Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Distaclor LA Forte 500 mg prolonged release tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains cefaclor monohydrate equivalent to 500 mg of cefaclor as active ingredient.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release film-coated tablet
Blue, capsule-shaped, film-coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Distaclor LA Forte is indicated in the treatment of the following infections when caused by susceptible strains of the designated organisms:
Acute bronchitis and acute exacerbations of chronic bronchitis caused by *Streptococcus pneumoniae, Haemophilus influenzae* (including beta-lactamase producing strains), *Haemophilus parainfluenzae, Moraxella catarrhalis* (including beta-lactamase producing strains) and *Staphylococcus aureus*.
Pharyngitis and tonsillitis caused by *Streptococcus pyogenes* (group A streptococci).
Pneumonia caused by *S.pneumoniae, H. influenzae* (including beta-lactamase producing strains) and *M. catarrhalis* (including beta-lactamase producing strains).
Uncomplicated lower urinary tract infections, including cystitis and asymptomatic bacteriuia, caused by *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis* and *Staphylococcus saprophyticus*.
Skin and skin structure infections caused by *S. pyogenes* (group A streptococci), *S. aureus* (including beta-lactamase producing strains) and *Staphylococcus epidermidis* (including beta-lactamase producing strains).
Bacteriological studies, to determine the causative organism and its susceptibility to cefaclor, should be performed. Therapy may be started while awaiting the results of these studies. Once these results become available antimicrobial therapy should be adjusted accordingly.
Distaclor LA Forte is generally effective in the eradication of streptococci from the oropharynx. However, data establishing the efficacy of this antibiotic in the subsequent prevention of rheumatic fever are not available.

4.2 Posology and method of administration

Posology

Adults, including the elderly:
Pharyngitis, tonsillitis, skin and skin structure infections: 375mg twice daily.

Lower urinary tract infections:
357mg twice daily or 500mg once daily.

Bronchitis:
375mg or 500mg twice daily.

Pneumonia:
750mg twice daily.

If prolonged therapy is required, it should be noted that in clinical trials doses of 1.5g/day of Distaclor LA Forte have been administered safely for 14 days, and doses of 4g/day of cefaclor have been administered safely to normal subjects for 28 days.

Cefaclor should be administered with caution in the presence of markedly impaired renal function. Since the half-life of cefaclor in anuric patients is 2.3 to 2.8 hours, dosage adjustments for patients with moderate or severe renal impairment are not usually required. Clinical experience with cefaclor under such conditions is limited, therefore, careful clinical observation and laboratory studies should be made.

If regular haemodialysis is required for renal failure, a loading dose of 250 to 1000mg of cefaclor can be given prior to dialysis and 250 to 500mg every 6 to 8 hours during the intervals between dialysis.
Elderly subjects with normal renal function do not require dosage adjustment.

Children:
The safety and effectiveness of Distaclor LA Forte have not been established. Cefaclor suspensions are available (see Distaclor Summary of Product Characteristics for dosages).

In the treatment of infections caused by *S. pyogenes* (group A streptococci), a therapeutic dosage should be administered for at least 10 days.

Distaclor LA Forte is well absorbed from the gastro-intestinal tract and may be given orally without regard to meals. However, absorption is enhanced when administered with food. The tablets should not be cut, crushed or chewed.

Methodof Administration

Distaclor LA Forte is administered orally.

4.3 Contraindications

Hypersensitivity to cephalosporins.

4.4 Special warnings and precautions for use

Before instituting therapy with cefaclor, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins or other drugs. Cefaclor should be given cautiously to penicillin-sensitive patients and to any patient who has demonstrated some form of allergy, particularly to drugs.

If an allergic reaction to cefaclor occurs, the drug should be discontinued and the patient treated with the appropriate agents.

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.

Prolonged use of cefaclor may result in the overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

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

A positive Coombs' test may occur with cephalosporins.

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

Reports of neurotoxicity have been identified in association with cephalosporin treatment. Symptoms may include encephalopathy, myoclonus and seizures. Elderly patients, patients with severe renal impairment or central nervous system disorders are particularly at risk. If cefaclor associated neurotoxicity is suspected, discontinuation of cefaclor should be considered (see Section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

There have been rare reports of increased prothrombin time, with or without clinical bleeding, in patients receiving cefaclor and warfarin concomitantly. It is recommended that in such patients, regular monitoring of prothrombin time should be considered, with adjustment of dosage if necessary.

The extent of absorption of Distaclor LA Forte is diminished if magnesium hydroxide or aluminium hydroxide containing antacids are taken within 1 hour of administration.

H2 blockers do not alter either the rate or extent of absorption.

The renal excretion of cefaclor is inhibited by probenecid.

4.6 Fertility, pregnancy and lactation

Pregnancy:
Although animal studies have shown no evidence of impaired fertility or harm to the foetus due to cefaclor, there are no adequate and well-controlled studies in pregnant women. Distaclor LA Forte should be used during pregnancy only if clearly needed.

Breast-feeding:
Small amounts of cefaclor have been detected in breast milk following administration of single 500mg doses. Average levels of about 0.2 micrograms/ml or less were detected up to 5 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. No studies have been done with Distaclor LA Forte.

Labour and delivery:
Treatment should be given only if clearly needed.

4.7 Effects on ability to drive and use machines

Distaclor has no known influence on the ability to drive and use machines.

4.8 Undesirable effects

The majority of adverse reactions observed in clinical trials of Distaclor LA Forte were mild and transient. Drug-related adverse reactions requiring discontinuation of therapy occurred in 1.7% of patients. The following adverse reactions were reported in clinical trials. Incidence rates were less than 1 in 100 (less than 1%), except as stated:

Gastro-intestinal:
Diarrhoea (3.4%), nausea (2.5%), vomiting and dyspepsia.

Hypersensitivity:
Rash, urticaria or pruritus occurred in approximately 1.7% of patients. One serum sickness-like reaction (0.03%) was reported among the 3,272 patients treated with Distaclor LA Forte during the controlled clinical trials.
Serum sickness-like reactions (Erythema multiforme minor, rashes or other skin manifestations accompanied by arthritis/arthralgia, with or without fever) have been reported with cefaclor. Lymphadenopathy and proteinuria are infrequent, there are no circulating immune complexes and no evidence of sequelae.

Occasionally, solitary symptoms may occur, but do not represent a serum sickness-like reaction. 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.

Haematological and lymphatic systems: Eosinophilia. Genitourinary: Vaginal moniliasis (2.5%) and vaginitis (1.7%).

The following adverse effects have been reported, but causal relationship is uncertain:
Central nervous system: Headache, dizziness and somnolence.

Hepatic: Transient elevations in AST, ALT and alkaline phosphatase.
Renal: Transient increase in BUN or creatinine.
Laboratory tests: Transient thrombocytopenia, leucopenia, lymphocytosis, neutropenia and abnormal urinalysis.

In addition to the adverse reactions listed above that have been observed in patients taking Distaclor LA Forte, the following have been reported in patients treated with cefaclor:

Erythema multiforme, fever, anaphylaxis (may be more common in patients with a history of penicillin allergy), Stevens-Johnson syndrome, positive direct Coombs' test and genital pruritus. Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.

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

Rarely, hypersensitivity symptoms may persist for several months.

The following reactions have been reported rarely in patients treated with cefaclor:

Toxic epidermal necrolysis, reversible interstitial nephritis, hepatic dysfunction, including cholestasis, increased prothrombin time in patients receiving cefaclor and warfarin concomitantly, reversible hyperactivity, nervousness, insomnia, confusion, hallucinations, hypertonia, aplastic anaemia, agranulocytosis and haemolytic anaemia.

The following adverse reactions have been reported in patients treated with other beta-lactam antibiotics: Colitis, renal dysfunction and toxic nephropathy.

Several beta-lactam antibiotics have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated. There have also been reports of neurological adverse reactions including encephalopathy, tremor and myoclonia associated with the use of cephalosporins. Most cases occurred in patients with severe renal impairment (see Section 4.4).

Reportingofsuspectedadversereactions
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
Website: www.hpra.ie

4.9 Overdose

Symptoms of nausea, vomiting, epigastric distress and diarrhoea would be anticipated.
General management consists of supportive therapy.
Consider activated charcoal instead of, or in addition to, gastric emptying.
Forced diuretics, peritoneal dialysis, haemodialysis or charcoal haemoperfusion have not been established as beneficial.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Second generation cephalosporins, ATC code: J01DC04

Distaclor LA Forte has been shown to be active *in vitro* against most strains of the following organisms, although clinical efficacy has not been established:

Gram-negative organisms:
Citrobacter diversus
Neisseria gonorrhoeae.
Anaerobic organisms:

Propionibacterium acnes
Bacteroides species (excluding Bacteroides fragilis)
Peptococci
Peptostreptococci.

Note: Pseudomonas sp., Acinetobacter calcoaceticus, most strains of enterococci, Enterobacter sp., indole-positive Proteus and Serratia sp. are resistant to cefaclor. Cefaclor is inactive against methicillin-resistant staphylococci.
Cefaclor is a broad spectrum semi-synthetic cephalosporin antibiotic.

5.2 Pharmacokinetic properties

'Long Acting' (sustained release) cefaclor differs from cefaclor in its rate of dissolution, producing a lower peak serum concentration, but retaining sustained measurable serum concentrations, which provides the advantage of twice daily dosing. It is well absorbed giving peak levels after 2.5-3 hours. It is excreted without metabolism in urine. Plasma half-life in healthy subjects is independent of dosage form and ranges from 0.6 to 1.2 hours. Elderly subjects with normal, or mildly diminished renal function, do not require dosage adjustment.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber in addition to that summarised in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Mannitol (E421)
Hypromellose (E464)
Hyprolose
Methacrylic acid copolymer, Type C
Stearic acid
Magnesium stearate (E572)

Tablet coating
Colour mixture - Dark blue (includes Hypromellose (E464), Titanium dioxide (E171), Macrogol 8000, Propylene glycol (E1520), Indigo carmine aluminium lake (E132))
Propylene glycol (E1520)
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original container.

6.5 Nature and contents of container

The product is packaged in PVC/Aclar/Aluminium foil blister packs of 2 or 14.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Flynn Pharma Limited
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40 Mespil Road
Dublin 4
D04 C2N4
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1226/001/005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 June 1994

Date of last renewal: 16 June 2008

10 DATE OF REVISION OF THE TEXT

January 2025