Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pinaclor Hard Capsules 500 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains Cefaclor monohydrate 524.4 mg equivalent to anhydrous Cefaclor 500 mg.

Excipients: Each capsule contains 0.0068mg Ponceau 4R (E124), 0.017mg Carmoisine (E122), 0.02415-0.0273mg Ethanol, 0.05mg Sodium, 0.5515mg Methyl Parahydroxybenzoate (E218) and 0.1378mg Propyl Parahydroxybenzoate (E216).

For full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Hard capsules
Purple/grey, hard gelatin, self locked capsules of size “0el” marked with “CEFACLOR 500” on cap and body in black edible ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Cefaclor Capsules are indicated for the treatment of the following infections due to susceptible microorganisms including *Streptococcus pyogenes* (group A beta haemolytic streptococci) and *Branhamella catarrhalis.*

Respiratory tract infections, including pneumonia, (bronchitis), exacerbations of chronic bronchitis, pharyngitis and tonsillitis and as part of the management of sinusitis

Otis media

Skin and soft tissue infections.

Urinary tract infections, including pyelonephritis and cystitis. Cefaclor has been found to be effective in both acute and chronic urinary tract infections.

Cefaclor is generally effective in the eradication of streptococci from the nasopharynx, however, data estabilishing efficacy in the subsequent prevention

of either rheumatic fever or bacterial endocarditis are not available.

Consideration should be given to the local guidance regarding the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Cefaclor is administered orally.

Adults: The usual adult dosage is 250 mg every eight hours. For more severe infections or those caused by less susceptible organisms, doses may be doubled. Doses of 4 g per day have been administered safely to normal subjects for 28 days but the total daily dosage should not exceed this amount.

Cefaclor may be administered in the presence of impaired renal function. Under such conditions dosage is usually unchanged (see Special warnings and special precautions for use).

Patients undergoing haemodialysis: Haemodialysis shortens serum half-life by 25-30%. In patients undergoing regular haemodialysis, a loading dose of 250mg-1g administered prior to dialysis and a therapeutic dose of 250-500mg every six to eight hours maintained during interdialytic periods is recommended.

The elderly: As for adults

Children: The usual recommended daily dosage for children is 20mg/kg/day in divided doses every eight hours. For streptococcal pharyngitis or tonsillitis or otitis media and soft tissue infections, the total daily dosage may be divided and administered every 12 hours. Safety and efficacy have not been established for use in infants aged less than one month.

In more severe infections, otitis media, sinusitits and infections caused by less susceptible organisms, 40mg/kg/day in divided doses is recommended up to a daily maximum of 1g.

In the treatment of beta-haemolytic streptococcal infections, therapy should be continued for at least 10 days.

As small children cannot swallow capsules, an appropriate paediatric formulation should be used.

4.3 Contraindications

Cefaclor is contra-indicated in patients with known hypersensitivity to cefaclor and other cephalosporins.

4.4 Special warnings and precautions for use

Warnings:
Before instituting therapy with cefaclor, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross-sensitivity amont beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy.
If an allergic reaction to cefaclor occurs, the drug should be discontinued and the patient treated with the appropriate supportive measures.

Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, macrolides, semi-synthetic penicillins and cephalosporins, including cefaclor and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increase morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile,* and surgical evaluation should be instituted as clinically indicated.

Some excipients (e.g. Ponceau 4R and carmoisine) may cause allergic reactions.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics including macrolides, semi-synthetic penicillins and cephalosporins. It is important, therefore, to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening. Mild cases usually respond to drug discontinuance alone. In moderate to severe cases, appropriate measures should be taken.

Precautions

Prescribing cefaclor in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Prolonged use of cefaclor may result in the overgrowth of non-susceptible organisms. Superinfection (overgrowth by non-susceptible organisms) should always be considered a possibility in a patient being treatment with a broad spectrum antimicrobial. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Renal Insufficiency

Cefaclor should be administered with caution in the presence of markedly impaired renal function. In patients with reduced renal function, the serum half-life of cefaclor is slightly prolonged. Since the half-life of cefaclor in anuric patients is 2.3 to 2.8 hours (compared to 0.6 – 0.9 hours in normal subjects), dosage adjustments for patients with moderate or severe renal impairment are not usually required. Excretion pathways in patients with markedly impaired renal function have not been determined. Haemodialysis shortens the half-life by 25% to 30%.

Clinical experience cefaclor under such conditions is limited; therefore, careful clinical observation and laboratory studies should be made.

Geriatric patients
In elderly subjects (over age 65) with normal serum creatinine values, higher peak plasma concentrations and AUCs have been observed. This is considered to be primarily as a result of an age-related decrement in renal function, and has no apparent clinical significance. Therefore, dosage adjustment is not necessary in elderly subjects with normal serum creatinine values.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastro-intestinal disease, particularly colitis.

Patients should be counselled that antibacterial drugs including cefaclor should only be used to treat bacterial infections. They do not treat viral infections (e.g. the common cold). When cefaclor are prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by cefaclor or other antibacterial drugs in the future.

Drug and/or Laboratory Test interactions

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematological studies or in transfusion cross

matching procedures, when anti-globulin tests are performed on the minor side, or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs' test may be due to the drug.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets.

4.5 Interaction with other medicinal products and other forms of interaction

Antacids
The extent of absorption of cefaclor is diminished if magnesium or aluminium hydroxide-containing antacids are taken within 1 hour of administration; H2 blockers do not alter either the rate or the extent of absorption of cefaclor.

Probenecid
The renal excretion of cefaclor is inhibited by probenecid leading to increased plasma cephalosporin concentrations.

Warfarin
There have been rare reports of increased prothrombin time, with or without clinical bleeding, in patients receiving cefaclor and warfarin concomitantly.

No specific studies have been performed to rule in or rule out this potential drug/drug interaction. It is recommended that in such patients, regular monitoring of prothrombin time should be considered, with adjustment of dosage if necessary.

Cefaclor may decrease the efficacy of estrogen-contianing oral contraceptives.

4.6 Fertility, pregnancy and lactation

Pregnancy
Animal studies have shown no evidence of impaired fertility or teratogenicity. However, since there are no adequate or well-controlled studies in pregnant women, cefaclor should not be administered during pregnancy or lactation unless considered essential by the physician

Breast-feeding
Small amounts of cefaclor have been detected in breast milk following administration of single 500 mg doses. Average levels of about 0.2 micrograms/ml or less were detected up to five hours later. Trace amounts were detected at one hour. As the effect on nursing infants is not known, caution should be exercised when cefaclor is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

No effect has been reported

4.8 Undesirable effects

In one paediatric study cefaclor was associated with 53.3% of oral antibiotic related skin and joint adverse reactions and 84.1% of serum sickness like reactions.

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated form the available data).

Infections and infestations
Frequency not known: Genital pruritus, vaginitis and vaginal moniliasis.

Blood and lymphatic system disorders
Rare: thrombocytopenia, transient lymphocytosis, leucopenia. Other haematological reactions include haemolytic anaemia, aplastic anaemia, agranulocytosis and reversible neutropenia of possible clinical significance.
Frequency not known: Eosinophilia, lymphadenopathy

Immune system disorders:
Rare: Allergic reactions such as morbilliform euruptions, pruritus and urticaria have been observed. These reactions usually subside upon discontinuation of therapy. Rarely, hypersensitivity symptoms may persist for several months.
Frequency not known: Serum sickness-like reactions (erythema multiforme minor, rashes or other skin manifestations accompanied by arthritis/arthralgia, with or without fever) have been reported.

Anaphylactoid events may present as solitary symptoms, including angioedema, asthenia, oedema (including face and limbs), dyspnoea, paraesthesias, syncope, or vasodilation.

Serum sickness-like reactions are apparently due to hypersensitivity and have usually occurred during or following a second (or subsequent) course of therapy with cefaclor. Such reactions have been reported more frequently in children than in adults. Signs and symptoms usually occur a few days after initiation of therapy and usually subside within a few

days of cessation of therapy. Antihistamines and corticosteroids appear to enhance resolution of the syndrome. No serious sequelae have been reported.

Psychiatric disorders:
Frequency not known: Reversible hyperactivity nervousness, insomnia, confusion, hypertonia, hallucinations

Nervous system disorders:
Common: Headache
Frequency not known: agitation, dizziness, drowsiness and somnolence.

Gastrointestinal disorders:
Common: diarrhoea, colitis, nausea and vomiting.
Rare: pseudomembranous colitis

Hepato-biliary disorders:
Frequency not known: Transient hepatitis and cholestatic jaundice

Skin and subcutaneous tissue disorders:
Rare: erythema multiforme major (Stevens-Johnson syndrome), toxic epidermal necrolysis, and anaphylaxis) may be more common in patients with a history of penicillin allergy).

Renal and urinary disorders:
Rare: Reversible interstitial nephritis, slight elevations in blood urea or serum creatinine or abnormal urinarlysis.
Frequency not known: proteinuria

General disorders and administration site conditions:
Rare: slight elevations in AST, ALT or alkaline phosphatise values.
Frequency not known: positive Coombs' tests

It should be noted that there is a lack of modem frequency data for cefaclor adverse events.
Cephalosporin-Class Reactions
In addition to the adverse ractions listed above, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:
Clinical: Confusion, erythema multiforme, genital pruritus, hepatic dysfunction including cholestatis, haemolytic anemia, reversible hyperactivity, hypertonia and reversible interstitial nephritis.
Laboratory: Positive direct Coombs' test

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms:
The toxic symptoms following an overdose of cefaclor are non-specific and may include nausea, vomiting, epigastric distress and diarrhoea. The severity of the epigastric distress and the diarrhoea are dose-related.

Treatment:
Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage. Consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Although cefaclor is considered dialyzable, neither forced dieresis, peritoneal dialysis, haemodialysis, nor charcoal hemoperfusion have been demonstrated to be beneficial in an overdose of cefaclor.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC-code: J01DC04 Second generation cephalosporins

Cefaclor is a semi-synthetic second generation cephalosporin antibiotic.

Cefaclor is a broad-spectrum, second generation cephalosporin. It is bactericidal against a wide range of Gram-positive and Gram-negative microorganisms. The reported mode of action is predominantly by the inhibition of cell wall synthesis in susceptible bacteria. This is mainly achieved by inhibiting the trans-peptidation reaction, the final stage of the cell wall synthesis process, thus preventing the complete formation of peptidoglycan cross links. Other earlier stages in this synthesis process may also be inhibited and there may be some induction of bacterial lysis.

Cefaclor is active against the following organisms *in vitro:*
Alpha-and beta- haemolytic streptococci
Staphylococci; including coagulase-positive, coagulase-negative and penicillinase-producting strains.
Streptococcus penumoniae
Streptococcus pyogenes (group A beta-haemolytic streptococci)
Moraxella catarrhalis
Escherichia coli
Proteus mirabilis
Klebsiella species
Haemophilus influenza, including ampicillin-resistant strains

Cefaclor has no activity against *Pseudomonas* species or *Acinetobaster* species. Methicillin-resistant staphylococci and most strains of *Enterobacter spp, Serratia spp, Morganella morganii, Proeus vulgaris* and *Providencia rettgeri.*

5.2 Pharmacokinetic properties

Cefaclor is well absorbed after oral administration to fasting subjects. Total absorption is the same whether the drug is given with or without food; when it is taken with food, the peak concentration achieved is 50% to 75% of that observed when the drug is administered to fasting subjects and generally appears from ¾ to one hour later. Following administration of 250 mg, 500 mg and 1 g doses to fasting subjects, average peak serum levels of approximately 7, 13 and 23 g/l, respectively, were obtained within 30 to 60 minutes. Approximately 60% to 85% of the drug is excreted unchanged in the urine within eight hours, the greater portion being excreted within the first two hours. During the eight hour period, peak urine concentrations following the 250 mg, 500 mg and 1 g doses were approximately 600, 900 and 1900 g/l respectively.

The serum half-life in normal subjects is 0.6 to 0.9 hours. In patients with reduced renal function, the serum half-life of cefaclor is slightly prolonged. In those with complete absence of renal function, the plasma half-life of the intact molecules is 2.3 to 2.8 hours. Excretion pathways in patients with markedly impaired renal function have not been determined. Haemodialysis shortens the half-life by 25% to 30%.

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 SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Colloidal anhydrous silica
Croscarmellose sodium (E466)
Magnesium Stearate (E572)

Capsule Shell

Gelatin
Ponceau 4R (E124)
Carmoisine (E122)
Brilliant Blue (E133)
Titanium Dioxide (E171)
Black Iron Oxide (E172)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)

Black Ink
Shellac
Ethanol
Isopropyl Alcohol
n-Butyl Alcohol
Propylene Glycol
Purified Water
Strong Ammonia Solution
Black Iron Oxide (E172)
Potassium Hydroxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Two years

6.4 Special precautions for storage

The capsules are sensitive to light and moisture.
Blister: Do not store above 25°C. Keep the blister in the outer carton. Store in the original package.
Bottle: Do not store above 25°C. Keep the bottle in the outer carton. Keep the container tightly closed.

6.5 Nature and contents of container

Plastic (HDPE) bottles with polypropylene child resistant closure containing 50 capsules.
Packs with blister strips (PVC PVdC) with aluminium foil backing containing 8, 12, 15, 16, 20, 30 or 100 capsules. Not all pack sizes may be marketed.

Bottles contain dessicant.

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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Ltd
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0281/155/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14th May 1999
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10 DATE OF REVISION OF THE TEXT

July 2016