Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ceporex Granules for Oral Suspension 250 mg/5ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

When reconstituted, each 5ml contains Cephalexin .equivalent to 250mg Cephalexin (anhydrous).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Granules for oral suspension
Pale orange granules with a characteristic odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ceporex is indicated in the management of moderate and serious infections due to micro-organisms sensitive to this anti-infective, for example beta-haemolytic Streptococci, Staphylococci, *Proteus mirabilis* etc.

4.2 Posology and method of administration

Adults:

Many infections in adults will respond to oral dosage of 1 gram to 2 grams per day in divided doses; however, for most infections, the following simple scheme will be found satisfactory:

Adults and children over 12 years: 500mg t.d.s. (three times daily). To aid compliance, especially in ambulatory patients, the daily dosage may be given in two equal doses, e.g. 1g twice daily in adult with urinary tract infections.

The following additional information should also be considered:

For severe or deep-seated infections, especially when less sensitive organisms are involved, the dosage should be increased to 1g t.d.s. or 1.5g q.d.s. (four times daily).

For prophylaxis of recurrent urinary tract infections in adults, a dose of 125mg each night is recommended and may be continued for several months (the 125mg/5ml suspension is suitable for this purpose).

Children:

Ideally, dosage should be calculated on a body-weight basis, particularly in infants. The following dosage recommendations for children are derived from a normal dosage of 25 to 60mg/kg/day. For chronic, severe or deep-seated infections, this should be increased to 100mg/kg/day (maximum 4g/day).

0 to 1 year:	25 to 60mg/kg/day.
1 year to 2 years:	62.5 to 125mg four times daily or 125 to 250mg twice daily.
3 to 6 years:	125 to 250mg four times daily or 250 to 500mg twice daily.
7 to 12 years:	250 to 500mg four times daily or 500mg to 1g twice daily.

For most acute infections, treatment should continue for at least two days after signs have returned to normal and symptoms have subsided, but in chronic, recurrent or complicated urinary tract infections, treatment for two weeks (giving 500 mg four times daily) is recommended. For gonorrhoea, a single dose of 3 g with 1 g probenecid for males or 2 g with 0.5 g probenecid for females is usually effective. Concurrent administration of probenecid delays excretion of cephalexin and raises the serum levels by 50-100%.

Ceporex has not been shown to have a toxic effect on the kidney, but as with other antibiotics which are excreted mainly by the kidneys, unnecessary accumulation may occur in the body when renal function is below about half of normal. Clinical practice indicates that in view of the wide therapeutic window of Ceporex, the standard recommended doses should be halved only in those patients with severe renal impairment (creatinine clearance <10ml/min).

The maximum recommended dosages (i.e. adults 6g/day, children 4g/day) should be reduced by 50% in mild, 75% in moderate and 87.5% in severe renal failure.

In elderly patients, the possibility of renal impairment should be considered.

If dialysis is required for renal failure the daily dose of cephalexin should not exceed 500 mg without dialysis.

Adult patients receiving intermittent dialysis should be given an additional 500 mg Ceporex after each dialysis, i.e. a total dosage of up to 1 gram on that day. Children should receive an additional 8 mg per kg.

In skin and soft tissue infection, streptococcal pharyngitis and uncomplicated urinary tract infections dosage may be given 12 hourly.

4.3 Contraindications

Use in patients hypersensitive to cephalosporins.

4.4 Special warnings and precautions for use

As with other broad-spectrum antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci, *Clostridium difficile*), which may require interruption of treatment. Pseudomembranous colitis due to clostridia has been reported with the use of broad-spectrum antibiotics; therefore, it is important to consider its diagnosis in patients who develop severe diarrhoea during or after antibiotic use.

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

As with other antibiotics that are excreted mainly by the kidneys, when renal function is poor, dosage of Ceporex should be suitably reduced (see dosage and administration).

In patients receiving Ceporex, a false-positive reaction for glucose in the urine may be given, with Benedict's or Fehling's solution or with 'Clinitest' tablets, but not with enzyme-based tests.

Ceporex can interfere with the alkaline picrate assay for creatinine, giving a falsely high reading, but the degree of elevation is unlikely to be of clinical importance.

Cross-resistance and cross sensitisation may exist between penicillins and cephalosporins.

Use of the anti-infective in the presence of renal dysfunction requires careful monitoring of serum levels of drug to avoid levels in excess of those desired.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent treatment with high doses of cephalosporins and nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. frusemide, ethacrynic acid and piretanide) may adversely effect renal function and may increase the risk

of nephrotoxicity.

Cephalexin may interfere with tests for glucose using copper reagents, and for creatinine by the alkaline picrate assay.

4.6 Pregnancy and lactation

The product should not be used during pregnancy unless considered essential by the physician. Cephalexin is excreted in human milk in low concentrations and should be used with caution in nursing mothers.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

A small proportion of patients receiving cephalexin have experienced gastrointestinal symptoms including nausea, vomiting and diarrhoea. As with other broad-spectrum antibiotics, there have been rare reports of headache, increased levels of liver enzymes and pseudomembranous colitis.

Prolonged use can result in the overgrowth of Candida causing vulvo-vaginitis.

Reversible neutropenia has occurred in a few patients, but is very rare. Drug rashes - both urticarial and maculopapular. Severe skin reactions including very rarely toxic epidermal necrolysis (exanthematic necrolysis) and Stevens-Johnson syndrome and hypersensitivity reactions including angioedema and anaphylaxis.

There have been reports of positive Coombs' test.

As with other cephalosporins there have been rare reports of reversible interstitial nephritis.

4.9 Overdose

Serum levels of cephalexin can be reduced greatly by peritoneal dialysis or haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Bacteriology:
Cephalexin is a bactericidal antibiotic of the cephalosporin group, which is active against a wide range of Gram-positive and Gram-negative organisms.

Gram-positive organisms:
Cephalexin is stable to Staphylococcal penicillinase and so is active against penicillin-resistant *Staphylococcus aureus* and other staphylococcal species (excluding methicillin-resistant isolates).
Streptococcus pyrogenes, *Streptococcus pneumoniae*, *Streptococcus agalactiae* (Group B), other beta-haemolytic streptococci and most viridans group streptococci are also susceptible to cephalexin. Cephalexin has *in-vitro* activity against *Corynebacterium diphtheria*.

Gram-negative organisms:
Cephalexin has *in-vitro* activity against *E. coli*, Klebsiella species, *Proteus mirabilis*, Salmonella and Shigella species. *Neisseria gonorrhoeae* and *N. meningitidis* are also susceptible.

5.2 Pharmacokinetic properties

Absorption: Cephalexin is almost completely absorbed in the upper portions of the gastrointestinal tract. Following oral administration, absorption is rapid and peak serum levels (4.5microg/ml for a 125mg dose, 9microg/ml for 250mg dose, 18microg/ml for 500mg dose and 32microg/ml for a 1000mg dose) are usually reached at one hour. Inpatients with normal renal function, serum levels persist for 4 to 6 hours and disappear within 8 hours.
Absorption is delayed when cephalexin is given with or shortly after food, but the total amount absorbed is not altered. Absorption of cephalexin is not adversely affected by coeliac disease, partial gastrectomy, achlorhydria, jaundice or diverticulosis (duodenal or jejunal).

The serum half-life is normally about one hour, but is longer in the newborn (see 4.2 Posology and Method of Administration). In patients with impaired renal function, an increase in serum half-life of cephalexin occurs. Clinical practice indicates that in view of the wide therapeutic window of cephalexin, the standard recommended doses should be halved only in those patients with severe renal impairment (creatinine clearance <10ml/min).

Distribution: Cephalexin is widely distributed in body tissues and high concentrations are found in all organs, particularly the liver and kidneys. Cephalexin reaches therapeutic levels in the blood, urine, bile, synovial fluid, pus, tonsillar tissue, amniotic fluid, cord blood and foetal blood.

Metabolism and Elimination: Cephalexin is not metabolised in the body and is rapidly excreted unchanged in the urine. High concentrations (80-100%) of an orally administered dose are recoverable in the urine within 6-8 hours. Cephalexin is excreted in human milk in low concentrations.

Concurrent administration of probenecid delays excretion of cephalexin and raises serum levels by 50 to 100%. (see 4.2 Posology and Method of Administration).

5.3 Preclinical safety data

Cephalexin is not anticipated to cause any genotoxic or carcinogenic effects, although no specific studies have been performed to determine this.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Calcium Edetate
Acacia
Citric Acid (Anhydrous)
Sodium Citrate (Anhydrous)
Eurocert Sunset Yellow 311831 (E110)
Orange-bramble flavour
Sucrose

6.2 Incompatibilities

The reconstituted syrups should not be diluted with syrup (See 6.4 Special Precautions for Storage).

6.3 Shelf Life

Unconstituted granules:	3 years.
Reconstituted granules:	10 days.

6.4 Special precautions for storage

Unconstituted granules: Do not store above 30°C.
Reconstituted granules: Store at 2-8°C in a refrigerator.

6.5 Nature and contents of container

Screw-capped amber glass bottles containing dry granules.

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

Ceporex Syrup prepared by adding 60ml of water to the granules to give 100ml of a uniform orange suspension with a characteristic odour and containing 250mg cephalexin in each 5ml.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 44/9/5

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