In this leaflet:

1 Xorim 1500 mg vial contains 1500 mg cefuroxime equivalent to 1578 mg cefuroxime sodium.

The active substance is cefuroxime sodium

Pharmaceutical form: Powder for solution for injection.
White to off-white powder.

Presentation: Packs of 1, 5, 10, 25, 50 100 vials.

Marketing authorization holder and manufacturer:
Sandoz GmbH, Kundl, Austria

1. WHAT XORIM IS AND WHAT IT IS USED FOR

Xorim inhibits the formation of the cell wall in bacteria, which kills the microbes. The active substance is also resistant to bacteria which comprise a substance (beta-lactamase) that inactivates some antibiotics. The medicine therefore possesses a broad range of activity.

The antibacterial activity of Xorim encompasses gram-positive (e.g. some staphylococcal strains, specific streptococci), gram-negative (e.g. Escherichia coli, Haemophilus influenzae and neisseria) and anaerobic bacteria.

Cefuroxime is suitable for parenteral treatment of the following infections caused by cefuroxime-sensitive microbes:

- infections of the airways, e.g. acute and chronic bronchitis, bacterial pneumonia
- infections of the ears, nose and throat
- infections of the urinary tract
- infections of the skin and soft tissue
- infections of the bones and joints
- infections occurring in obstetrics and gynaecology

2. BEFORE YOU USE XORIM

Do not use Xorim if

- you are hypersensitive (allergic) to cefuroxime or other cephalosporin antibiotics.
- you have a history of immediate allergic reactions and/or severe hypersensitivity reactions to penicillin or other beta-lactam antibiotics.

Take special care with Xorim

In patients with a history of an allergic reaction to penicillin or other beta-lactam antibiotics.
If hypersensitivity reactions occur after the administration of cefuroxime sodium, the medicine must be discontinued immediately and appropriate treatment be instituted.
Particular care is necessary for patients with liver function impairment.

As with other broad-spectrum antibiotics, prolonged use of cefuroxime sodium may lead to overgrowth of insensitive organisms (e.g. *Candida*, *Enterococci* and *Clostridium difficile*), which may require discontinuation of therapy.

If patients develop severe diarrhoea during or after the treatment with cefuroxime sodium, the risk of a life-threatening inflammation of the large intestine (pseudomembranous colitis) must be considered. Cefuroxime sodium must be discontinued and appropriate treatment be instituted. The use of products which inhibit the movement of the intestines (peristalsis) is contraindicated (see Side Effects section).

Long-term use of cefuroxime sodium may lead to overgrowth of microbes which are resistant to cefuroxime sodium. Careful monitoring of the patients is essential. If superinfection occurs during treatment, the doctor must institute appropriate measures (see Side Effects section).

Cefuroxime is excreted via the kidneys. Patients with impaired kidney function will therefore require a dose adjustment.

Pregnancy

Data available on the use of cefuroxime sodium during pregnancy are insufficient to assess its potential harmfulness. Animal studies have to date not yielded any indication of a harmful effect. Cefuroxime crosses the placental barrier. Cefuroxime sodium should not be used during pregnancy if the treating doctor feels that this is not absolutely necessary.
Please inform your doctor if you have become pregnant.

Gastrointestinal complaints:
Common
Gastrointestinal disturbances such as diarrhoea, nausea and vomiting were observed.

Liver and biliary system disorders:
Uncommon
A transient elevation in liver enzymes (AST, ALT and LDH) and in serum bilirubin were observed.
Very rare
Jaundice

Skin and subcutaneous cellular tissue disorders:
Common
Skin rashes, nettle rash, itching
Rare
Severe skin diseases (erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis)

Kidney and urinary system disorders:
Common
Disturbances of serum creatinine and urea levels were reported commonly, especially in patients with impaired kidney function.
Uncommon
Acute kidney inflammation may occur occasionally.
There have been reports of kidney damage. Acute tubular necrosis was induced by overdosage and was moreover associated with the use of cefuroxime in elderly patients and patients with underlying kidney damage.

Generalized disorders and administration site reactions:
Rare
Drug fever
Common
Transient pain and induration may occur commonly at the site of intramuscular injection. The likeliness of such a reaction increases with the dose. Intravenous injection is commonly associated with clot formation and inflammation in the superficial vein, and pain. But it is unlikely that this will require discontinuation of therapy. Sensation of warmth or nausea may occur after rapid intravenous administration of cefuroxime. Dizziness and headache was reported for patients on cefuroxime treatment.

Investigations:
The Coombs' test may yield false-positive results during cefuroxime treatment. Interference with crossmatching is possible.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. STORING XORIM

Keep out of the reach of children!

Note the expiry date on the package.
Do not use Xorim after the expiry date indicated.

Do not store above 30°C. Keep vials in the outer carton to protect the contents from light.

Reconstituted solution: The product must be used immediately. Keep vials in the outer carton to protect the contents from light.

Reconstituted solution: Chemical and physical stability has been demonstrated for 2 hours at 25°C and for 24 hours at 2°C – 8°C.

From a microbiological point of view, the product should be used immediately.
If it is not used immediately, the user holds responsibility for duration and conditions of storage which usually will not exceed 24 hours at 2-8°C, unless preparation was carried out under controlled and validated aseptic conditions.

You can dispose of expired and unused medicines in any pharmacy.

6. Notes on handling and use for doctors and healthcare professionals

6.1 Dosage

Xorim may be administered only by a doctor.
Notes for the doctor

Mode of administration:
Xorim 1500 mg: intravenous injection.

Usual dosage for adults and the elderly:
Most infections respond to 750 mg cefuroxime three times a day. For more severe infections, the dose can be increased to 1500 mg three times a day given by intravenous injection.

Where necessary, the frequency of cefuroxime administration can be increased to four times daily up to a total daily dose of 3 g to 6 g.

Infants, toddlers and children:

The daily dose is in a range from 30 to 100 mg/kg/day and is divided

Breast-feeding
Small amounts of cefuroxime pass into breast milk; women should therefore suspend breast-feeding while being treated with cefuroxime sodium.

Driving and using machines:

Attention: This medicine may impair the speed of reactions and the ability to drive.

Cefuroxime may in some cases cause side effects such as dizziness, which may impair the ability to drive a vehicle, to operate machinery or to work safely (see Side Effects section).

Important information about some of the ingredients of Xorim:

Interactions with other medicines:
Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.

Particular caution is required if high doses of cephalosporin antibiotics are administered to patients being treated with potent diuretics (water pills), such as furosemide, aminoglycosides and amphotericin, as concurrent administration increases the risk of kidney damage.

Concomitant treatment with probenecid may diminish the renal excretion of cephalosporins.

Since bacteriostatic antibiotics may impair the bactericidal activity of cephalosporins, cefuroxime should not be combined with tetracyclines, macrolides or chloramphenicol.

Cefuroxime sodium may influence urine sugar determination.

For intravenous administration, no other medicines must be admixed in the solution.

The Coombs´ test may yield false-positive results during cefuroxime sodium treatment. Interference with crossmatching is possible.

3. HOW TO USE XORIM

Xorim may be administered only by a doctor.

Xorim 250 mg - dry vials, Xorim 750 mg - dry vials and Xorim 1500 mg – dry vials are available for accurate dosing.

Mode of administration:
Xorim 1500 mg: intravenous injection.

For more detailed information see section 6. Notes on handling and use for doctors and healthcare professionals

If you have the impression that the effect of Xorim is too strong or too weak, talk to your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Xorim can have side effects.

Common (10% or less, but more than 1%)
Uncommon (1% or less, but more than 0.1%)
Rare (0.1% or less, but more than 0.01%)
Very rare (0.01% or less)

Infections and infestations:
Rare
Inflammation of the large intestine (pseudomembranous colitis)
As with other antibiotics, long-term use may lead to superinfections caused by insensitive microbes such as candida, enterococci and Clostridium difficile.

Blood and lymphatic system disorders:
Some patients may develop a blood count abnormality (decreased haemoglobin value, eosinophilia, leucopenia, neutropenia and thrombocytopenia).
Very rare
Anaemia

Immune system disorders:
Rare
Serum sickness
Very rare
Hypersensitivity symptoms

Nervous system disorders:
Uncommon
Headache, somnolence
Very rare
Dizziness, restlessness, nervousness, confusion

Disorders of the ear and labyrinth:
Mild to moderate hearing impairment was reported occasionally in conjunction with the use of cefuroxime for the treatment of meningitis in children.

The daily dose is in a range from 30 to 100 mg/kg/day and is divided into three or four doses. Most infections respond to a dose of 60 mg/kg/day.

Newborn babies:

The daily dose is in a range from 30 to 100 mg/kg/day and is divided into two or three doses. In the first weeks of life, the serum half-life of cefuroxime may be three to five times longer than that in adults.

When kidney function is impaired:

A dose reduction is not necessary if creatinine clearance is above 20 ml/minute. If kidney function is more severely impaired, your doctor will adjust the dose appropriately.
Specific precautionary measures with appropriate medical supervision are required if creatinine clearance is <10 ml/minute.

Haemodialysis patients require an additional dose of 750 mg cefuroxime at the end of each dialysis treatment. The appropriate dosage for patients undergoing continuous peritoneal dialysis is generally 750 mg twice daily.

The recommended dosage for patients suffering from kidney failure and undergoing continuous arteriovenous haemodialysis or high-flux haemofiltration in the ICU is 750 mg twice daily.

Cefuroxime is often effective as monotherapy in the treatment of the above-listed infections.

Overdosage

A cephalosporin overdose may cause an irritation of the brain and consequently induce seizures. The serum cefuroxime concentration can be reduced by dialysis (peritoneal or haemodialysis).

6.2 Notes on handling

Compatibility with intravenous solutions

Cefuroxim remains stable for 2 hours at room temperature and for 24 hours at 2°C-8°C when dissolved in:
- water for injections
- 0.9 % sodium chloride solution
- 5 % glucose solution

Instructions for preparation

Xorim 1500 mg – dry vials must not be administered intramuscularly.

Xorim 1500 mg – dry vials, for intravenous injection:
The powder is dissolved in at least 15 ml of water for injections, 0.9 % sodium chloride solution or 5 % glucose solution.
The vial is shaken cautiously to obtain a clear solution.

For contents and concentrations of cefuroxime as a solution: see table below

mg cefuroxime per vial	ml of solvent added	Volume of the ready-for-use solution in ml	Concentration mg/ml
1500	15	16.5	91

Note: Antibiotics must not be added to the customary infusion fluids. Most infusion fluids are administered over the course of 6 to 8 hours, which is inappropriate for antibiotics therapy. Cefuroxime should be administered over short periods of time (30 minutes).

Once prepared for intravenous injection, the white to off-white powder gives a colourless to brownish-yellow solution.

Like all medicinal products for parenteral administration, the prepared solution must be inspected for visible particles and discoloration before administration. The prepared solution is clear. The medicinal product is intended for single use only. Residues of the solution must be discarded.

Incompatibilities
Cefuroxime must not be mixed with aminoglycoside antibiotics in a syringe.
The colour of the solution is strongly affected when cefuroxime is mixed with sodium bicarbonate solutions. Said solution is therefore not recommended for dilution of cefuroxime. For patients receiving sodium bicarbonate solution by infusion, where required, the cefuroxime solution in water for injections can be introduced into the tube of the infusion pump.

Date of the information: April 2005

If you need further information regarding this medicine, please contact your local representative of the marketing authorization holder.

Sandoz GmbH, Kundl, Austria

E