/kg. The dose for newborn babies born at full term is the same as that for premature babies.
- Infants and children up to 12 years of age: 20-50 mg/kg. In extremely severe infections, the daily dose can be raised up to 80 mg/kg. The dose must never exceed 80 mg/kg. Intravenous doses of more than 50 mg/kg must be administered as an infusion over a period of 30 minutes.
- The usual adult dose is recommended for children weighing at least 50 kg.

Impaired kidney function:

Patients with impaired kidney function require a change in the ceftriaxone dose only if the liver function is also impaired. The daily dose must be reduced to 2 g or below only if kidney function is extremely impaired (creatinine clearance < 10 ml/min).

In patients suffering from both kidney and liver function impairment, plasma ceftriaxone concentrations must be checked regularly, and the dose be adjusted appropriately.

Patients undergoing dialysis or peritoneal dialysis require no additional supplementary dose of ceftriaxone following the dialysis. Plasma concentrations must, however, be monitored in order to determine whether a dose adjustment is required, since the elimination rate may be lower in these patients.

Impaired liver function:

Patients with normal kidney function require no dose adjustment. In patients suffering from both kidney and liver function impairment, plasma ceftriaxone concentrations must be monitored regularly, and the dose be adjusted appropriately.

Mode of administration

The product may be administered only by a doctor.

Megion 1 g can be administered as an intramuscular or intravenous injection or as intravenous infusion. It is recommended to use the solution immediately after preparation. For detailed information, see "Note on expiry date and storage".

Instructions for handling

Ceftriaxone must not be mixed in the same syringe with other medicines, except 1% lidocaine hydrochloride solution (exclusively for intramuscular injection).

Intramuscular injection: Megion 1 g must be dissolved in 3.5 ml of 1% lidocaine hydrochloride solution. The solution should be administered by deep intramuscular injection. Dosages of more than 1 g should be divided and injected at multiple sites.

Intravenous administration of solutions containing lidocaine must be avoided.

Intravenous injection: Megion 1 g is dissolved in 10 ml of water for injections. The injection must be administered directly into the vein or by infusion via the tube of an intravenous infusion system over a period of at least 2-4 minutes.

Liver and biliary function disorders

Rare

Symptomatic precipitation of calcium ceftriaxone in the gallbladder, elevated liver enzyme levels.

In some ultrasound scans of the gallbladder of patients treated with ceftriaxone, abnormalities including symptoms of gallbladder disorders were found. These were echoes without acoustic shadows, suggesting the presence of sludge, or echoes with acoustic shadows, which may erroneously be interpreted as gallstones. The chemical basis for the shadow detected by ultrasound is predominantly a calcium salt of ceftriaxone. The shadow appears temporarily and disappears after treatment is completed and conservative therapy instituted. Ceftriaxone treatment should therefore be discontinued if patients present with symptoms of a suspected gallbladder disorder and/or the ultrasound findings described above. The risk of precipitates in the gallbladder increases if treatment lasts longer than 14 days or in cases of kidney failure, reduced body fluid (dehydration) or total parenteral feeding. Isolated cases of inflammation of the pancreas (pancreatitis) were reported, but treatment with ceftriaxone could not be identified as the definite cause. Ceftriaxone can precipitate out in the gallbladder in patients of any age, but the probability of this happening is greater in infants, because the ceftriaxone dose is higher in proportion to the body weight. Owing to the increasing risk of precipitation in the gallbladder, doses above 80 mg/kg must be avoided in children if possible. There is no clear evidence that children or infants treated with ceftriaxone develop gallstones or acute inflammation of the gallbladder. Any ceftriaxone precipitations in the gallbladder should be treated by conservative measures.

Skin and subcutaneous tissue disorders

Uncommon

Skin rashes, allergic dermatitis, rashes, swelling, erythema multiforme exudativum.

Very rare

Severe skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis).

Kidney and urinary tract disorders

Rare

Reduced urine volume, elevated serum creatinine concentration.

Very rare

Precipitation in children's kidneys, haematuria.

Generalized disorders and administration site reactions

Rare

Inflammation of the vein in connection with intravenous injection. This can be minimized by injecting the product slowly over a period of 2-4 minutes.

The intramuscular injection of ceftriaxone without lidocaine is painful.

Investigations

Glucosuria may occur.

If you notice any undesirable 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/infusion 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 the information: February 2004

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