

ANNEX I

**LIST OF THE NAMES, PHARMACEUTICAL FORM, STRENGTHS OF THE MEDICINAL
PRODUCTS, ROUTE OF ADMINISTRATION, MARKETING AUTHORISATION HOLDER
/ APPLICANTS IN THE MEMBER STATES**

<u>Member State</u>	<u>Marketing Authorisation Holder</u>	<u>Applicant</u>	<u>Invented name Name</u>	<u>Strength</u>	<u>Pharmaceutical Form</u>	<u>Route of administration</u>
The Netherlands	Sandoz B.V. Veluwezoom 22 1327 Almere The Netherlands		Cefuroximaxetil 125, omhulde tabletten 125 mg Cefuroximaxetil 250, omhulde tabletten 250 mg Cefuroximaxetil 500, omhulde tabletten 500 mg	125 mg 250 mg 500 mg	Coated tablets	oral use
Estonia		1A Pharma GmbH Keltenring 1 + 3 D-82041 Oberhaching Germany	Cefuroxim 1A Pharma 125 mg Cefuroxim 1A Pharma 250 mg Cefuroxim 1A Pharma 500 mg	125 mg 250 mg 500 mg	Coated tablets	oral use
Greece		Sandoz GmbH Biochemiestrasse 10 6250 Kundl Austria	Cefuroxime axetil Sandoz 250 mg Cefuroxime axetil Sandoz 500 mg	250 mg 500 mg	Coated tablets	oral use
Portugal		Sandoz Farmacêutica Lda. Alameda da Quinta da Beloura, Edifício 1-Esc. 15 2710-693 Sintra Portugal	CEFUROXIMA Sandoz 250 mg COMPRIMIDOS CEFUROXIMA Sandoz 500 mg COMPRIMIDOS	250 mg 500 mg	Coated tablets	oral use
Spain		SANDOZ FARMACÉUTICA, S.A. Gran Vía de les Corts Catalanes, 764 08013 Barcelona Spain	Cefuroxima Sandoz 125 mg comprimidos recubiertos con película EFG Cefuroxima Sandoz 250 mg comprimidos recubiertos con película EFG Cefuroxima Sandoz 500 mg comprimidos recubiertos con película EF	125 mg 250 mg 500 mg	Coated tablets	oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF CEFUROXIMAXETIL (see Annex I)

The active substance, cefuroxime axetil, owes its *in vivo* bactericidal activity to the parent compound cefuroxime. All cephalosporins (β -lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. In the Reference Member State, Cefuroxime axetil tablets are indicated for the treatment of mild to moderately severe infections caused by micro-organisms susceptible to cefuroxime, such as:

- upper respiratory tract infections: acute otitis media, sinusitis, tonsillitis and pharyngitis
- acute bronchitis, acute exacerbations of chronic bronchitis
- lower uncomplicated urinary tract infections: cystitis
- skin and soft tissue infections: furunculosis, pyoderma and impetigo
- uncomplicated gonorrhoea: urethritis and cervicitis
- treatment of early stage Lyme disease (stadium I) and subsequent prevention of late complications in adults and children above 12 years of age.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

During CMD (h) referral, Member States could agree on the indications, except the one referring to gonococcal infections.

During CHMP arbitration, the applicant was asked to further justify the indication “uncomplicated gonorrhoea: urethritis and cervicitis”. The applicant had to address the safety and efficacy of cefuroximaxetil in uncomplicated gonorrhoea and to conclude on the risk-benefit balance for this sought indication.

To address the concerns of the CHMP, **the Applicant** submitted an extensive review of the literature supporting the efficacy of cefuroxime axetil in the treatment of uncomplicated gonorrhoea and specifically in cervicitis and urethritis. The experience with cefuroxime axetil in limited numbers of patients with uncomplicated anorectal gonorrhoea or pharyngeal gonorrhoea is not sufficient and the efficacy is not established and therefore not acceptable and should not be included in the product information.

Taking into account the originator SPCs of cefuroxime axetil and recommendations from the literature on the use of cefuroxime in the treatment of uncomplicated gonorrhoea, it was argued that the inclusion of this indication is fully justified from a clinical and pharmacological point of view. Official guidance should be sought for its use and data on resistance just like for the other recommended antibiotics for this indication.

In order to comply with the NfG on Evaluation of Medicinal Products Indicated for Treatment of Bacterial Infections (CPMP/EWP/558/95 rev.1), the applicant accepted that proposed SPC should be updated in due time to include EUCAST breakpoints.

The **CHMP** nonetheless considered that not sufficient evidence supported the optimal efficacy of cefuroxime axetil in treating uncomplicated gonorrhoea, restricted to urethritis and cervicitis. The efficacy of cefuroxime axetil on other anatomical locations, (which often remain asymptomatic), is highly questionable and consequently treatment with cefuroxime axetil might not curtail further transmission of the infection. Therefore, the inclusion of uncomplicated gonococcal disease is a matter of major concern from a public health perspective, both at individual and community level.

GROUND FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Whereas

- CMD(h) referral agreed on all therapeutic indications, except uncomplicated gonorrhoea: urethritis and cervicitis.
- The scope of the referral was to address the safety and efficacy of cefuroxime axetil in uncomplicated gonorrhoea (cervicitis and urethritis) and to conclude on the risk-benefit balance for this sought indication
- The Summary of Products Characteristic, labelling and package leaflet proposed by the applicant has been assessed based on the documentation submitted and the scientific discussion within the Committee.

the CHMP has recommended by consensus that the indication pertaining uncomplicated gonorrhoea (cervicitis and urethritis) should not be included in the product information. Consequently, the Summary of Product Characteristics and package leaflet should be amended as set out in Annex III. Existing Marketing Authorisations should be varied and pending Marketing Authorisation Applications (see Annex I) should be granted to include these amendments.

ANNEX III

**SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET**

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cefuroximaxetil 125, coated tablets 125 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefuroximaxetil 125 contain 150.36 mg cefuroxime axetil which is equivalent to 125 mg cefuroxime per tablet

Excipient:

Cefuroxime axetil 125 mg coated tablets contain 0.2 mg aspartame.

Cefuroxime axetil 250 mg coated tablets contain 0.3 mg aspartame.

Cefuroxime axetil 500 mg coated tablets contain 0.4 mg aspartame.

For a full list of excipients: see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablets

Cefuroximaxetil 125: white to slightly yellowish, biconvex, oblong tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime axetil is indicated for the treatment of mild to moderately severe infections caused by micro-organisms susceptible to cefuroxime, such as:

- upper respiratory tract infections: acute otitis media, sinusitis, tonsillitis and pharyngitis
- acute bronchitis, acute exacerbations of chronic bronchitis
- lower uncomplicated urinary tract infections: cystitis
- skin and soft tissue infections: furunculosis, pyoderma and impetigo
- treatment of early stage Lyme disease (stadium I) and subsequent prevention of late complications in adults and children above 12 years of age.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Cefuroxime axetil tablets are coated to mask their taste: they should not be chewed.

The usual duration of therapy is 7 days (ranging from 5 to 10 days). In case of pharyngotonsillitis caused by *Streptococcus pyogenes* a therapy duration of at least 10 days is indicated. The duration of treatment of early Lyme disease should be 20 days. In order to achieve optimum absorption cefuroxime axetil tablets should be taken shortly after meals.

The dosage depends on the severity of the infection. For severe infections parenteral forms of cefuroxime are recommended. Where appropriate cefuroxime axetil is effective when used following initial parenteral cefuroxime sodium in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

Dosage schedule for tablets:

Adults and children over 12 years of age	Dosage
Upper respiratory tract infections	250 (– 500) mg twice daily
Lower respiratory tract infections	500 mg twice daily
Lower uncomplicated urinary tract infections	125 – 250 mg twice daily
Skin and soft tissue infections	250 – 500 mg twice daily
Early Lyme disease	500 mg twice daily during 20 days
Children from 5 to 12 years of age	
Above-mentioned indications, if relevant for this group of children	125 – 250 mg twice daily
Acute otitis media	250 mg twice daily

Children under 5 years of age:

Cefuroxime axetil tablets are not suitable for use in children under the age of 5. For patients in this age group it is advised to use an oral suspension. There is no experience in children under 3 months of age.

Dosage regimen in renal impairment, in dialysis patients and elderly :

No special precautions are necessary in patients with renal impairment, or in elderly patients if the daily dosage does not exceed 1 gram. In patients with renal impairment and creatinine clearance below 20 ml/min cefuroxime axetil tablets should be dosed carefully. Patients undergoing haemodialysis will require a supplementary dose of cefuroxime at the end of each dialysis treatment.

4.3 Contra-indications

Hypersensitivity to cefuroxime, other cephalosporins or to any of the excipients.

Previous immediate and /or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam medicinal products.

4.4 Special warnings and precautions for use

If after administration of cefuroxime axetil sensitivity reactions occur, the use should be discontinued immediately and an appropriate treatment should be established.

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.

As with other broad spectrum antibiotics, prolonged use of cefuroxime axetil may result in the overgrowth of non-susceptible organisms (e.g., candida, enterococci and clostridium difficile, which may require interruption of treatment.

In patients who develop severe diarrhoea during or after use of cefuroxime axetil, the risk of life threatening pseudomembranous colitis should be taken into account. The use of cefuroxime axetil should be discontinued and the appropriate treatment established. The use of preparations inhibiting the intestinal peristalsism is contra-indicated (see section 4.8).

A 20-day treatment of Lyme disease may cause the frequency of developing diarrhoea to increase.

Long term use of cefuroxime axetil may lead to an excess of pathogens resistant to cefuroxime axetil. It is of high importance that the patient is carefully checked. If a superinfection occurs during treatment, appropriate measures should be taken (see section 4.8).

The use of cefuroxime axetil is not recommended in patients with severe intestinal tract disorders accompanied by vomiting and diarrhoea, since in these situations a sufficient absorption can not be guaranteed. Administration of a parenteral formulation of cefuroxime should be considered.

The Jarisch-Herxheimer reaction has been reported following cefuroxime axetil treatment of Lyme disease. The reaction results directly from the bactericidal activity of cefuroxime axetil on the spirochaete *Borrelia burgdorferi*. Patients should be informed of this common and usually self-limited reaction being a consequence of antibiotic treatment of Lyme disease.

Simultaneous use of medicines enhancing the pH of the stomach is not recommended (see section 4.5).

There is no clinical experience with the use of cefuroxime axetil in children under the age of 3 months. With respect to the treatment of early Lyme disease there is only clinical experience with children from the age of 12 and with adults.

Special care should be taken with phenylketonuric patients because of the aspartame containing coating.

Cefuroximaxetil 125 contains 0,2 mg aspartame per tablet

Either the glucose oxidase or the hexokinase methods are recommended to determine the blood and plasma glucose levels in patients receiving cefuroxime axetil. Cefuroxime does not interfere in the alkaline picrate assay for creatinine (see section 4.5).

During the treatment with cefuroxime sodium, some children have experienced slight to moderate hearing loss.

4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous use of medicines enhancing the pH of the stomach decreases the bioavailability of cefuroxime axetil. It is recommended to avoid this combination (see section 4.4).

Since bacteriostatic drugs may interfere with the bactericidal action of cephalosporins, it is advisable to avoid giving tetracyclines, macrolides, or chloramphenicol in conjunction with cefuroxime axetil.

The concomitant administration of probenecid can produce higher and sustained concentrations of cefuroxime in the serum and in the bile.

Cefuroxime may interfere with the determination of glucose in urine with copper containing reagentia (Benedict- or Fehling-solution, Clinitest). For the determination of blood- and plasma sugar levels in patients receiving cefuroxime axetil, the glucose-oxidase- or hexokinase method is recommended (see section 4.4).

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood (see section 4.8).

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving potent diuretics, aminoglycosides, or amphotericin as these combinations increases the risk of nephrotoxicity.

4.6 Pregnancy and lactation

Use in pregnancy

There are not sufficient data on the use of cefuroxime axetil during pregnancy to assess its possible harmfulness. So far, animal tests have not yielded evidence of harmfulness. Cefuroxime crosses the placenta. Cefuroxime axetil should not be used during pregnancy unless considered essential by the physician.

Use during lactation

Cefuroxime is excreted to a small degree in human milk; breast feeding should be avoided in women using cefuroxime axetil.

4.7 Effects on ability to drive and use machines

There are no studies of the effect of cefuroxime axetil on the ability to drive and to handle machines. However, any effects are not to be expected.

4.8 Undesirable effects

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very rare ($< 1/10,000$)

Infections and infestations:

Rare

Pseudomembranous colitis

As with other antibiotics prolonged use may lead to secondary superinfections caused by insusceptible organisms, e.g. *Candida*, *Enterococci* and *Clostridium difficile* (see section 4.4).

Blood and the lymphatic system disorders

Rare

Decreased haemoglobin concentration, eosinophilia, leucopenia, neutropenia and thrombocytopenia

Very rare

Haemolytic anaemia

Immune system disorders:

Common

Jarisch-Herxheimer reaction following cefuroxime axetil treatment of Lyme disease (see section 4.4).

Rare

Serum sickness

Very rare

Anaphylaxis

Nervous system disorders

Uncommon

Headache, dizziness

Very rare

Restlessness, nervousness, confusion

Gastrointestinal disorders:

Common

Diarrhoea, nausea and vomiting. The frequency of diarrhoea is related to the administered dose and may rate up to 10% with tablets. The incidence is even higher (approx. 13%) at prolonged treatment of 20 days of early Lyme disease.

Hepato-biliary disorders:

Rare

Transient increases of hepatic enzyme levels (AST, ALT and LDH) and serum bilirubin.

Very rare

Jaundice.

Skin and subcutaneous tissue disorders:

Common

Skin rashes, urticaria, pruritus.

Very rare

Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis

Renal and urinary disorders

Common

Increased levels of creatinine and urea in serum, especially in patients with impaired renal function.

Uncommon

Acute interstitial nephritis

General disorders and administration site conditions:

Rare

Drug fever

Investigations

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood (see 4.5. Interactions).

4.9 Overdose

Overdose of cephalosporins may cause cerebral irritancy leading to convulsions. In case of overdose cefuroxime serum levels can be reduced by haemodialysis and peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: cephalosporins and related substances, ATC-Code: J01D A06

Mode of action

Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime.

All cephalosporins (β -lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. The initial step in drug action consists of binding of the drug to cell receptors, called Penicillin-Binding Proteins. After a β -lactam antibiotic has bound to these receptors, the transpeptidation reaction is inhibited and peptidoglycan synthesis is blocked. Bacterial lysis is the end result.

Mechanism of resistance

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- hydrolysis by beta-lactamases. Cefuroxime may be efficiently hydrolysed by certain of the extended-spectrum beta-lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme that may be induced or stably derepressed in certain aerobic gram-negative bacterial species
- reduced affinity of penicillin-binding proteins for cefuroxime

- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in gram-negative organisms
- drug efflux pumps

Methicillin-resistant staphylococci (MRS) are resistant to all currently available β -lactam antibiotics including cefuroxime.

Penicillin-resistant *Streptococcus pneumoniae* are cross-resistant to cephalosporins such as cefuroxime through alteration of penicillin binding proteins.

Beta-lactamase negative, ampicillin resistant (BLNAR) strains of *H. influenzae* should be considered resistant to cefuroxime despite apparent in vitro susceptibility.

Strains of Enterobacteriaceae, in particular *Klebsiella* spp. and *Escherichia coli* that produce ESBLs (extended spectrum β -lactamase) may be clinically resistant to therapy with cephalosporins despite apparent in vitro susceptibility and should be considered as resistant.

Breakpoints:

According to the NCCLS (National Committee on Clinical Laboratory Standards) in 2001 the following breakpoints have been defined for cefuroxime axetil:

Enterobacteriaceae: $\leq 4 \mu\text{g/ml}$ susceptible, $\geq 32 \mu\text{g/ml}$ resistant

Staphylococcus spp.: $\leq 4 \mu\text{g/ml}$ susceptible, $\geq 32 \mu\text{g/ml}$ resistant

Haemophilus spp.: $\leq 4 \mu\text{g/ml}$ susceptible; $\geq 16 \mu\text{g/ml}$ resistant

Streptococcus pneumoniae: $\leq 1 \mu\text{g/ml}$ susceptible, $\geq 4 \mu\text{g/ml}$ resistant

Streptococcus spp. other than *S. pneumoniae*:

Streptococcal isolates susceptible to penicillin ($\text{MIC}_{90} \leq 0.12 \mu\text{g/ml}$) may be considered susceptible to cefuroxime.

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
<u>Aerobes, Gram positive:</u> <i>Staphylococcus aureus</i> (methicillin-susceptible) Coagulase-negative staphylococci (methicillin-susceptible) <i>Streptococcus agalactiae</i> <i>Streptococcus pneumoniae</i> <i>Streptococcus pyogenes</i>
<u>Aerobes, Gram negative:</u> <i>Escherichia coli</i> <i>Haemophilus influenzae</i> <i>Klebsiella</i> species <i>Moraxella catarrhalis</i> <i>Proteus mirabilis</i> <i>Proteus rettgeri</i>
<u>Anaerobes:</u> <i>Peptococcus</i> species <i>Peptostreptococcus</i> species
<u>Other organisms:</u>

<i>Borrelia burgdorferi.</i>
Species for which resistance may be a problem
<i>Acinetobacter</i> species <i>Citrobacter</i> species <i>Enterobacter</i> species <i>Morganella morganii</i>
<u>Resistant</u> <i>Bacteroides fragilis</i> <i>Clostridium difficile</i> Enterococci <i>Listeria monocytogenes</i> <i>Proteus vulgaris</i> <i>Pseudomonas</i> species <i>Serratia</i> species

5.2 Pharmacokinetic properties

Absorption: After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood causing the release of the active compound cefuroxime into the circulation. Optimum absorption occurs when Cefuroximaxetil is taken shortly after a meal (50-60%). Under these circumstances maximum serum concentration is achieved after 2-3 hours.

Distribution: Cefuroxime is widely distributed in the body including pleural fluid, sputum, bone, synovial fluid, and aqueous humour, but only achieves therapeutic concentrations in the CSF when the meninges are inflamed. About 50% of cefuroxime in the circulation is bound to plasma proteins. It diffuses across the placenta and has been detected in breast milk.

Metabolism: Cefuroxime is not metabolised.

Elimination: Most of the dose of cefuroxime is excreted unchanged. About 50% is excreted by glomerular filtration and about 50% through renal tubular secretion within 24 hours, with the majority being eliminated within 6 hours; high concentrations are achieved in the urine. Small amounts of cefuroxime are excreted in bile.

Probenecid competes with cefuroxime for renal tubular secretion resulting in higher and more prolonged plasma concentrations of cefuroxime.

The plasma half-life ranges between 60 and 90 minutes and is prolonged in patients with renal impairment and in neonates.

Dialysis causes the decrease of cefuroxime serum levels.

5.3 Preclinical safety data

Preclinical effects were observed in dosages far above the maximal human dosage which are therefore hardly relevant for the clinical use of cefuroxime axetil.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core: sodium lauryl sulphate, copovidone, croscarmellose sodium (E468), magnesium stearate (E470B), colloidal anhydrous silica (E551), granulated mannitol (E421), microcrystalline cellulose (E460), crospovidone (E1202), talc (E553B).

Coat: mannitol (E421), soluble starch (potato), talc (E553B), titanium dioxide (E171), aspartame (E951)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Al/Al strip: 36 months

Al/Al blister: 36 months

6.4 Special precautions for storage

Al/Al strip: Store in the original packaging

Al/Al blister: Store in the original packaging

6.5. Nature and contents of container

Al/Al strip packaging

Al/Al blister packaging

Pack sizes:

125 mg: 8, 10, 12, 14, 24 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I – to be completed nationally]

8. MARKETING AUTHORISATION NUMBERS

[to be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

[to be completed nationally]

10. DATE OF REVISION OF THE TEXT

[to be completed nationally]

1. NAME OF THE MEDICINAL PRODUCT

Cefuroximaxetil 250, coated tablets 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefuroximaxetil 250 contain 300.72 mg cefuroxime axetil which is equivalent to 250 mg cefuroxime per tablet

Excipient:

Cefuroxime axetil 250 mg coated tablets contain 0.3 mg aspartame.

For a full list of excipients: see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablets

Cefuroximaxetil 250: white to slightly yellowish, biconvex, oblong tablets, scored on both sides

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime axetil is indicated for the treatment of mild to moderately severe infections caused by micro-organisms susceptible to cefuroxime, such as:

- upper respiratory tract infections: acute otitis media, sinusitis, tonsillitis and pharyngitis
- acute bronchitis, acute exacerbations of chronic bronchitis
- lower uncomplicated urinary tract infections: cystitis
- skin and soft tissue infections: furunculosis, pyoderma and impetigo
- treatment of early stage Lyme disease (stadium I) and subsequent prevention of late complications in adults and children above 12 years of age.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Cefuroxime axetil tablets are coated to mask their taste: they should not be chewed.

The usual duration of therapy is 7 days (ranging from 5 to 10 days). In case of pharyngotonsillitis caused by *Streptococcus pyogenes* a therapy duration of at least 10 days is indicated. The duration of treatment of early Lyme disease should be 20 days. In order to achieve optimum absorption cefuroxime axetil tablets should be taken shortly after meals.

The dosage depends on the severity of the infection. For severe infections parenteral forms of cefuroxime are recommended. Where appropriate cefuroxime axetil is effective when used following initial parenteral cefuroxime sodium in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

Dosage schedule for tablets:

Adults and children over 12 years of age	Dosage
Upper respiratory tract infections	250 (– 500) mg twice daily
Lower respiratory tract infections	500 mg twice daily
Lower uncomplicated urinary tract infections	125 – 250 mg twice daily
Skin and soft tissue infections	250 – 500 mg twice daily
Early Lyme disease	500 mg twice daily during 20 days
Children from 5 to 12 years of age	
Above-mentioned indications, if relevant for this group of children	125 – 250 mg twice daily
Acute otitis media	250 mg twice daily

Children under 5 years of age:

Cefuroxime axetil tablets are not suitable for use in children under the age of 5. For patients in this age group it is advised to use an oral suspension. There is no experience in children under 3 months of age.

Dosage regimen in renal impairment, in dialysis patients and elderly :

No special precautions are necessary in patients with renal impairment, or in elderly patients if the daily dosage does not exceed 1 gram. In patients with renal impairment and creatinine clearance below 20 ml/min cefuroxime axetil tablets should be dosed carefully. Patients undergoing haemodialysis will require a supplementary dose of cefuroxime at the end of each dialysis treatment.

4.3 Contra-indications

Hypersensitivity to cefuroxime, other cephalosporins or to any of the excipients.

Previous immediate and /or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam medicinal products.

4.4 Special warnings and precautions for use

If after administration of cefuroxime axetil sensitivity reactions occur, the use should be discontinued immediately and an appropriate treatment should be established.

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.

As with other broad spectrum antibiotics, prolonged use of cefuroxime axetil may result in the overgrowth of non-susceptible organisms (e.g., candida, enterococci and clostridium difficile, which may require interruption of treatment.

In patients who develop severe diarrhoea during or after use of cefuroxime axetil, the risk of life threatening pseudomembranous colitis should be taken into account. The use of cefuroxime axetil should be discontinued and the appropriate treatment established. The use of preparations inhibiting the intestinal peristalsism is contra-indicated (see section 4.8).

A 20-day treatment of Lyme disease may cause the frequency of developing diarrhoea to increase.

Long term use of cefuroxime axetil may lead to an excess of pathogens resistant to cefuroxime axetil. It is of high importance that the patient is carefully checked. If a superinfection occurs during treatment, appropriate measures should be taken (see section 4.8).

The use of cefuroxime axetil is not recommended in patients with severe intestinal tract disorders accompanied by vomiting and diarrhoea, since in these situations a sufficient absorption can not be guaranteed. Administration of a parenteral formulation of cefuroxime should be considered.

The Jarisch-Herxheimer reaction has been reported following cefuroxime axetil treatment of Lyme disease. The reaction results directly from the bactericidal activity of cefuroxime axetil on the spirochaete *Borrelia burgdorferi*. Patients should be informed of this common and usually self-limited reaction being a consequence of antibiotic treatment of Lyme disease.

Simultaneous use of medicines enhancing the pH of the stomach is not recommended (see section 4.5).

There is no clinical experience with the use of cefuroxime axetil in children under the age of 3 months. With respect to the treatment of early Lyme disease there is only clinical experience with children from the age of 12 and with adults.

Special care should be taken with phenylketonuric patients because of the aspartame containing coating.

Cefuroximaxetil 250 contains 0,3 mg aspartame per tablet

Either the glucose oxidase or the hexokinase methods are recommended to determine the blood and plasma glucose levels in patients receiving cefuroxime axetil. Cefuroxime does not interfere in the alkaline picrate assay for creatinine (see section 4.5).

During the treatment with cefuroxime sodium, some children have experienced slight to moderate hearing loss.

4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous use of medicines enhancing the pH of the stomach decreases the bioavailability of cefuroxime axetil. It is recommended to avoid this combination (see section 4.4).

Since bacteriostatic drugs may interfere with the bactericidal action of cephalosporins, it is advisable to avoid giving tetracyclines, macrolides, or chloramphenicol in conjunction with cefuroxime axetil.

The concomitant administration of probenecid can produce higher and sustained concentrations of cefuroxime in the serum and in the bile.

Cefuroxime may interfere with the determination of glucose in urine with copper containing reagentia (Benedict- or Fehling-solution, Clinitest). For the determination of blood- and plasma sugar levels in patients receiving cefuroxime axetil, the glucose-oxidase- or hexokinase method is recommended (see section 4.4).

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood (see section 4.8).

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving potent diuretics, aminoglycosides, or amphotericin as these combinations increases the risk of nephrotoxicity.

4.6 Pregnancy and lactation

Use in pregnancy

There are not sufficient data on the use of cefuroxime axetil during pregnancy to assess its possible harmfulness. So far, animal tests have not yielded evidence of harmfulness. Cefuroxime crosses the placenta. Cefuroxime axetil should not be used during pregnancy unless considered essential by the physician.

Use during lactation

Cefuroxime is excreted to a small degree in human milk; breast feeding should be avoided in women using cefuroxime axetil.

4.7 Effects on ability to drive and use machines

There are no studies of the effect of cefuroxime axetil on the ability to drive and to handle machines. However, any effects are not to be expected.

4.8 Undesirable effects

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very rare ($< 1/10,000$)

Infections and infestations:

Rare

Pseudomembranous colitis

As with other antibiotics prolonged use may lead to secondary superinfections caused by insusceptible organisms, e.g. *Candida*, *Enterococci* and *Clostridium difficile* (see section 4.4).

Blood and the lymphatic system disorders

Rare

Decreased haemoglobin concentration, eosinophilia, leucopenia, neutropenia and thrombocytopenia

Very rare

Haemolytic anaemia

Immune system disorders:

Common

Jarisch-Herxheimer reaction following cefuroxime axetil treatment of Lyme disease (see section 4.4).

Rare

Serum sickness

Very rare

Anaphylaxis

Nervous system disorders

Uncommon

Headache, dizziness

Very rare

Restlessness, nervousness, confusion

Gastrointestinal disorders:

Common

Diarrhoea, nausea and vomiting. The frequency of diarrhoea is related to the administered dose and may rate up to 10% with tablets. The incidence is even higher (approx. 13%) at prolonged treatment of 20 days of early Lyme disease.

Hepato-biliary disorders:

Rare

Transient increases of hepatic enzyme levels (AST, ALT and LDH) and serum bilirubin.

Very rare

Jaundice.

Skin and subcutaneous tissue disorders:

Common

Skin rashes, urticaria, pruritus.

Very rare

Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis

Renal and urinary disorders

Common

Increased levels of creatinine and urea in serum, especially in patients with impaired renal function.

Uncommon

Acute interstitial nephritis

General disorders and administration site conditions:

Rare

Drug fever

Investigations

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood (see 4.5. Interactions).

4.9 Overdose

Overdose of cephalosporins may cause cerebral irritancy leading to convulsions. In case of overdose cefuroxime serum levels can be reduced by haemodialysis and peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: cephalosporins and related substances, ATC-Code: J01D A06

Mode of action

Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime. All cephalosporins (β -lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. The initial step in drug action consists of binding of the drug to cell receptors, called Penicillin-Binding Proteins. After a β -lactam antibiotic has bound to these receptors, the transpeptidation reaction is inhibited and peptidoglycan synthesis is blocked. Bacterial lysis is the end result.

Mechanism of resistance

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- hydrolysis by β -lactamases. Cefuroxime may be efficiently hydrolysed by certain of the extended-spectrum β -lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme that may be induced or stably derepressed in certain aerobic gram-negative bacterial species
- reduced affinity of penicillin-binding proteins for cefuroxime

- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in gram-negative organisms
- drug efflux pumps

Methicillin-resistant staphylococci (MRS) are resistant to all currently available β -lactam antibiotics including cefuroxime.

Penicillin-resistant *Streptococcus pneumoniae* are cross-resistant to cephalosporins such as cefuroxime through alteration of penicillin binding proteins.

Beta-lactamase negative, ampicillin resistant (BLNAR) strains of *H. influenzae* should be considered resistant to cefuroxime despite apparent in vitro susceptibility.

Strains of Enterobacteriaceae, in particular *Klebsiella* spp. and *Escherichia coli* that produce ESBLs (extended spectrum β -lactamase) may be clinically resistant to therapy with cephalosporins despite apparent in vitro susceptibility and should be considered as resistant.

Breakpoints:

According to the NCCLS (National Committee on Clinical Laboratory Standards) in 2001 the following breakpoints have been defined for cefuroxime axetil:

Enterobacteriaceae: $\leq 4 \mu\text{g/ml}$ susceptible, $\geq 32 \mu\text{g/ml}$ resistant

Staphylococcus spp.: $\leq 4 \mu\text{g/ml}$ susceptible, $\geq 32 \mu\text{g/ml}$ resistant

Haemophilus spp.: $\leq 4 \mu\text{g/ml}$ susceptible; $\geq 16 \mu\text{g/ml}$ resistant

Streptococcus pneumoniae: $\leq 1 \mu\text{g/ml}$ susceptible, $\geq 4 \mu\text{g/ml}$ resistant

Streptococcus spp. other than *S. pneumoniae*:

Streptococcal isolates susceptible to penicillin ($\text{MIC}_{90} \leq 0.12 \mu\text{g/ml}$) may be considered susceptible to cefuroxime.

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
<u>Aerobes, Gram positive:</u> <i>Staphylococcus aureus</i> (methicillin-susceptible) Coagulase-negative staphylococci (methicillin-susceptible) <i>Streptococcus agalactiae</i> <i>Streptococcus pneumoniae</i> <i>Streptococcus pyogenes</i>
<u>Aerobes, Gram negative:</u> <i>Escherichia coli</i> <i>Haemophilus influenzae</i> <i>Klebsiella</i> species <i>Moraxella catarrhalis</i> <i>Proteus mirabilis</i> <i>Proteus rettgeri</i>
<u>Anaerobes:</u> <i>Peptococcus</i> species <i>Peptostreptococcus</i> species
<u>Other organisms:</u>

<i>Borrelia burgdorferi.</i>
Species for which resistance may be a problem
<i>Acinetobacter</i> species <i>Citrobacter</i> species <i>Enterobacter</i> species <i>Morganella morganii</i>
<u>Resistant</u> <i>Bacteroides fragilis</i> <i>Clostridium difficile</i> Enterococci <i>Listeria monocytogenes</i> <i>Proteus vulgaris</i> <i>Pseudomonas</i> species <i>Serratia</i> species

5.2 Pharmacokinetic properties

Absorption: After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood causing the release of the active compound cefuroxime into the circulation. Optimum absorption occurs when Cefuroximaxetil is taken shortly after a meal (50-60%). Under these circumstances maximum serum concentration is achieved after 2-3 hours.

Distribution: Cefuroxime is widely distributed in the body including pleural fluid, sputum, bone, synovial fluid, and aqueous humour, but only achieves therapeutic concentrations in the CSF when the meninges are inflamed. About 50% of cefuroxime in the circulation is bound to plasma proteins. It diffuses across the placenta and has been detected in breast milk.

Metabolism: Cefuroxime is not metabolised.

Elimination: Most of the dose of cefuroxime is excreted unchanged. About 50% is excreted by glomerular filtration and about 50% through renal tubular secretion within 24 hours, with the majority being eliminated within 6 hours; high concentrations are achieved in the urine. Small amounts of cefuroxime are excreted in bile.

Probenecid competes with cefuroxime for renal tubular secretion resulting in higher and more prolonged plasma concentrations of cefuroxime.

The plasma half-life ranges between 60 and 90 minutes and is prolonged in patients with renal impairment and in neonates.

Dialysis causes the decrease of cefuroxime serum levels.

5.3 Preclinical safety data

Preclinical effects were observed in dosages far above the maximal human dosage which are therefore hardly relevant for the clinical use of cefuroxime axetil.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core: sodium lauryl sulphate, copovidone, croscarmellose sodium (E468), magnesium stearate (E470B), colloidal anhydrous silica (E551), granulated mannitol (E421), microcrystalline cellulose (E460), crospovidone (E1202), talc (E553B).

Coat: mannitol (E421), soluble starch (potato), talc (E553B), titanium dioxide (E171), aspartame (E951)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Al/Al strip: 36 months

Al/Al blister: 36 months

6.4 Special precautions for storage

Al/Al strip: Store in the original packaging

Al/Al blister: Store in the original packaging

6.5. Nature and contents of container

Al/Al strip packaging

Al/Al blister packaging

Pack sizes:

250 mg: 8, 10, 12, 14, 24 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I – to be completed nationally]

8. MARKETING AUTHORISATION NUMBERS

[to be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

[to be completed nationally]

10. DATE OF REVISION OF THE TEXT

[to be completed nationally]

1. NAME OF THE MEDICINAL PRODUCT

Cefuroximaxetil 500, coated tablets 500 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefuroximaxetil 500 contain 601.44 mg cefuroxime axetil which is equivalent to 500 mg cefuroxime per tablet

Excipient:

Cefuroxime axetil 500 mg coated tablets contain 0.4 mg aspartame.

For a full list of excipients: see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablets

Cefuroximaxetil 500: white to slightly yellowish, biconvex, oblong tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefuroxime axetil is indicated for the treatment of mild to moderately severe infections caused by micro-organisms susceptible to cefuroxime, such as:

- upper respiratory tract infections: acute otitis media, sinusitis, tonsillitis and pharyngitis
- acute bronchitis, acute exacerbations of chronic bronchitis
- lower uncomplicated urinary tract infections: cystitis
- skin and soft tissue infections: furunculosis, pyoderma and impetigo
- treatment of early stage Lyme disease (stadium I) and subsequent prevention of late complications in adults and children above 12 years of age.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Cefuroxime axetil tablets are coated to mask their taste: they should not be chewed.

The usual duration of therapy is 7 days (ranging from 5 to 10 days). In case of pharyngotonsillitis caused by *Streptococcus pyogenes* a therapy duration of at least 10 days is indicated. The duration of treatment of early Lyme disease should be 20 days. In order to achieve optimum absorption cefuroxime axetil tablets should be taken shortly after meals.

The dosage depends on the severity of the infection. For severe infections parenteral forms of cefuroxime are recommended. Where appropriate cefuroxime axetil is effective when used following initial parenteral cefuroxime sodium in the treatment of pneumonia and acute exacerbations of chronic bronchitis.

Dosage schedule for tablets:

Adults and children over 12 years of age	Dosage
Upper respiratory tract infections	250 (– 500) mg twice daily
Lower respiratory tract infections	500 mg twice daily
Lower uncomplicated urinary tract infections	125 – 250 mg twice daily
Skin and soft tissue infections	250 – 500 mg twice daily
Early Lyme disease	500 mg twice daily during 20 days
Children from 5 to 12 years of age	
Above-mentioned indications, if relevant for this group of children	125 – 250 mg twice daily
Acute otitis media	250 mg twice daily

Children under 5 years of age:

Cefuroxime axetil tablets are not suitable for use in children under the age of 5. For patients in this age group it is advised to use an oral suspension. There is no experience in children under 3 months of age.

Dosage regimen in renal impairment, in dialysis patients and elderly :

No special precautions are necessary in patients with renal impairment, or in elderly patients if the daily dosage does not exceed 1 gram. In patients with renal impairment and creatinine clearance below 20 ml/min cefuroxime axetil tablets should be dosed carefully. Patients undergoing haemodialysis will require a supplementary dose of cefuroxime at the end of each dialysis treatment.

4.3 Contra-indications

Hypersensitivity to cefuroxime, other cephalosporins or to any of the excipients.

Previous immediate and /or severe hypersensitivity reaction to a penicillin or to any other type of beta-lactam medicinal products.

4.4 Special warnings and precautions for use

If after administration of cefuroxime axetil sensitivity reactions occur, the use should be discontinued immediately and an appropriate treatment should be established.

Special care is indicated in patients who have experienced an allergic reaction to penicillins or other beta-lactams.

As with other broad spectrum antibiotics, prolonged use of cefuroxime axetil may result in the overgrowth of non-susceptible organisms (e.g., candida, enterococci and clostridium difficile, which may require interruption of treatment.

In patients who develop severe diarrhoea during or after use of cefuroxime axetil, the risk of life threatening pseudomembranous colitis should be taken into account. The use of cefuroxime axetil should be discontinued and the appropriate treatment established. The use of preparations inhibiting the intestinal peristalsism is contra-indicated (see section 4.8).

A 20-day treatment of Lyme disease may cause the frequency of developing diarrhoea to increase.

Long term use of cefuroxime axetil may lead to an excess of pathogens resistant to cefuroxime axetil. It is of high importance that the patient is carefully checked. If a superinfection occurs during treatment, appropriate measures should be taken (see section 4.8).

The use of cefuroxime axetil is not recommended in patients with severe intestinal tract disorders accompanied by vomiting and diarrhoea, since in these situations a sufficient absorption can not be guaranteed. Administration of a parenteral formulation of cefuroxime should be considered.

The Jarisch-Herxheimer reaction has been reported following cefuroxime axetil treatment of Lyme disease. The reaction results directly from the bactericidal activity of cefuroxime axetil on the spirochaete *Borrelia burgdorferi*. Patients should be informed of this common and usually self-limited reaction being a consequence of antibiotic treatment of Lyme disease.

Simultaneous use of medicines enhancing the pH of the stomach is not recommended (see section 4.5).

There is no clinical experience with the use of cefuroxime axetil in children under the age of 3 months. With respect to the treatment of early Lyme disease there is only clinical experience with children from the age of 12 and with adults.

Special care should be taken with phenylketonuric patients because of the aspartame containing coating.

Cefuroximaxetil 500 contains 0,4 mg aspartame per tablet

Either the glucose oxidase or the hexokinase methods are recommended to determine the blood and plasma glucose levels in patients receiving cefuroxime axetil. Cefuroxime does not interfere in the alkaline picrate assay for creatinine (see section 4.5).

During the treatment with cefuroxime sodium, some children have experienced slight to moderate hearing loss.

4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous use of medicines enhancing the pH of the stomach decreases the bioavailability of cefuroxime axetil. It is recommended to avoid this combination (see section 4.4).

Since bacteriostatic drugs may interfere with the bactericidal action of cephalosporins, it is advisable to avoid giving tetracyclines, macrolides, or chloramphenicol in conjunction with cefuroxime axetil.

The concomitant administration of probenecid can produce higher and sustained concentrations of cefuroxime in the serum and in the bile.

Cefuroxime may interfere with the determination of glucose in urine with copper containing reagentia (Benedict- or Fehling-solution, Clinitest). For the determination of blood- and plasma sugar levels in patients receiving cefuroxime axetil, the glucose-oxidase- or hexokinase method is recommended (see section 4.4).

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood (see section 4.8).

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving potent diuretics, aminoglycosides, or amphotericin as these combinations increases the risk of nephrotoxicity.

4.6 Pregnancy and lactation

Use in pregnancy

There are not sufficient data on the use of cefuroxime axetil during pregnancy to assess its possible harmfulness. So far, animal tests have not yielded evidence of harmfulness. Cefuroxime crosses the placenta. Cefuroxime axetil should not be used during pregnancy unless considered essential by the physician.

Use during lactation

Cefuroxime is excreted to a small degree in human milk; breast feeding should be avoided in women using cefuroxime axetil.

4.7 Effects on ability to drive and use machines

There are no studies of the effect of cefuroxime axetil on the ability to drive and to handle machines. However, any effects are not to be expected.

4.8 Undesirable effects

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Very rare ($< 1/10,000$)

Infections and infestations:

Rare

Pseudomembranous colitis

As with other antibiotics prolonged use may lead to secondary superinfections caused by insusceptible organisms, e.g. *Candida*, *Enterococci* and *Clostridium difficile* (see section 4.4).

Blood and the lymphatic system disorders

Rare

Decreased haemoglobin concentration, eosinophilia, leucopenia, neutropenia and thrombocytopenia

Very rare

Haemolytic anaemia

Immune system disorders:

Common

Jarisch-Herxheimer reaction following cefuroxime axetil treatment of Lyme disease (see section 4.4).

Rare

Serum sickness

Very rare

Anaphylaxis

Nervous system disorders

Uncommon

Headache, dizziness

Very rare

Restlessness, nervousness, confusion

Gastrointestinal disorders:

Common

Diarrhoea, nausea and vomiting. The frequency of diarrhoea is related to the administered dose and may rate up to 10% with tablets. The incidence is even higher (approx. 13%) at prolonged treatment of 20 days of early Lyme disease.

Hepato-biliary disorders:

Rare

Transient increases of hepatic enzyme levels (AST, ALT and LDH) and serum bilirubin.

Very rare

Jaundice.

Skin and subcutaneous tissue disorders:

Common

Skin rashes, urticaria, pruritus.

Very rare

Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis

Renal and urinary disorders

Common

Increased levels of creatinine and urea in serum, especially in patients with impaired renal function.

Uncommon

Acute interstitial nephritis

General disorders and administration site conditions:

Rare

Drug fever

Investigations

The use of cefuroxime axetil may be accompanied by a false positive Coombs test. This may interfere with the performance of cross matching tests with blood (see 4.5. Interactions).

4.9 Overdose

Overdose of cephalosporins may cause cerebral irritancy leading to convulsions. In case of overdose cefuroxime serum levels can be reduced by haemodialysis and peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: cephalosporins and related substances, ATC-Code: J01D A06

Mode of action

Cefuroxime axetil owes its *in vivo* bactericidal activity to the parent compound cefuroxime.

All cephalosporins (β -lactam antibiotics) inhibit cell wall production and are selective inhibitors of peptidoglycan synthesis. The initial step in drug action consists of binding of the drug to cell receptors, called Penicillin-Binding Proteins. After a β -lactam antibiotic has bound to these receptors, the transpeptidation reaction is inhibited and peptidoglycan synthesis is blocked. Bacterial lysis is the end result.

Mechanism of resistance

Bacterial resistance to cefuroxime may be due to one or more of the following mechanisms:

- hydrolysis by beta-lactamases. Cefuroxime may be efficiently hydrolysed by certain of the extended-spectrum beta-lactamases (ESBLs) and by the chromosomally-encoded (AmpC) enzyme that may be induced or stably derepressed in certain aerobic gram-negative bacterial species
- reduced affinity of penicillin-binding proteins for cefuroxime

- outer membrane impermeability, which restricts access of cefuroxime to penicillin binding proteins in gram-negative organisms
- drug efflux pumps

Methicillin-resistant staphylococci (MRS) are resistant to all currently available β -lactam antibiotics including cefuroxime.

Penicillin-resistant *Streptococcus pneumoniae* are cross-resistant to cephalosporins such as cefuroxime through alteration of penicillin binding proteins.

Beta-lactamase negative, ampicillin resistant (BLNAR) strains of *H. influenzae* should be considered resistant to cefuroxime despite apparent in vitro susceptibility.

Strains of Enterobacteriaceae, in particular *Klebsiella* spp. and *Escherichia coli* that produce ESBLs (extended spectrum β -lactamase) may be clinically resistant to therapy with cephalosporins despite apparent in vitro susceptibility and should be considered as resistant.

Breakpoints:

According to the NCCLS (National Committee on Clinical Laboratory Standards) in 2001 the following breakpoints have been defined for cefuroxime axetil:

Enterobacteriaceae: $\leq 4 \mu\text{g/ml}$ susceptible, $\geq 32 \mu\text{g/ml}$ resistant

Staphylococcus spp.: $\leq 4 \mu\text{g/ml}$ susceptible, $\geq 32 \mu\text{g/ml}$ resistant

Haemophilus spp.: $\leq 4 \mu\text{g/ml}$ susceptible; $\geq 16 \mu\text{g/ml}$ resistant

Streptococcus pneumoniae: $\leq 1 \mu\text{g/ml}$ susceptible, $\geq 4 \mu\text{g/ml}$ resistant

Streptococcus spp. other than *S. pneumoniae*:

Streptococcal isolates susceptible to penicillin ($\text{MIC}_{90} \leq 0.12 \mu\text{g/ml}$) may be considered susceptible to cefuroxime.

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
<u>Aerobes, Gram positive:</u> <i>Staphylococcus aureus</i> (methicillin-susceptible) Coagulase-negative staphylococci (methicillin-susceptible) <i>Streptococcus agalactiae</i> <i>Streptococcus pneumoniae</i> <i>Streptococcus pyogenes</i>
<u>Aerobes, Gram negative:</u> <i>Escherichia coli</i> <i>Haemophilus influenzae</i> <i>Klebsiella</i> species <i>Moraxella catarrhalis</i> <i>Proteus mirabilis</i> <i>Proteus rettgeri</i>
<u>Anaerobes:</u> <i>Peptococcus</i> species <i>Peptostreptococcus</i> species
<u>Other organisms:</u>

<i>Borrelia burgdorferi.</i>
Species for which resistance may be a problem
<i>Acinetobacter</i> species <i>Citrobacter</i> species <i>Enterobacter</i> species <i>Morganella morganii</i>
<u>Resistant</u> <i>Bacteroides fragilis</i> <i>Clostridium difficile</i> Enterococci <i>Listeria monocytogenes</i> <i>Proteus vulgaris</i> <i>Pseudomonas</i> species <i>Serratia</i> species

5.2 Pharmacokinetic properties

Absorption: After oral administration cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolysed in the intestinal mucosa and blood causing the release of the active compound cefuroxime into the circulation. Optimum absorption occurs when Cefuroximaxetil is taken shortly after a meal (50-60%). Under these circumstances maximum serum concentration is achieved after 2-3 hours.

Distribution: Cefuroxime is widely distributed in the body including pleural fluid, sputum, bone, synovial fluid, and aqueous humour, but only achieves therapeutic concentrations in the CSF when the meninges are inflamed. About 50% of cefuroxime in the circulation is bound to plasma proteins. It diffuses across the placenta and has been detected in breast milk.

Metabolism: Cefuroxime is not metabolised.

Elimination: Most of the dose of cefuroxime is excreted unchanged. About 50% is excreted by glomerular filtration and about 50% through renal tubular secretion within 24 hours, with the majority being eliminated within 6 hours; high concentrations are achieved in the urine. Small amounts of cefuroxime are excreted in bile.

Probenecid competes with cefuroxime for renal tubular secretion resulting in higher and more prolonged plasma concentrations of cefuroxime.

The plasma half-life ranges between 60 and 90 minutes and is prolonged in patients with renal impairment and in neonates.

Dialysis causes the decrease of cefuroxime serum levels.

5.3 Preclinical safety data

Preclinical effects were observed in dosages far above the maximal human dosage which are therefore hardly relevant for the clinical use of cefuroxime axetil.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core: sodium lauryl sulphate, copovidone, croscarmellose sodium (E468), magnesium stearate (E 470B), colloidal anhydrous silica (E551), granulated mannitol (E421), microcrystalline cellulose (E460), crospovidone (E1202), talc (E553B).

Coat: mannitol (E421), soluble starch (potato), talc (E553B), titanium dioxide (E171), aspartame (E951)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Al/Al strip: 36 months

Al/Al blister: 36 months

6.4 Special precautions for storage

Al/Al strip: Store in the original packaging

Al/Al blister: Store in the original packaging

6.5. Nature and contents of container

Al/Al strip packaging

Al/Al blister packaging

Pack sizes:

500 mg: 8, 10, 12, 14, 20, 24 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I – to be completed nationally]

8. MARKETING AUTHORISATION NUMBERS

[to be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

[to be completed nationally]

10. DATE OF REVISION OF THE TEXT

[to be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON / BOX****1. NAME OF THE MEDICINAL PRODUCT**

Cefuroximaxetil 125, coated tablets 125 mg

Cefuroxime axetil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 coated tablet contains cefuroxime axetil equivalent to 125 mg cefuroxime

3. LIST OF EXCIPIENTS

Aspartame (E951).

See the package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Coated tablets

125 mg

8 tablets

10 tablets

12 tablets

14 tablets

24 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
--

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)
--

To be completed nationally

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY
--

To be completed nationally

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

To be completed nationally

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON / BOX****1. NAME OF THE MEDICINAL PRODUCT**

Cefuroximaxetil 250, coated tablets 250 mg

Cefuroxime axetil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 coated tablet contains cefuroxime axetil equivalent to 250 mg cefuroxime

3. LIST OF EXCIPIENTS

Aspartame (E951).

See the package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Coated tablets

250 mg

8 tablets

10 tablets

12 tablets

14 tablets

24 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

To be completed nationally

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

To be completed nationally

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON / BOX****1. NAME OF THE MEDICINAL PRODUCT**

Cefuroximaxetil 500, coated tablets 500 mg

Cefuroxime axetil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 coated tablet contains cefuroxime axetil equivalent to 500 mg cefuroxime

3. LIST OF EXCIPIENTS

Aspartame (E951).

See the package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Coated tablets

500 mg

8 tablets

10 tablets

12 tablets

14 tablets

20 tablets

24 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in the original package.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

Batch:

14. GENERAL CLASSIFICATION FOR SUPPLY

To be completed nationally

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

To be completed nationally

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cefuroximaxetil 125, coated tablets 125 mg

Cefuroxime axetil

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Cefuroxime axetil is and what it is used for
2. Before you take Cefuroxime axetil
3. How to take Cefuroxime axetil
4. Possible side effects
5. How to store Cefuroxime axetil
6. Further information

1. WHAT CEFUROXIME AXETIL IS AND WHAT IT IS USED FOR

Cefuroxime axetil is an antibiotic. It belongs to a group of antibiotics that are called cephalosporins. These types of antibiotics are similar to penicillin.

Cefuroxime axetil kills bacteria and it can be used against various sorts of infections.

Like all antibiotics Cefuroxime axetil is only effective against some types of bacteria. So, it is only suitable for treating some types of infection.

Cefuroxime axetil can be used to treat:

- ear, sinus and throat infections
- chest infections such as bronchitis
- infections of the bladder
- infections in the skin and the layers just under the skin (such as furuncles, impetigo-an infection on the surface of the skin)
- early Lyme disease (from a tick bite) and to prevent late complications in adults and children above the age of 12.

2. BEFORE YOU TAKE CEFUROXIME AXETIL

Do not take this medicine if:

- You are allergic (hypersensitive) to Cefuroxime axetil or to any of the other ingredients of this medicine (See "Further Information").
- You are allergic (hypersensitive) to any other cephalosporin type of antibiotic
- You have ever had a severe allergic reaction to any sort of penicillin antibiotic

Not all people who are allergic to penicillins are also allergic to cephalosporins. However, you should not take this medicine if you have ever had a severe allergic

reaction to any penicillin. This is because you might also be allergic to this medicine.

If you are not sure about anything, ask your doctor or pharmacist.

Take special care with this medicine if:

- You have ever had an allergic reaction to penicillins, tell your doctor or pharmacist before you take this medicine.
- If you have severe and persistent diarrhea while using or after using cefuroxime axetil – contact your doctor and use no medicines for diarrhea that inhibit peristalsis;
- if you have abdominal complaints such as vomiting and diarrhoea. It is possible that insufficient cefuroxime axetil will be absorbed by the body, your doctor will recommend an injection of cefuroxime;
- if you get fever and feel ill a short time after using cefuroxime axetil for the treatment of Lyme disease (this is a sign of a disease called Jarisch Herxheimer disease)
- if you are also using medicines that decrease stomach acidity. It is possible that insufficient Cefuroximaxetil will be absorbed by the body (see: “Using other medicines”);
- some children have experienced mild to moderate hearing loss during treatment with cefuroxime sodium
- Having a course of cefuroximeaxetil can temporarily increase the chance that you can get infections caused by other sorts of germs. For example, thrush may occur.

Talk to your doctor or pharmacist if any of the above apply to you.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In some cases, medicines can affect the way other medicines work. This may be the case when Cefuroximaxetil is used together with:

- medicines that decrease stomach acidity (medicines for heartburn);
- certain other medicines for the prevention or control of infections (antibiotics), such as tetracyclines, macrolides, chloramphenicol, aminoglycosids;
- probenecid (a medicine for gout and other ailments). Taking this medicine with cefuroxime axetil can cause higher and more persistent levels of cefuroxime in the blood and bile;
- Water tablets or injections (diuretics)
- Certain medicines against fungal infections (Amphotericin)
- certain tests, such as tests for determining the amount of glucose (sugar) in the blood or urine
- certain tests, such as tests for determining some substances in your blood (Coombs test)

Taking Cefuroxime axetil coated tablets with food and drink

Take this medicine after meals. This is because it helps this medicine to be absorbed into the body.

Pregnancy and breast-feeding

- Are you pregnant, or do you think you might be pregnant? Although this medicine is not known to harm the unborn child, it will only be given to a pregnant woman if it is really necessary.
- Are you breast-feeding? This medicine should not be given to women who are breastfeeding. This is because small amounts of it enter the milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Cefuroxime axetil tablets will not affect your ability to drive or operate machinery.

Important information about some of the ingredients of this medicine

Cefuroxime axetil 125 mg coated tablets contain 0.2 mg aspartame.

If you have been told by your doctor that you have a metabolic disorder called phenylketonuria or if you are on a low-phenylalanine diet, contact your doctor before taking this medicinal product.

3. HOW TO TAKE CEFUROXIME AXETIL

Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The dispensing label will tell you much of this medicine you should take and how often you should take. Please read it carefully. The dose your doctor prescribes depends on the type of infection and how bad the infection is. Your doctor will explain this to you.

Information on how many tablets and how often they should be taken will exactly be written on the dispensing label. Please read it carefully.

The tablets should be taken after meals because this improves the absorption of Cefuroxime axetil into the body.

The recommended doses are given below. However, your doctor may prescribe a different dose to those below: if this applies to you, discuss it with your doctor if you have not already done so. The dose you are prescribed will depend on the type and severity of the infection.

The usual dose is:

Adults and children above the age of 12

For upper respiratory tract infections such as tonsillitis, otitis media, sinusitis and pharyngitis:

1 tablet of Cefuroximaxetil 250 or 500 twice a day for 5-10 days.

For lower respiratory tract infections such as bronchitis and pneumonia:

1 tablet of Cefuroximaxetil 500 twice a day for 5-10 days.

For bladder infections:

1 tablet of Cefuroximaxetil 125 or 250 twice a day for 5-10 days.

For skin infections:

1 tablet of Cefuroximaxetil 250 or 500 twice a day for 5-10 days.

For the treatment of early Lyme disease:

1 tablet of Cefuroximaxetil 500 twice a day for 20 days.

Children between the ages of 5 and 12

For the conditions listed above:

1 tablet of Cefuroximaxetil 125 or 250 twice a day for 5-10 days.

For acute otitis media:

1 tablet of Cefuroximaxetil 250 twice a day for 5-10 days.

Using cefuroxim containing suspension is recommended for children under the age of 5.
There is no experience in the use of cefuroxime axetil in children under 3 months of age.

If you take more Cefuroxime axetil than you should

If you have taken more of this medicine than you should, talk to your doctor straight away or go to the nearest hospital accident and emergency department.

Take the medicine with you in the carton, so that staff will know exactly what has been taken.

Overdose with Cefuroximaxetil can lead to convulsions.

If you forget to take this medicine

If you forget to take a dose of this medicine at the right time, take it as soon as you remember. Do not take a double dose to make up for forgotten doses.

If you stop taking this medicine

It is important that you take this medicine until you finish the prescribed course. You should not stop the medicine just because you feel better. If you stop too soon, the infection may start up again. If the person being treated still feels unwell at the end of the prescribed course of treatment, or feels worse during treatment, tell your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergic reactions to this medicine are very rare (affecting less than 1 in 10,000 people) or rare (affecting less than 1 in 1,000 people). These can include:

- (high) fever
- joint pain
- Swelling of eyelids, face or lips
- Severe skin rashes that can blister and may involve the eyes, mouth and throat and genitals.
- Loss of consciousness (fainting)
- severe diarrhoea or if you see blood in your diarrhoea.

All of these reactions need urgent medical attention. If you think you are having any of these types of reaction, stop taking this medicine and contact your doctor or your nearest hospital accident and emergency department.

Common side effects (affecting less than 1 in 10 people) include:

Fever and a feeling of generally being unwell a short time after taking Cefuroxime axetil for the treatment of Lyme disease (Jarisch-Herxheimer reaction)

Stomach problems: diarrhoea nausea and vomiting.

Skin rash with or without severe itching and wheal formation (urticaria)

Renal and urinary problems: If you have been told that your kidneys do not work very well, changes in kidney function may occur (higher levels of creatinine and urea)

Uncommon side effects (affecting less than 1 in 100 people) include:

Nervous system disorders: headaches, dizziness

Kidneys and urinary tract: blood in the urine, fever and pain in the side (acute interstitial nephritis)

Rare side effects (affecting less than 1 in 1000 people) include:

Blood and lymphatic system disorders: abnormal blood count (such as decreased haemoglobin level;, drops in the numbers of different cells in the blood (leucopenia,neutropenia), increases in some types of white blood cells (eosinophilia), decreases in the numbers of small cells that are needed for clotting of the blood . This may result in easy bleeding or bruising.

Immune system disorders: allergic reactions with fever, swelling of joints, muscle pain, skin rash

Liver and bile ducts: changes in blood tests that check how your liver is working (AST,ALT,LDH, bilirubin: temporary increase)

General: drug fever

Very rare side effects (affecting less than 1 in 10 000 people) include:

Blood and lymphatic system disorders: anemia (a type of anaemia that is caused by red blood cells breaking up);

Nervous system: restlessness, nervousness, confusion

Liver and bile ducts: yellow discolouration of skin or eyes (jaundice)

Skin and subcutaneous tissue: skin rash with irregular red (moist) patches (erythema multiforme);

Certain tests for determining some substances in your blood might show different results while you take cefuroxime axetil (Coombs test).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE THIS MEDICINE

Keep out of the reach and sight of children.

Keep Cefuroximaxetil in the original packaging.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month. Do not use the medicine after the expiry date.

You should not throw away any medicine through wastewater or household waste. Ask your pharmacist how to dispose of medicines that you no longer need. This will help to protect the environment.

6. FURTHER INFORMATION

What Cefuroxime axetil contains

- The active substance is: Cefuroxime. Cefuroximaxetil 125 contains 150.36 mg of Cefuroximaxetil per tablet, equivalent to 125 mg of cefuroxime. Cefuroximaxetil 250 contains 300.72 mg of Cefuroximaxetil per tablet equivalent to 250 mg of cefuroxime. Cefuroximaxetil 500 contains 601.44 mg of Cefuroximaxetil per tablet (equivalent to 500 mg of cefuroxime).
- The other ingredients (excipients) are in the *tablet core*: sodium laurylsulphate, copovidone, croscarmellose sodium (E468), magnesium stearate (E470B), anhydrous colloidal silicon dioxide (E551), mannitol (E421), microcrystalline cellulose (E 460), crospovidone (E1202)and talc (E553B); in the *tablet coating*: mannitol (E421), soluble (potato) starch, talc (E553B), titanium dioxide (E171) and aspartame (E951).

What Cefuroxime axetil looks like and contents of the pack

Cefuroximaxetil tablets are coated.

Cefuroximaxetil 125 are white to slightly yellowish capsule-shaped tablets.

Cefuroximaxetil 125 mg coated tablets are available in carton boxes with blister(s) tear-off or strips containing 8, 10, 12, 14 and 24 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

To be completed nationally.

Manufacturer

Sandoz GmbH,
Biochemiestrasse 10,
6250 Kundl,
Austria

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Cefuroximaxetil Sandoz 125 mg – Filmtabletten
Czech Republic	Xorimax 125 mg potahované tablety
Estonia	Cefuroxim 1A Pharma 125 mg
Hungary	Xorimax 125 mg bevont tableta
Ireland	Cefuroxime 125mg Tablets (PA 372/9/1)
Lithuania	Xorimax 125 mg dengtos tabletės
Latvia	Xorimax 125 mg apvalkotās tabletes
Netherlands	Cefuroximaxetil 125, omhulde tabletten 125 mg
Poland	Xorimax 125 mg tabletki powlekane
Slovak Republic	Xorimax 125 mg
Spain	Cefuroxima Sandoz 125 mg comprimidos recubiertos con película EFG
United Kingdom	Cefuroxime 125mg Tablets (PL 04416/0626)

This leaflet is last approved in: MM/YYYY

To be completed nationally

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cefuroximaxetil 250, coated tablets 250 mg

Cefuroxime axetil

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Cefuroxime axetil is and what it is used for
2. Before you take Cefuroxime axetil
3. How to take Cefuroxime axetil
4. Possible side effects
5. How to store Cefuroxime axetil
6. Further information

7. WHAT CEFUROXIME AXETIL IS AND WHAT IT IS USED FOR

Cefuroxime axetil is an antibiotic. It belongs to a group of antibiotics that are called cephalosporins. These types of antibiotics are similar to penicillin.

Cefuroxime axetil kills bacteria and it can be used against various sorts of infections.

Like all antibiotics Cefuroxime axetil is only effective against some types of bacteria. So, it is only suitable for treating some types of infection.

Cefuroxime axetil can be used to treat:

- ear, sinus and throat infections
- chest infections such as bronchitis
- infections of the bladder
- infections in the skin and the layers just under the skin (such as furuncles, impetigo-an infection on the surface of the skin)
- early Lyme disease (from a tick bite) and to prevent late complications in adults and children above the age of 12.

8. BEFORE YOU TAKE CEFUROXIME AXETIL

Do not take this medicine if:

- You are allergic (hypersensitive) to Cefuroxime axetil or to any of the other ingredients of this medicine (See "Further Information").
- You are allergic (hypersensitive) to any other cephalosporin type of antibiotic
- You have ever had a severe allergic reaction to any sort of penicillin antibiotic

Not all people who are allergic to penicillins are also allergic to cephalosporins. However, you should not take this medicine if you have ever had a severe allergic

reaction to any penicillin. This is because you might also be allergic to this medicine.

If you are not sure about anything, ask your doctor or pharmacist.

Take special care with this medicine if:

- You have ever had an allergic reaction to penicillins, tell your doctor or pharmacist before you take this medicine.
- If you have severe and persistent diarrhea while using or after using cefuroxime axetil – contact your doctor and use no medicines for diarrhea that inhibit peristalsis;
- if you have abdominal complaints such as vomiting and diarrhoea. It is possible that insufficient cefuroxime axetil will be absorbed by the body, your doctor will recommend an injection of cefuroxime;
- if you get fever and feel ill a short time after using cefuroxime axetil for the treatment of Lyme disease (this is a sign of a disease called Jarisch Herxheimer disease)
- if you are also using medicines that decrease stomach acidity. It is possible that insufficient Cefuroximaxetil will be absorbed by the body (see: “Using other medicines”);
- some children have experienced mild to moderate hearing loss during treatment with cefuroxime sodium
- Having a course of cefuroximeaxetil can temporarily increase the chance that you can get infections caused by other sorts of germs. For example, thrush may occur.

Talk to your doctor or pharmacist if any of the above apply to you.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In some cases, medicines can affect the way other medicines work. This may be the case when Cefuroximaxetil is used together with:

- medicines that decrease stomach acidity (medicines for heartburn);
- certain other medicines for the prevention or control of infections (antibiotics), such as tetracyclines, macrolides, chloramphenicol, aminoglycosids;
- probenecid (a medicine for gout and other ailments). Taking this medicine with cefuroxime axetil can cause higher and more persistent levels of cefuroxime in the blood and bile;
- Water tablets or injections (diuretics)
- Certain medicines against fungal infections (Amphotericin)
- certain tests, such as tests for determining the amount of glucose (sugar) in the blood or urine
- certain tests, such as tests for determining some substances in your blood (Coombs test)

Taking Cefuroxime axetil coated tablets with food and drink

Take this medicine after meals. This is because it helps this medicine to be absorbed into the body.

Pregnancy and breast-feeding

- Are you pregnant, or do you think you might be pregnant? Although this medicine is not known to harm the unborn child, it will only be given to a pregnant woman if it is really necessary.
- Are you breast-feeding? This medicine should not be given to women who are breastfeeding. This is because small amounts of it enter the milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Cefuroxime axetil tablets will not affect your ability to drive or operate machinery.

Important information about some of the ingredients of this medicine

Cefuroxime axetil 250 mg coated tablets contain 0.3 mg aspartame.

If you have been told by your doctor that you have a metabolic disorder called phenylketonuria or if you are on a low-phenylalanine diet, contact your doctor before taking this medicinal product.

9. HOW TO TAKE CEFUROXIME AXETIL

Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The dispensing label will tell you much of this medicine you should take and how often you should take. Please read it carefully. The dose your doctor prescribes depends on the type of infection and how bad the infection is. Your doctor will explain this to you.

Information on how many tablets and how often they should be taken will exactly be written on the dispensing label. Please read it carefully.

The tablets should be taken after meals because this improves the absorption of Cefuroxime axetil into the body.

The recommended doses are given below. However, your doctor may prescribe a different dose to those below: if this applies to you, discuss it with your doctor if you have not already done so. The dose you are prescribed will depend on the type and severity of the infection.

The usual dose is:

Adults and children above the age of 12

For upper respiratory tract infections such as tonsillitis, otitis media, sinusitis and pharyngitis:

1 tablet of Cefuroximaxetil 250 or 500 twice a day for 5-10 days.

For lower respiratory tract infections such as bronchitis and pneumonia:

1 tablet of Cefuroximaxetil 500 twice a day for 5-10 days.

For bladder infections:

1 tablet of Cefuroximaxetil 125 or 250 twice a day for 5-10 days.

For skin infections:

1 tablet of Cefuroximaxetil 250 or 500 twice a day for 5-10 days.

For the treatment of early Lyme disease:

1 tablet of Cefuroximaxetil 500 twice a day for 20 days.

Children between the ages of 5 and 12

For the conditions listed above:

1 tablet of Cefuroximaxetil 125 or 250 twice a day for 5-10 days.

For acute otitis media:

1 tablet of Cefuroximaxetil 250 twice a day for 5-10 days.

Using cefuroxim containing suspension is recommended for children under the age of 5.
There is no experience in the use of cefuroxime axetil in children under 3 months of age.

If you take more Cefuroxime axetil than you should

If you have taken more of this medicine than you should, talk to your doctor straight away or go to the nearest hospital accident and emergency department.
Take the medicine with you in the carton, so that staff will know exactly what has been taken.
Overdose with Cefuroximaxetil can lead to convulsions.

If you forget to take this medicine

If you forget to take a dose of this medicine at the right time, take it as soon as you remember. Do not take a double dose to make up for forgotten doses.

If you stop taking this medicine

It is important that you take this medicine until you finish the prescribed course. You should not stop the medicine just because you feel better. If you stop too soon, the infection may start up again. If the person being treated still feels unwell at the end of the prescribed course of treatment, or feels worse during treatment, tell your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

10. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergic reactions to this medicine are very rare (affecting less than 1 in 10,000 people) or rare (affecting less than 1 in 1,000 people). These can include:

- (high) fever
- joint pain
- Swelling of eyelids, face or lips
- Severe skin rashes that can blister and may involve the eyes, mouth and throat and genitals.
- Loss of consciousness (fainting)
- severe diarrhoea or if you see blood in your diarrhoea.

All of these reactions need urgent medical attention. If you think you are having any of these types of reaction, stop taking this medicine and contact your doctor or your nearest hospital accident and emergency department.

Common side effects (affecting less than 1 in 10 people) include:

Fever and a feeling of generally being unwell a short time after taking Cefuroxime axetil for the treatment of Lyme disease (Jarisch-Herxheimer reaction)

Stomach problems: diarrhoea nausea and vomiting.

Skin rash with or without severe itching and wheal formation (urticaria)

Renal and urinary problems: If you have been told that your kidneys do not work very well, changes in kidney function may occur (higher levels of creatinine and urea)

Uncommon side effects (affecting less than 1 in 100 people) include:

Nervous system disorders: headaches, dizziness

Kidneys and urinary tract: blood in the urine, fever and pain in the side (acute interstitial nephritis)

Rare side effects (affecting less than 1 in 1000 people) include:

Blood and lymphatic system disorders: abnormal blood count (such as decreased haemoglobin level;, drops in the numbers of different cells in the blood (leucopenia,neutropenia), increases in some types of white blood cells (eosinophilia), decreases in the numbers of small cells that are needed for clotting of the blood . This may result in easy bleeding or bruising.

Immune system disorders: allergic reactions with fever, swelling of joints, muscle pain, skin rash

Liver and bile ducts: changes in blood tests that check how your liver is working (AST,ALT,LDH, bilirubin: temporary increase)

General: drug fever

Very rare side effects (affecting less than 1 in 10 000 people) include:

Blood and lymphatic system disorders: anemia (a type of anaemia that is caused by red blood cells breaking up);

Nervous system: restlessness, nervousness, confusion

Liver and bile ducts: yellow discolouration of skin or eyes (jaundice)

Skin and subcutaneous tissue: skin rash with irregular red (moist) patches (erythema multiforme);

Certain tests for determining some substances in your blood might show different results while you take cefuroxime axetil (Coombs test).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

11. HOW TO STORE THIS MEDICINE

Keep out of the reach and sight of children.

Keep Cefuroximaxetil in the original packaging.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month. Do not use the medicine after the expiry date.

You should not throw away any medicine through wastewater or household waste. Ask your pharmacist how to dispose of medicines that you no longer need. This will help to protect the environment.

12. FURTHER INFORMATION

What Cefuroxime axetil contains

- The active substance is: Cefuroxime. Cefuroximaxetil 125 contains 150.36 mg of Cefuroximaxetil per tablet, equivalent to 125 mg of cefuroxime. Cefuroximaxetil 250 contains 300.72 mg of Cefuroximaxetil per tablet equivalent to 250 mg of cefuroxime. Cefuroximaxetil 500 contains 601.44 mg of Cefuroximaxetil per tablet (equivalent to 500 mg of cefuroxime).
- The other ingredients (excipients) are in the *tablet core*: sodium laurylsulphate, copovidone, croscarmellose sodium (E468), magnesium stearate (E470B), anhydrous colloidal silicon dioxide (E551), mannitol (E421), microcrystalline cellulose (E 460), crospovidone (E1202)and talc (E553B); in the *tablet coating*: mannitol (E421), soluble (potato) starch, talc (E553B), titanium dioxide (E171) and aspartame (E951).

What Cefuroxime axetil looks like and contents of the pack

Cefuroximaxetil tablets are coated.

Cefuroximaxetil 250 are white to slightly yellowish capsule-shaped tablets with a break-line on both sides.

Cefuroximaxetil 250 mg coated tablets are available in carton boxes with blister(s) tear-off or strips containing 8, 10, 12, 14 and 24 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

To be completed nationally.

Manufacturer

Sandoz GmbH,
Biochemiestrasse 10,
6250 Kundl,
Austria

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Cefuroximaxetil Sandoz 250 mg – Filmdabletten
Belgium	Cefuroxim Sandoz 250 mg filmomhulde tableten
Czech Republic	Xorimax 250 mg potahované tablety
Estonia	Cefuroxim 1A Pharma 250 mg
Greece	Cefuroxime axetil Sandoz 250 mg
Hungary	Xorimax 250 mg bevont tableta
Ireland	Cefuroxime 250mg Tablets (PA 372/9/2)
Lithuania	Xorimax 250 mg dengtos tabletės
Luxemburg	Cefuroxim Sandoz 250 mg comprimés pelliculés
Latvia	Xorimax 250 mg apvalkotās tabletes
Netherlands	Cefuroximaxetil 250, omhulde tableten 250 mg
Poland	Xorimax 250 mg tabletki powlekane
Portugal	CEFUROXIMA Sandoz 250 mg COMPRIMIDOS
Slovak Republic	Xorimax 250 mg
Spain	Cefuroxima Sandoz 250 mg comprimidos recubiertos con película EFG

United Kingdom Cefuroxime 250mg Tablets (PL 04416/0627)

This leaflet is last approved in: MM/YYYY

To be completed nationally

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cefuroximaxetil 500, coated tablets 500 mg

Cefuroxime axetil

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Cefuroxime axetil is and what it is used for
2. Before you take Cefuroxime axetil
3. How to take Cefuroxime axetil
4. Possible side effects
5. How to store Cefuroxime axetil
6. Further information

13. WHAT CEFUROXIME AXETIL IS AND WHAT IT IS USED FOR

Cefuroxime axetil is an antibiotic. It belongs to a group of antibiotics that are called cephalosporins. These types of antibiotics are similar to penicillin.

Cefuroxime axetil kills bacteria and it can be used against various sorts of infections.

Like all antibiotics Cefuroxime axetil is only effective against some types of bacteria. So, it is only suitable for treating some types of infection.

Cefuroxime axetil can be used to treat:

- ear, sinus and throat infections
- chest infections such as bronchitis
- infections of the bladder
- infections in the skin and the layers just under the skin (such as furuncles, impetigo-an infection on the surface of the skin)
- early Lyme disease (from a tick bite) and to prevent late complications in adults and children above the age of 12.

14. BEFORE YOU TAKE CEFUROXIME AXETIL

Do not take this medicine if:

- You are allergic (hypersensitive) to Cefuroxime axetil or to any of the other ingredients of this medicine (See "Further Information").
- You are allergic (hypersensitive) to any other cephalosporin type of antibiotic
- You have ever had a severe allergic reaction to any sort of penicillin antibiotic

Not all people who are allergic to penicillins are also allergic to cephalosporins. However, you should not take this medicine if you have ever had a severe allergic

reaction to any penicillin. This is because you might also be allergic to this medicine.

If you are not sure about anything, ask your doctor or pharmacist.

Take special care with this medicine if:

- You have ever had an allergic reaction to penicillins, tell your doctor or pharmacist before you take this medicine.
- If you have severe and persistent diarrhea while using or after using cefuroxime axetil – contact your doctor and use no medicines for diarrhea that inhibit peristalsis;
- if you have abdominal complaints such as vomiting and diarrhoea. It is possible that insufficient cefuroxime axetil will be absorbed by the body, your doctor will recommend an injection of cefuroxime;
- if you get fever and feel ill a short time after using cefuroxime axetil for the treatment of Lyme disease (this is a sign of a disease called Jarisch Herxheimer disease)
- if you are also using medicines that decrease stomach acidity. It is possible that insufficient Cefuroximaxetil will be absorbed by the body (see: “Using other medicines”);
- some children have experienced mild to moderate hearing loss during treatment with cefuroxime sodium
- Having a course of cefuroximeaxetil can temporarily increase the chance that you can get infections caused by other sorts of germs. For example, thrush may occur.

Talk to your doctor or pharmacist if any of the above apply to you.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In some cases, medicines can affect the way other medicines work. This may be the case when Cefuroximaxetil is used together with:

- medicines that decrease stomach acidity (medicines for heartburn);
- certain other medicines for the prevention or control of infections (antibiotics), such as tetracyclines, macrolides, chloramphenicol, aminoglycosids;
- probenecid (a medicine for gout and other ailments). Taking this medicine with cefuroxime axetil can cause higher and more persistent levels of cefuroxime in the blood and bile;
- Water tablets or injections (diuretics)
- Certain medicines against fungal infections (Amphotericin)
- certain tests, such as tests for determining the amount of glucose (sugar) in the blood or urine
- certain tests, such as tests for determining some substances in your blood (Coombs test)

Taking Cefuroxime axetil coated tablets with food and drink

Take this medicine after meals. This is because it helps this medicine to be absorbed into the body.

Pregnancy and breast-feeding

- Are you pregnant, or do you think you might be pregnant? Although this medicine is not known to harm the unborn child, it will only be given to a pregnant woman if it is really necessary.
- Are you breast-feeding? This medicine should not be given to women who are breastfeeding. This is because small amounts of it enter the milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Cefuroxime axetil tablets will not affect your ability to drive or operate machinery.

Important information about some of the ingredients of this medicine

Cefuroxime axetil 500 mg coated tablets contain 0.4 mg aspartame.

If you have been told by your doctor that you have a metabolic disorder called phenylketonuria or if you are on a low-phenylalanine diet, contact your doctor before taking this medicinal product.

15. HOW TO TAKE CEFUROXIME AXETIL

Always take this medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The dispensing label will tell you much of this medicine you should take and how often you should take. Please read it carefully. The dose your doctor prescribes depends on the type of infection and how bad the infection is. Your doctor will explain this to you.

Information on how many tablets and how often they should be taken will exactly be written on the dispensing label. Please read it carefully.

The tablets should be taken after meals because this improves the absorption of Cefuroxime axetil into the body.

The recommended doses are given below. However, your doctor may prescribe a different dose to those below: if this applies to you, discuss it with your doctor if you have not already done so. The dose you are prescribed will depend on the type and severity of the infection.

The usual dose is:

Adults and children above the age of 12

For upper respiratory tract infections such as tonsillitis, otitis media, sinusitis and pharyngitis:

1 tablet of Cefuroximaxetil 250 or 500 twice a day for 5-10 days.

For lower respiratory tract infections such as bronchitis and pneumonia:

1 tablet of Cefuroximaxetil 500 twice a day for 5-10 days.

For bladder infections:

1 tablet of Cefuroximaxetil 125 or 250 twice a day for 5-10 days.

For skin infections:

1 tablet of Cefuroximaxetil 250 or 500 twice a day for 5-10 days.

For the treatment of early Lyme disease:

1 tablet of Cefuroximaxetil 500 twice a day for 20 days.

Children between the ages of 5 and 12

For the conditions listed above:

1 tablet of Cefuroximaxetil 125 or 250 twice a day for 5-10 days.

For acute otitis media:

1 tablet of Cefuroximaxetil 250 twice a day for 5-10 days.

Using cefuroxim containing suspension is recommended for children under the age of 5.
There is no experience in the use of cefuroxime axetil in children under 3 months of age.

If you take more Cefuroxime axetil than you should

If you have taken more of this medicine than you should, talk to your doctor straight away or go to the nearest hospital accident and emergency department.

Take the medicine with you in the carton, so that staff will know exactly what has been taken.

Overdose with Cefuroximaxetil can lead to convulsions.

If you forget to take this medicine

If you forget to take a dose of this medicine at the right time, take it as soon as you remember. Do not take a double dose to make up for forgotten doses.

If you stop taking this medicine

It is important that you take this medicine until you finish the prescribed course. You should not stop the medicine just because you feel better. If you stop too soon, the infection may start up again. If the person being treated still feels unwell at the end of the prescribed course of treatment, or feels worse during treatment, tell your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

16. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergic reactions to this medicine are very rare (affecting less than 1 in 10,000 people) or rare (affecting less than 1 in 1,000 people). These can include:

- (high) fever
- joint pain
- Swelling of eyelids, face or lips
- Severe skin rashes that can blister and may involve the eyes, mouth and throat and genitals.
- Loss of consciousness (fainting)
- severe diarrhoea or if you see blood in your diarrhoea.

All of these reactions need urgent medical attention. If you think you are having any of these types of reaction, stop taking this medicine and contact your doctor or your nearest hospital accident and emergency department.

Common side effects (affecting less than 1 in 10 people) include:

Fever and a feeling of generally being unwell a short time after taking Cefuroxime axetil for the treatment of Lyme disease (Jarisch-Herxheimer reaction)

Stomach problems: diarrhoea nausea and vomiting.

Skin rash with or without severe itching and wheal formation (urticaria)

Renal and urinary problems: If you have been told that your kidneys do not work very well, changes in kidney function may occur (higher levels of creatinine and urea)

Uncommon side effects (affecting less than 1 in 100 people) include:

Nervous system disorders: headaches, dizziness

Kidneys and urinary tract: blood in the urine, fever and pain in the side (acute interstitial nephritis)

Rare side effects (affecting less than 1 in 1000 people) include:

Blood and lymphatic system disorders: abnormal blood count (such as decreased haemoglobin level;, drops in the numbers of different cells in the blood (leucopenia,neutropenia), increases in some types of white blood cells (eosinophilia), decreases in the numbers of small cells that are needed for clotting of the blood . This may result in easy bleeding or bruising.

Immune system disorders: allergic reactions with fever, swelling of joints, muscle pain, skin rash

Liver and bile ducts: changes in blood tests that check how your liver is working (AST,ALT,LDH, bilirubin: temporary increase)

General: drug fever

Very rare side effects (affecting less than 1 in 10 000 people) include:

Blood and lymphatic system disorders: anemia (a type of anaemia that is caused by red blood cells breaking up);

Nervous system: restlessness, nervousness, confusion

Liver and bile ducts: yellow discolouration of skin or eyes (jaundice)

Skin and subcutaneous tissue: skin rash with irregular red (moist) patches (erythema multiforme);

Certain tests for determining some substances in your blood might show different results while you take cefuroxime axetil (Coombs test).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

17. HOW TO STORE THIS MEDICINE

Keep out of the reach and sight of children.

Keep Cefuroximaxetil in the original packaging.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month. Do not use the medicine after the expiry date.

You should not throw away any medicine through wastewater or household waste. Ask your pharmacist how to dispose of medicines that you no longer need. This will help to protect the environment.

18. FURTHER INFORMATION

What Cefuroxime axetil contains

- The active substance is: Cefuroxime. Cefuroximaxetil 125 contains 150.36 mg of Cefuroximaxetil per tablet, equivalent to 125 mg of cefuroxime. Cefuroximaxetil 250 contains 300.72 mg of Cefuroximaxetil per tablet equivalent to 250 mg of cefuroxime. Cefuroximaxetil 500 contains 601.44 mg of Cefuroximaxetil per tablet (equivalent to 500 mg of cefuroxime).
- The other ingredients (excipients) are in the *tablet core*: sodium laurylsulphate, copovidone, croscarmellose sodium (E468), magnesium stearate (E470B), anhydrous colloidal silicon dioxide (E551), mannitol (E421), microcrystalline cellulose (E 460), crospovidone (E1202)and talc (E553B); in the *tablet coating*: mannitol (E421), soluble (potato) starch, talc (E553B), titanium dioxide (E171) and aspartame (E951).

What Cefuroxime axetil looks like and contents of the pack

Cefuroximaxetil tablets are coated.

Cefuroximaxetil 500 are white to slightly yellowish capsule-shaped tablets.

Cefuroximaxetil 500 mg coated tablets are available in carton boxes with blister(s) tear-off or strips containing 8, 10, 12, 14, 20 and 24 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

To be completed nationally.

Manufacturer

Sandoz GmbH,
Biochemiestrasse 10,
6250 Kundl,
Austria

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Cefuroximaxetil Sandoz 500 mg – Filmtabletten
Belgium	Cefuroxim Sandoz 500 mg filmomhulde tabletten
Czech Republic	Xorimax 500 mg potahované tablety
Estonia	Cefuroxim 1A Pharma 500 mg
Greece	Cefuroxime axetil Sandoz 500 mg
Hungary	Xorimax 500 mg bevont tabletta
Lithuania	Xorimax 500 mg dengtos tabletės
Luxemburg	Cefuroxim Sandoz 500 mg comprimés pelliculés
Latvia	Xorimax 500 mg apvalkotās tabletes
Netherlands	Cefuroximaxetil 500, omhulde tabletten 500 mg
Poland	Xorimax 500 mg tabletki powlekane
Portugal	CEFUROXIMA Sandoz 500 mg COMPRIMIDOS
Slovak Republic	Xorimax 500 mg
Spain	Cefuroxima Sandoz 500 mg comprimidos recubiertos con película EFG

This leaflet is last approved in: MM/YYYY

To be completed nationally