FLADINIR® Suspension

Cefdinir 125 mg/5 ml Powder for Oral Suspension

1. NAME OF THE MEDICINAL PRODUCT

FLADINIR® Suspension125 mg/5 ml powder for oral suspension**.**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION Active substance: Cefdinir.

Excipients: *For the complete list of the excipients, see section 6.1.*

3. PHARMACEUTICAL FORM

Powder for oral suspension. Cream-yellow coloured, strawberry and cream flavoured, homogeneous granule powder.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

FLADINIR® Suspension is indicated for pediatric patients:

- **Acute otitis media** caused by *Haemophilus influenzae* (including beta lactamase producing strains), *Streptococcus pneumoniae* (penicillin-sensitive strains only) and *Moraxella catarrhalis* (including beta-lactamase producing strains);
- **Angina/tonsillitis** caused by *Streptococcus pyogenes;*
- **Uncomplicated skin infections** caused by *Staphylococcus aureus* (including beta-lactamase producing strains) and *Streptococcus pyogenes.*

4.2. Posology and method of administration

The recommended dosage and duration of treatment in paediatric patients aged 6 months to 12 years are described in the dosing chart below.

The total daily dose for all infections is 14 mg/kg up to a maximum dose of 600 mg per day. Once daily dosing for 10 days is as effective as BID dosing.

Once-daily dosing have not been studied in skin infections; therefore, FLADINIR® suspension should be administrated twice daily in this infection.

FLADINIR® suspension may be administrated without regard to meals.

FLADINIR® suspension DOSAGE CHART for patients aged between 6 months to 12 years of age.

Type of Infection	Dosage	Duration
Acute Otitis Media	7 mg/kg per12 hour period 14 mg/kg single daily dose	5 to 10 days 10 days
Acute Maxillary Sinusitis	7 mg/kg per 12 hours or 14 mg/kg single daily dose	10 days 10 days
Pharyngitis/Tonsillitis	7 mg/kg per12 hour period	5 to 10 days

Type of Infection	Dosage	Duration
	or 14 mg/ kg single daily dose	10 days
Uncomplicated Skin Infections	7 mg/kg per12 hour period	10 days

Paediatric patients ≥ 43 kg should receive the maximum daily dose of 600 mg.

Weight	*Quantity of suspension (125 mg/5 ml) to be administered*
9 kg	2.5 ml per 12 hours or 5 ml single daily dose
18 kg	5 ml per 12 hours or 10 ml single daily dose
27 kg	7.5 ml per 12 hours or 15 ml single daily dose
36 kg	10 ml per 12 hours or 20 ml single daily dose
≥43 kg	12 ml per 12 hours or 24 ml single daily dose

Directions for the reconstitution and use of the oral suspension

- Put clean and fresh water up to the half level of the sign on the bottle than shake well, wait for 5 minutes to get a homogeneous dispersal.
- Add water up to the sign level and then shake again.
- Shake the suspension well before and close the bottle tightly after each use.
- After reconstitution, the suspension is stored at controlled room temperature; it may be used for 10 days after which any unused portion should be discarded.

Use in patients with renal insufficiency: For paediatric patients with creatinine clearance <30ml/min/1.73m², the dose should be 7 mg/kg (up to 300 mg) given once daily.

Use in patients with haemodialysis: Haemodialysis removes cefdinir from the body. The recommended initial dosage is 300 mg (or 7 mg/kg) every other day. At the conclusion of each haemodialysis session, 300 mg (or 7 mg/kg) dose should be administrated. Subsequent doses should be 300 mg (or 7 mg/kg) every other day.

Efficacy and safety are not established in new-borns and in children less than 6 months.

4.3. Contraindications

FLADINIR® suspension is contraindicated in patients with known hypersensitivity to the cephalosporin class of antibiotics.

4.4. Special warnings and Precautions for use

Before starting therapy with cefdinir, inquiry should be made to determine whether the patient has shown previous hypersensitivity *reactions* to cefdinir, other cephalosporins, penicillins or other drugs. If cefdinir is to be given to penicillin-sensitive patients, caution should be exercised because cross-hypersensitivity among 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 cefdinir occurs, the drug should be discontinued. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures including intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management with oxygen.

Pseudomembranous colitis has been reported with nearly all antibacterial agents including cefdinir. Therefore, it is important to be careful in patients reporting diarrhea subsequent to the administration of antibacterial agents. Treatment with antibacterial agents alters the normal flora of the colon. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated colitis. After diagnosis of pseudomembranous colitis has been established, appropriate therapy should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *Clostridium difficile*.

As with other broad-spectrum antibiotics, prolonged treatment may result in overgrowth of resistant organisms. Careful observation of the patient is essential. If superinfection occurs, appropriate alternative therapy should be administrated.

Cefdinir, as with other broad-spectrum antibiotics, should be administrated carefully to the patients with a history of colitis.

In patients with renal insufficiency (creatinine clearance <30 ml/min), the dose of cefdinir should be adjusted.

4.5. Interactions with other medicinal products and food

Cefdinir should be taken at least 2 hours before or after intake of an antiacid medicine. As with other drugs, probenecid inhibits the renal excretion of cefdinir.

In the case of concomitant administration of cefdinir with iron containing drugs, cefdinir should be taken at least 2 hours before or after this drug.

Alcohol may interfere with the actions of the medicine.

4.6. Use in Pregnancy and Lactation

Pregnancy category: B.

There are no adequate and well-controlled studies in pregnant women, therefore it should be used during pregnancy only if clearly needed.

After administration of single 600 mg doses, it was not detected in breast milk.

4.7. Effects on ability to drive and use machines

Adverse effects on the ability to drive or to operate machinery have not been observed.

4.8. Undesirable effects

Undesirable effects after the use of cefdinir are mild and self-limiting.

The most common reported side effects are: **>10%:** diarrhea (8-15%); **1-10%:** vaginal moniliasis (<4%), nausea (3%), rash (3%), headache (2%), increased urine leukocytes (2%), increased urine protein (1-2%), decreased lymphocytes (1%), glycosuria (1%), increased alkaline phosphatase (1%), increased eosinophils (1%), increased platelets (1%).

4.9. Overdosage

Information on cefdinir overdosage in humans is not available. Toxic signs and symptoms following overdosage with other beta-lactam antibiotics are nausea, vomiting, epigastric distress, diarrhea and convulsions. Hemodialysis removes cefdinir from the body.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ATC code: J01DD15 (Other beta-lactam antibacterials, third-generation cephalosporins). FLADINIR® suspension contains the active ingredient cefdinir which is a broad-spectrum semisynthetic cephalosporin.
Cefdinir is a third generation cephalosporin having a bactericidal effect by disrupting the synthesis of bacterial cell walls. Micro-organisms resistant to penicillins and certain cephalosporins are sensitive to cefdinir. Cefdinir has more affinity to penicillin binding protein (PBP) 3,2,1 of *S.aureus* and penicillin binding protein (PBP) 2 and 3 of *E.faecalis* than the other cephalosporins. Cefdinir inhibits the myeloperoxidase excretion of neutrophils at
the time of neutrophil stimulation by the mediators.

Microbiology

Cefdinir is effective on the following micro-organisms:

Aerobic Gram-Positive:

Staphylococcus aureus (including beta-lactamase producing strains, excluding methicillin- resistant strains); *Streptococcus pneumoniae* (penicillin- sensitive strains only);

Streptococcus pyogenes;

Staphylococcus epidermidis (methicillin- sensitive strains only);

Streptococcus agalactiae;

Streptococcus viridans species;

Aerobic Gram-Negative:

Haemophilus influenzae (including beta-lactamase producing strains); *Haemophilus parainfluenzae* (including beta-lactamase producing strains); *Moraxella catarrhalis* (including beta-lactamase producing strains); *Citrobacter diversus; Escherichia coli; Klebsiella pneumoniae; Proteus mirabilis*.

5.2. Pharmacokinetic properties:

Absorption:

Maximal plasma concentrations occur 2 to 4 hours following oral administration. The absolute bioavailability of cefdinir suspension is 25%. After administration of a single 7mg/kg dose of cefdinir to children between 6 months- 12

years of age, the values of C_{max} (µg/ml), T_{max} (hour) and AUC (µg. hour/ml) were 2.30, 2.2, 8.31, respectively and after administration of single 14 mg/kg dose of cefdinir, values were 3.86, 1.8, 13.4, respectively.

Multiple dosing: Cefdinir does not accumulate in plasma after once or twice daily administration to patients with normal renal function.

Distribution: The mean volume of distribution in children is 0.67 L/kg (±0.29). Cefdinir is 60% to 70% bound to plasma proteins in both adults and children; binding is independent of concentration.

Metabolism and excretion: Cefdinir is not appreciably metabolised. It is eliminated via renal excretion with a mean plasma elimination half-life ($t_{½}$) of 1.7 hours. Cefdinir clearance is reduced in patients with renal dysfunction. Because renal excretion is the predominant pathway of elimination, dosage should be adjusted in patients with renal function disorder or who are undergoing hemodialysis.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Aerosil, Sodium Carboxymethylcellulose, sodium benzoate, aspartame, camousine, lactose, sucrose, raspberry flavour

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30°C in in its original package.

After reconstitution, the suspension is stored at controlled room temperature; it may be used for 10 days after which any unused portion should be discarded.

6.5 Nature and contents of container:

FLADINIR® Suspension is 30 g of a cream-yellow powder, packaged in a 100 ml graduated Polypropylene bottle with plastic screw-cap and dosage cup.

6.6 Special precautions for disposal and other handlings

No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. CLASSIFICATION

Prescription only medicine.

8. MANUFACTURER

MIRAFLASH NIGERIA LIMITED

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