Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cefuroxime 1.5 g Powder for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 1.5g cefuroxime (as sodium salt).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Powder for solution for infusion
Vials containing white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the management of systemic infections due to micro-organisms susceptible to this anti-infective, including gram positive and gram negative organisms and such conditions as respiratory and urinary tract infections, gonorrhoea, septicaemia, meningitis.

Prophylaxis against infection in abdominal, orthopaedic and other surgical procedures, where there is increased risk from infection.

4.2 Posology and method of administration

Cefuroxime 1.5 g Powder for Infusion is for intravenous use only. Dosage instructions for intramuscular use are provided below; other product presentations are available for intramuscular administration.

Cefuroxime 1.5g powder for infusion must be used for intravenous infusion only.

For short intravenous infusion (e.g. up to 30 minutes), solutions containing 1.5 g cefuroxime in 50 ml water for injections may be used. These solutions may be given directly into the vein or introduced into the tubing of the giving set if the patient is receiving parenteral fluids.

Parenteral cefuroxime dosage recommendations (where intramuscular use is recommended, presentations of Cefuroxime Powder for injection licensed for such use should be administered):

Adults: The usual dose is 750 mg t.d.s (three times a day) by intravenous injection. The total daily dosage is in the range of 1500 mg to 6000 mg in divided doses.

Infants and children: Doses of 30 to 100 mg/kg/day given as three or four divided doses. A dose of 60 mg/kg/day will be appropriate for most infections.

Neonates: Doses of 30 to 100 mg/kg/day given as two or three divided doses. In the first weeks of life the serum half-life of cefuroxime can be three to five times that in adults.

Elderly: See dosage in adults.

Other recommendations:

Gonorrhoea: 1.5 g intramuscular injection should be given as a single dose. This may be given as 2 × 750 mg injections into different sites, e.g. each buttock.

Meningitis: Cefuroxime is suitable for sole therapy of bacterial meningitis due to sensitive strains. The following dosages are recommended:

Adults: 3 g intravenously every eight hours. Data are not yet sufficient to recommend a dose for intrathecal administration.

Infants and children: 200 to 240 mg/kg/day intravenously in three or four divided doses. This dosage may be reduced to 100 mg/kg/day intravenously after three days or when clinical improvement occurs.

Neonates: The initial dose should be 100 mg/kg/day intravenously. A reduction to 50 mg/kg/day intravenously may be made when clinically indicated.

Prophylaxis: The usual dose is 1.5 g intravenously with induction of anaesthesia for abdominal, pelvic and orthopaedic operations, but may be supplemented with two 750 mg intramuscular doses eight and sixteen hours later. In cardiac, pulmonary, oesophageal and vascular operations, the usual dose is 1.5 g intravenously with induction of anaesthesia continuing with 750 mg intramuscularly t.d.s. for a further 24 to 48 hours.

In total joint replacement, 1.5 g cefuroxime powder for infusion may be mixed dry with each pack of methyl methacrylate cement polymer before adding the liquid monomer.

Dosage in impaired renal function: Cefuroxime is excreted by the kidneys. Therefore, as with all such antibiotics, in patients with markedly impaired renal function it is recommended that the dosage of cefuroxime should be reduced to compensate for its slower excretion. However, it is not necessary to reduce the dose until the creatinine clearance falls below 20 ml/min. In adults with marked impairment (creatinine clearance 10-20 ml/min) 750 mg b.d.(twice daily) is recommended and with severe impairment (creatinine clearance <10 ml/min) 750 mg once daily is adequate. For patients on haemodialysis a further 750 mg dose should be given at the end of each dialysis. When continuous peritoneal dialysis is being used, a suitable dosage is usually 750 mg twice daily.

For patients in renal failure on continuous arteriovenous haemodialysis of high-flux haemofiltration in intensive therapy units a suitable dosage is 750 mg twice daily. For low-flux haemofiltration follow the dosage recommended under impaired renal function.

4.3 Contraindications

Hypersensitivity to cephalosporin antibiotics.
Use in patients with hepatic dysfunction.

4.4 Special warnings and precautions for use

Use of cefuroxime should be reserved for moderately serious or severe infections.

Cephalosporin antibiotics may in general be given safely to patients who are hypersensitive to penicillins, although cross-reactions have been reported. Special care is indicated in patients who have experienced an anaphylactic reaction to penicillin.

As a precaution, renal function should be monitored in the elderly, in patients taking concurrent potent diuretics or aminoglycosides, and in patients with pre-existing renal impairment.

Prolonged use of an anti-infective may result in the development of superinfection due to organisms resistant to that anti-infective.

There may be some variation on the results of biochemical tests of renal function, but these do not appear to be of clinical importance.

4.5 Interaction with other medicinal products and other forms of interaction

Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with potent diuretics such as frusemide and aminoglycosides, as these combinations are suspected of adversely affecting renal function. Clinical experience with cefuroxime has shown that this is not likely to be a problem at the recommended dose levels.

Cefuroxime does not interfere in enzyme-based tests for glycosuria. Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. However, this should not lead to false-positive results, as may be experienced with some other cephalosporins.

It is recommended that either the glucose oxidase or hexokinase methods are used to determine blood/plasma glucose levels in patients receiving cefuroxime. This antibiotic does not interfere in the alkaline picrate assay for creatinine.

4.6 Pregnancy and lactation

Studies in animals do not suggest any adverse effects on reproduction. There is no experience of use during pregnancy in human beings. Cefuroxime should not be used during pregnancy or lactation in breast feeding women unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Hypersensitivity reactions have been reported; these include skin rashes (maculopapular and urticarial), interstitial nephritis, drug fever and rarely anaphylaxis. As with other cephalosporins there have been rare reports of erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.

As with other antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms, e.g. candida. There have been reports of headache, gastrointestinal disturbances, including nausea and diarrhoea. Very rarely, pseudomembranous colitis may occur during or after treatment.

The principal changes in haematological parameters seen in some patients have been of decreased haemoglobin concentration and of eosinophilia, leukopenia and neutropenia.

As with other cephalosporins, there have been very rare reports of thrombocytopenia.

A positive Coombs' test has been found in some patients treated with cefuroxime – this phenomenon can interfere with the cross-matching of blood.

Although there are sometimes transient rises in serum liver enzymes or serum bilirubin, particularly in patients with pre-existing liver disease, there is no evidence of hepatic involvement.

Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed.

Transient pain may be experienced at the site of intramuscular injection. This is more likely to occur with higher doses. However, it is unlikely to be a cause for discontinuation of treatment. Occasionally, thrombophlebitis may follow intravenous injection.

As with other therapeutic regimens used in the treatment of meningitis, mild to moderate hearing loss has been reported in a few paediatric patients treated with cefuroxime.

4.9 Overdose

Overdosage of cephalosporins can cause cerebral irritation leading to convulsions. Serum levels of cefuroxime can be reduced by haemodialysis or peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code J01D A06.
Cefuroxime is a bactericidal cephalosporin antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms.

It is highly active against *Staphylococcus aureus* including strains which are resistant to penicillin (but not the rare methicillin-resistant strains), *Staph. epidermidis, Haemophilus influenzae,* Klebsiella spp, Enterobacter spp, *Streptococcus pyogenes, Escherichia coli, Str. mitis (viridans group),* Clostridium spp, *Proteus mirabilis, Pr. rettgeri, Salmonella typhi, S. typhimurium* and other Salmonella spp, Shigella spp, Neisseria spp (including beta-lactamase producing strains of *N. gonorrhoea*) and *Bordetella pertussis*. It is also moderately active against strains of *Pr. vulgaris, Morganella morganii* (formerly *Proteus morganii*) and *Bacteroides fragilis*.

The following organisms are not susceptible to cefuroxime: *Clostridium difficile*, Pseudomonas spp, Campylobacter spp, *Acinetobacter calcoaceticus*, Legionella spp and methicillin-resistant strains of *Staph. aureus* and *Staph. epidermidis*. Some strains of the following genera have also been found not to be susceptible to cefuroxime: *Strep. faecalis, Morganella morganii, Proteus vulgaris*, Enterobacter spp. Citrobacter spp, Serratia spp and *Bacteroides fragilis*.

In vitro the activities of cefuroxime and aminoglycoside antibiotics in combination have been shown to be at least additive with occasional evidence of synergy.

5.2 Pharmacokinetic properties

Peak levels of cefuroxime are achieved within 30 to 45 minutes after intramuscular administration. The serum half-life after either intramuscular or intravenous injection is approximately 70 minutes. Concurrent administration of probenecid prolongs the excretion of the antibiotic and produces an elevated peak serum level. There is almost complete recovery of unchanged cefuroxime in the urine within 24 hours of administration, the major part being eliminated in the first six hours. Approximately 50 % is excreted through the renal tubules and approximately 50 % by glomerular filtration. Concentrations of cefuroxime in excess of the minimum inhibitory levels for common pathogens can be achieved in bone, synovial fluid and aqueous humor. Cefuroxime passes the blood-brain barrier when the meninges are inflamed.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

Incompatible with sodium bicarbonate.

Cefuroxime should not be mixed in the syringe with aminoglycoside antibiotics.

6.3 Shelf Life

As packaged for sale: 30 months.
In use: Following reconstitution and dilution to a final concentration of 30mg/ml in sodium chloride 0.9%, dextrose 10%, M/6 sodium lactate injection, Lactated Ringers injection and Ringer's injection, chemical and physical in-use stability has been demonstrated for 48 hours at 2-8ºC. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8ºC, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

As packaged for sale: Do not store above 25^{o}C.
Keep the vial in the outer carton.

In use: see 6.3.

6.5 Nature and contents of container

1.5g (for intravenous infusion) –Type III uncoloured glass vials with rubber stoppers in packs of 1, 10 or 50.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Contains no preservative. For single use. Discard any unused contents.
May be added to most intravenous fluids and electrolyte solutions, e.g. Water for Injections, sodium chloride 0.9%, glucose 5%, sodium chloride 0.18% with glucose 4%.

7 MARKETING AUTHORISATION HOLDER

Mayne Pharma Plc
Queensway
Royal Leamington Spa
Warwickshire CV31 3RW
United Kingdom

8 MARKETING AUTHORISATION NUMBER

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