SCHEDULING STATUS: **S4**

1. NAME OF THE MEDICINE:

CEFIXIME 400 TABLETS RESMED

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains Cefixime trihydrate equivalent to Cefixime anhydrous 400 mg. Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Film coated tablets.

Off-white coloured, caplet-shaped, biconvex, film coated tablets, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CEFIXIME 400 TABLETS RESMED are indicated for the treatment of infections caused by susceptible micro-organisms.

Upper respiratory tract infections (infections of the ear, nose and throat); e.g. bacterial pharyngitis, tonsillitis, otitis media, sinusitis, laryngitis.

Lower respiratory tract infections, e.g. bronchitis.

Urinary tract infections, e.g. acute cystitis.

Uncomplicated gonorrhoea.

CEFIXIME 400 TABLETS RESMED is not suitable to treat staphylococcal infections since staphylococci are resistant.

4.2 Posology and method of administration

Posology

Absorption of CEFIXIME 400 TABLETS RESMED is not significantly modified by the presence of food. The usual course of treatment is 5 – 14 days. The tablet should be taken with liquid either before or during a meal.

Adults and children over 12 years:

The recommended adult dose is 400 mg daily given as a single dose.

In lower respiratory tract infections, 400 mg daily is recommended.

For uncomplicated infections of the lower urinary tract, in general, treatment over 1 to 3 days is sufficient.

For sinusitis the therapeutic dosage must be administered for 10 to 14 days.

Treatment of uncomplicated Gonorrhoea:

The recommended dosage is 400 mg as a single oral dose.

The elderly: Elderly patients may be given the same dose as recommended for adults. Renal function should be assessed, and dosage should be adjusted in severe renal impairment. (See “Dosage in Renal Impairment”).

Dosage in Renal Impairment:

Patients with impaired renal function may require a dose of CEFIXIME 400 TABLETS RESMED as follows:

Creatinine Clearance (ml/min/ ml/sec)	**Dose**
>60/1.00	400 mg once daily.

Method of administration

For oral use.

4.3 Contraindications

CEFIXIME 400 TABLETS RESMED must not be used in patients hypersensitive to Cefixime, to other cephalosporins, or to any of the excipients of Cefixime 400 Tablets Resmed.

4.4 Special warnings and precautions for use

CEFIXIME 400 TABLETS RESMED should be given with caution to patients who have shown hypersensitivity to other cephalosporins. CEFIXIME 400 TABLETS RESMED should be given with caution to patients allergic to beta-lactam antibiotics such as penicillin-sensitive patients, as there is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have had severe reactions (including anaphylaxis) to both classes of medicine. If an allergic effect occurs with CEFIXIME 400 TABLETS RESMED, the medicine should be discontinued, and the patient treated with appropriate medicines if necessary.

In patients with asthma and allergic diathesis particular caution is recommended.

CEFIXIME 400 TABLETS RESMED should be administered with caution in patients with impaired renal function (See section 4.2 “Dosage in Renal Impairment”).

Short or prolonged use of CEFIXIME 400 TABLETS RESMED may result in the overgrowth of non-susceptible organisms. Use of CEFIXIME 400 TABLETS RESMED has been shown to alter the normal flora of the colon and may permit overgrowth of Clostridia. Studies indicate a toxin(s) produced by Clostridium difficile is the primary cause of antibiotic associated pseudomembranous colitis. Severe and persistent diarrhoea requiring medical intervention may develop. CEFIXIME 400 TABLETS RESMED should be discontinued if diarrhoea occurs and corrective treatment must be started.

In patients with severe gastrointestinal disturbances involving vomiting and diarrhoea treatment with CEFIXIME 400 TABLETS RESMED is not recommended.

Caution is recommended in patients concomitantly treated with diuretics (e.g. furosemide) and/or other potentially nephrotoxic medicinal products (e.g. aminoglycoside antibiotics), especially in patients with underlying medical conditions, where renal ischaemia can be expected (e.g. severe infections, septicaemia).

In these patients, impairment of renal function and even acute renal failure, caused by such combinations, may occur. Careful monitoring of renal function is necessary.

Renal Impairment

In patients with severely impaired renal function particular caution is recommended. Close monitoring and dose adaptation are recommended.

Haemolytic anaemia

Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime) –associated haemolytic anaemia has also been reported

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in some patients on cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/or measures should be taken. Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs.

Neonates

Safety and efficacy have not been established in neonates including preterm neonates. Therefore, the administration of CEFIXIME 400 TABLETS RESMED is not recommended in neonates.

4.5 Interaction with other medicines and other forms of interaction

- Potentially nephrotoxic substances such as aminoglycoside antibiotics, colistin, polymyxin, viomycin or potent diuretics may increase the risk of impairment of renal function, when used concomitantly with CEFIXIME 400 TABLETS RESMED.
- The calcium-channel blocker nifedipine increases the bioavailability of CEFIXIME 400 TABLETS RESMED. However, no dose adaptation is recommended.
- Platelet aggregation inhibitors: hypoprothrombinemia induced by large doses of salicylates and/or cephalosporins and the gastrointestinal ulcerative or hemorrhagic potential of nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, or sulfinpyrazone may increase the risk of hemorrhage.
- Interference with laboratory tests.
- A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions. A false positive direct Coombs test has been reported during treatment with cephalosporin antibiotics, therefore it should be recognised that a positive Coombs test may be due to the medicine.
- Probenecid: decreases tubular secretions in increased and prolonged cephalosporin serum concentrations, prolonged elimination half-life, and increased risk of toxicity; however, cefixime as in Cefixime 400 Tablets Resmed and probenecid might be used concurrently in the treatment of infections such as sexually transmitted diseases (STDs) or other infections, in which high and/or prolonged antibiotic serum and tissue concentrations are required.
- Anticoagulants
- In common with other cephalosporins, increases in prothrombin times have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy.

- Cefixime should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since cefixime may enhance effects of the anticoagulants, prolonged prothrombin time with or without bleeding may occur.

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.

In the case of side effects such as encephalopathy (which may include convulsion, confusion, impairment of consciousness, movement disorders), the patient should not operate machines or drive a vehicle.

4.8 Undesirable effects

System Organ Class	More frequent	Less frequent
Blood and lymphatic system disorders:		Eosinophilia, leukopenia, agranulocytosis pancytopenia, thrombocytopenia, and further changes in blood count. These adverse reactions usually return to normal spontaneously after the end of therapy. Coagulation disorders, haemolytic anaemia.
Gastrointestinal disorders:	Loose stools Diarrhoea	Abdominal pain, indigestion, nausea and Vomiting.
Hepatobiliary disorders:		Reversible elevation in hepatic enzymes (transaminases, alkaline phosphatase) in serum. Hepatitis, cholestatic jaundice.
Infections and infestations:	Oral candidiasis (sore mouth and tongue) Vaginal candidiasis (vaginal itching and discharge)	Superinfections with resistant bacteria or fungi after long-term and repeated administration
Skin and Subcutaneous Tissue Disorders		Rashes Erythema, exanthema, pruritis, mucosal inflammation. Toxic epidermal necrolysis Stevens-Johnson syndrome, Erythema exudativum multiforme.

Nervous system disorders:		Headache, dizziness Transient hyperactivity Cases of convulsions have been reported with cephalosporins including cefixime (frequency not known) Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment (frequency not known).
Renal and urinary disorders: *		Transient elevation in urea concentrations. Elevation in serum creatinine, interstitial nephritis.
Immune system disorders:		Hypersensitivity reactions of varying degrees such as flush, palpitations, dyspnoea, hypotension, bronchospasm, angioedema. Anaphylactic shock, serum sickness-like reactions Drug rash with eosinophilia and systemic symptoms (DRESS)
General disorders and administration site conditions		Drug fever

* Caution is recommended in patients concomitantly treated with diuretics and/or other potentially nephrotoxic medicinal products, especially in patients with underlying medical conditions, where renal ischaemia can be expected. In these patients, impairment of renal function and even acute renal failure, caused by such combinations, may occur. Careful monitoring of renal function is necessary.

4.9 Overdose

CEFIXIME 400 TABLETS RESMED-400 mg TABLETS is not removed from the circulation in significant quantities by dialysis. No specific antidote exists. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.1.1 Antimicrobial (Chemotherapeutic) agents Broad and Medium Spectrum Antibiotics

Cefixime is an oral third generation cephalosporin antibiotic; it is bactericidal and acts by inhibiting synthesis of the bacterial cell wall.

Cefixime is stable to hydrolysis by many beta-lactamases.

It has in-vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms including *Streptococcus pneumonia, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenza* (beta-lactamase positive and negative), *Moraxella (Branhamella) catarrhalis* (beta-lactamase positive and negative).

(*In vitro* activity does not necessarily imply *in vivo* efficacy.)

Most strains of enterococci (*Streptococcus faecalis, group D Streptococci*) and *Staphylococci* (including coagulase positive and negative strains and methicillin-resistant strains) are resistant to Cefixime. In addition, most strains of *Enterobacter* and *Pseudomonas*, *Bacteroides fragilis*, *Listeria monocytogenes* and *Clostridia* are resistant to Cefixime.

5.2 Pharmacokinetic properties

Absorption: Only 40 to 50 % of an oral dose of Cefixime is absorbed from the gastrointestinal tract, whether taken before or after meals, however the rate of absorption may be decreased in the presence of food. Absorption is fairly slow; peak plasma concentration of 2 to 3 micrograms/ml and 3,7 to 4,6 micrograms /ml have been reported between 2 and 6 hours after single doses of 200 and 400 mg, respectively.

Distribution: Information on the distribution of Cefixime in body tissue and fluids is limited. Cefixime crosses the placenta.

The plasma half-life is usually about 3 to 4 hours and may be prolonged in cases of renal impairment. About 65% of Cefixime is bound to plasma proteins.

Relatively high concentrations may be achieved in bile and urine.

Excretion: About 20% of an oral dose (or 50% of an absorbed dose) is excreted unchanged in the urine within 24 hours. Up to 60% may be eliminated by non-renal mechanisms. There is no evidence of metabolism, but some is probably excreted in the faeces from bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients: Microcrystalline cellulose, pregelatinized starch, hydroxypropyl cellulose, croscarmellose sodium, colloidal silicon dioxide, magnesium stearate, hypromellose, polyethylene glycol, talc, and titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30^0C. Protect from light. KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Carton containing 1 x 10’s tablets in aluminium/aluminium blister packs.

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

53/20.1.1/0172

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/07/2023

10. DATE OF REVISION OF THE TEXT