SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Distaclor MR Tablets

Cefaclor Flynn 375 mg Prolonged-Release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains cefaclor monohydrate equivalent to 375 mg of cefaclor as active ingredient.

3 PHARMACEUTICAL FORM

Prolonged-release tablets.

Blue and engraved with GP5.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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 bacteriuria, 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.

Note: Cefaclor prolonged-release tablets are 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 and the elderly:
Pharyngitis, tonsillitis, skin and skin structure infections: 375mg twice daily.
Lower urinary tract infections: 375mg twice daily or 500mg once daily.
Bronchitis: 375mg or 500mg twice daily
Pneumonia: 750mg twice daily.

In clinical trials, doses of 1.5g/day of Cefaclor prolonged-release tablets have been administered safely for 14 days. Doses of 4g/day of cefaclor have been administered safely, to normal subjects, for 28 days.
Elderly subjects with normal renal function do not require dosage adjustment.

Paediatric population
The safety and efficacy of Cefaclor prolonged-release tablets in children have not been established. No data are available. Cefaclor suspensions are available (see Cefaclor data sheet 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.

Method of administration
Cefaclor prolonged-release tablets are administered orally.
Cefaclor prolonged-release tablets are well absorbed from the gastro-intestinal tract. Since absorption is enhanced by administration with food, Cefaclor prolonged-release tablets should be taken with meals.

The tablets should not be cut, crushed or chewed. There is no evidence of metabolism in humans.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypersensitivity to other cephalosporins.

4.4 Special warnings and precautions for use

Warnings
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.

Precautions
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.

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.

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 Cefaclor prolonged-release tablets 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. Cefaclor prolonged-release tablets 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 500 mg 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 Cefaclor prolonged-release tablets.

Usage during labour and delivery
Treatment should be given only if clearly needed.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The majority of adverse reactions observed in clinical trials of Cefaclor prolonged-release tablets 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 Cefaclor prolonged-release 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. There have been reports of neurological sequelae including tremor, myoclonia, convulsions, encephalopathy with drugs belonging to the class of cephalosporins. Most cases occurred in patients with renal impairment who received doses that exceeded the recommended dose and resolved following discontinuation of treatment.

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 Cefaclor prolonged-release tablets, 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, orvasodilatation.

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, agitation, 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.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continues monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard.

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 diuresis, peritoneal dialysis, haemodialysis or charcoal haemoperfusion have not been established as beneficial.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Second-generation cephalosporins antibiotics, ATC code: J01DC04
Cefaclor prolonged-release tablets have 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.

Using the NCCLS recommended methods for sensitivity testing, the criteria for dilution methods are:

MIC $\leq$ 8 micrograms/ml:	susceptible
MIC = 16 micrograms/ml:	moderately susceptible
MIC $\geq$ 32 micrograms/ml:	resistant

and for the standard disc test, using a 30 microgram cefaclor disc (zone diameters)

MIC $\geq$ 18 mm: susceptible
MIC = 15-17 mm: moderately susceptible
MIC $\leq$ 14 mm: resistant

Cefaclor is a semi-synthetic cephalosporin antibiotic.

5.2 Pharmacokinetic properties

Following administration of 375mg, 500mg and 750mg tablets to fed subjects, average peak serum concentrations of 4, 8 and 11 micrograms/ml respectively, were obtained within 2.5 to 3 hours. No drug accumulation was noted when this was given twice daily.

Plasma half-life in healthy subjects is independent of dosage form and averages 1 hour. Elderly subjects with normal, mildly diminished renal function, do not require dosage adjustment, since higher peak plasma concentrations and AUC had no apparent clinical significance.

There is no evidence of metabolism in humans.

5.3 Preclinical safety data

There are no pre-clinical 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

Mannitol
Methylhydroxypropylcellulose
Hydroxypropylcellulose
Methacrylic acid copolymer
Stearic acid
Magnesium stearate
Titanium dioxide (E171)
Polyethylene glycol
Propylene glycol
Indigo carmine aluminium lake (E132)
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Two years.

6.4 Special precautions for storage

Do not store above 25˚C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Blister packs consisting of clear PVC with aluminium foil backing containing either 2 or 14 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Flynn Pharma Ltd
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Dublin 4,
IRELAND, D04 C2N4

8 MARKETING AUTHORISATION NUMBER(S)

PL 13621/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 November 1978
Date of latest renewal: 06 December 2006

10 DATE OF REVISION OF THE TEXT

12/03/2024