SCHEDULING STATUS: **S4**

1. NAME OF THE MEDICINE:

CEFALEXIN 250 CAPSULES RESMED (Capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains as the active ingredient, Cefalexin monohydrate equivalent to Cefalexin anhydrous 250 mg.

Contains sugar (lactose) 6 mg per capsule.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Capsules.

Green/white coloured hard gelatin size ‘2’ capsules containing white to off white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin, as in Cefalexin 250 Capsules Resmed, is a first-generation cephalosporin antibacterial indicated for the treatment of the following infections caused by susceptible micro-organisms:

- Respiratory tract infections caused by *Streptococcus pneumonia* and group A β-*haemolytic Streptococci*.
- Otitis media due to *Streptococcus pneumonia*, *H. influenza, Staphylococci, Streptococci* and *N. catarrhalis.*
- Skin and soft tissue infections caused by *staphylococci* and/or s*treptococci*.
- Genitourinary tract infections, including acute prostatitis caused by *E. coli, P. mirabilis,* and *Klebsiella*.
- Dental infections caused by *staphylococci* and/or s*treptococci.*

Appropriate culture and susceptibility studies should be performed to determine susceptibility of causative organism to cefalexin. Renal function studies should be performed when indicated.

4.2 Posology and method of administration

Posology

Adults: The adult dosage ranges from 1-4 g daily in divided doses. The usual adult dose is 250 mg every 6 hours. For skin and soft tissue infections, streptococcal pharyngitis and mild uncomplicated urinary tract infections, the usual dosage is 250 mg every 6 hours or 500 mg every 12 hours.

For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses greater than 4 grams are required, parenteral cephalosporins, in appropriate doses, should be considered.

Special populations

The elderly and patients with impaired renal function: As for adults. Reduce dosage if renal function is markedly impaired.

Paediatric population

Children: The usual recommended dosage for children is 25 mg/kg/day to 50 mg/kg/day in divided doses every six hours. The use of capsules is not feasible in young children.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Method of administration

Capsules for oral use.

4.3 Contraindications

Hypersensitivity to cefalexin or to any of the excipients of Cefalexin 250 Capsules Resmed listed in section 6.1. Cefalexin is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics.

Safety in pregnancy and lactation has not been established.

4.4 Special warnings and precautions for use

Before therapy with cefalexin is instituted, careful enquiry should be made concerning previous hypersensitivity reactions to cephalosporins, penicillins and other medicine.

Cefalexin should be administered with caution to penicillin-sensitive patients. There is some evidence of cross-allergenicity between the penicillins and cephalosporins. Patients have been reported to have had severe reactions (including anaphylaxis) to both.

The diagnosis of pseudomembranous colitis must be considered in patients who develop diarrhoea in association with its use. Such colitis may be life-threatening and appropriate measures should be taken, including discontinuation of Cefalexin 250 Capsules Resmed.

Cefalexin 250 Capsules Resmed should be administered with caution to patients with renal impairment and dosage reduction may be necessary. Acute renal tubular necrosis may occur following excessive dosage and has been associated with its use in older patients, those with pre-existing renal impairment, or with concomitant administration of nephrotoxic medicines such as aminoglycosides.

Positive results to the direct Coombs' test have been found during treatment with cephalosporins, which can interfere with blood cross matching. A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with copper sulphate test tablets.

Prolonged use of Cefalexin 250 Capsules Resmed may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Acute generalised exanthematous pustulosis (AGEP) has been reported in association with cefalexin treatment. At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, cefalexin should be withdrawn immediately and an

alternative treatment considered. Most of these reactions occurred most likely in the first week during treatment.

Cefalexin 250 Capsules Resmed contains lactose. Patients with the rare hereditary conditions of galactose intolerance, total lactose deficiency, glucose-galactose malabsorption should not take Cefalexin 250 Capsules Resmed.

Contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

As cephalosporins like cefalexin are only active against proliferating microorganisms, they should not be combined with bacteriostatic antibiotics.

Concomitant use of uricosuric drugs (e.g. probenecid) suppresses renal drug elimination. As a result, cefalexin plasma levels are increased and sustained for longer periods.

If associated with highly potent diuretics (ethacrynic acid, furosemide) or other potentially nephrotoxic antibiotics (aminoglycosides, polymyxin, colistin), cephalosporins may show higher nephrotoxicity.

Combined use of cephalosporins and oral anticoagulants may prolong prothrombin time.

A potential interaction between cefalexin and metformin may result in an accumulation of metformin and could result in fatal lactic acidosis.

Hypokalaemia has been described in patient taking cytotoxic drugs for leukaemia when they were given gentamicin and cefalexin.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

4.7 Effects on ability to drive and use machines.

None known.

4.8 Undesirable effects

Blood and the lymphatic system disorders:	• Frequent: eosinophilia. • Less frequent: Hypoprothrombinaemia, neutropenia, thrombocytopenia, agranulocytosis; there may be a positive response to the Coombs' test, but haemolytic anaemia rarely occurs.
Nervous system disorders:	• Less frequent: convulsions and other signs of CNS toxicity have been associated with high doses, especially in patients with severe renal impairment.
Gastrointestinal disorders:	• Frequent: Nausea, vomiting and diarrhoea. • Less frequent: pseudomembranous colitis
Hepato-biliary disorders:	• Less frequent: Transient increases in hepatic enzyme levels, hepatitis, cholestatic jaundice.
Skin:	• Frequent: Rash • Less frequent: erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis.
Renal and urinary disorders:	• Less frequent: acute interstitial nephritis.
Other:	• Frequent: Hypersensitivity reactions including skin rashes, urticaria, eosinophilia, fever, reactions resembling serum sickness and anaphylaxis. • Frequency unknown: vulval irritation, abdominal cramps, headache, dizziness, drowsiness and fatigue.

4.9 Overdose

Treatment is symptomatic and supportive. Cefalexin is removed by haemodialysis and peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A20.1.1 Broad and medium spectrum antibiotics

Mechanism of action

It is a broad-spectrum bactericidal antibiotic which acts by inhibiting bacterial cell-wall synthesis.

Cefalexin is active against the following organisms *in vitro.*

Beta-haemolytic streptococci; staphylococci, including coagulase-positive, coagulase negative and penicillinase-producing strains; *Streptococcus pneumoniae*; *Escherichia coli; Proteus mirabilis; Klebsiella* species; *Haemophilus influenza; Neisseria catarrhalis*.

Most strains of enterococci (streptococcus faecalis) and a few strains of *staphylococci* are resistant to cefalexin. It is not active against most strains of *Enterobacter* species, *P. morganii* and *P. vulgaris*.

It has no activity against *Pseudomonas* or *Herellea* species. When tested by *in vitro* methods, *staphylococci* exhibit cross-resistance between cefalexin and methicillin-type antibiotics. *In-vitro* sensitivity does not necessarily imply *in-vivo* efficacy.

5.2 Pharmacokinetic properties

Absorption: Cefalexin is rapidly absorbed from the upper gastrointestinal tract, giving peak levels at 1 hour and following food at 2 hours.

Distribution: Following doses of 250 mg and 500 mg average serum levels of about 9 and 18 mcg per ml respectively were obtained at one hour. The serum half-life of cefalexin is 0,9 to 1,2 hours but is prolonged in neonates. In uremic patients half-life may increase to 5-30 hours.

Elimination: Over 90 % is recovered unchanged in urine within 8 hours. Peak urine concentrations are 1000 mcg per ml during this period following a 250 mg dosage of Cefalexin 250 Capsules Resmed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients: Lactose anhydrous, croscarmellose sodium, magnesium stearate, gelatin, sodium lauryl sulphate and colourants.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30^0C, protected from moisture.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Carton containing 10 x 10 capsules in blister packing.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Resmed Healthcare

71 Rochdale Road, Springfield Park, Durban, 4051.

8. REGISTRATION NUMBER

53/20.1.1/0169

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

Date of latest renewal:

10. DATE OF REVISION OF THE TEXT