1.3.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

Cefpodoxime 100 mg Alkem film-coated tablets

Cefpodoxime 200 mg Alkem film-coated tablets

Cefpodoxime proxetil

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefpodoxime 100 mg Alkem: Each film-coated tablet contains 130.44 mg cefpodoxime proxetil equivalent to 100 mg cefpodoxime.

Cefpodoxime 200 mg Alkem: Each film-coated tablet contains 260.88 mg cefpodoxime proxetil equivalent to 100 mg cefpodoxime.

Excipients with known effect:

Cefpodoxime 100 mg Alkem: 15 mg of Lactose monohydrate, 0.156 mg of FD&C yellow #6, 0.132 mg of FD&C yellow #5 and 0.0006 mg of red iron oxide.

Cefpodoxime 200 mg Alkem: 30 mg of Lactose monohydrate, 0.312 mg of FD&C yellow #6, 0.264 mg of FD&C yellow #5 and 0.0012 mg of red iron oxide.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Cefpodoxime 100 mg Alkem: Orange colored, oval shaped, film-coated tablets debossed with "A55" on one side and plain on other side.

Cefpodoxime 200 mg Alkem: Orange colored, oval shaped, film-coated tablets debossed with "A57" on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefpodoxime Alkem is indicated, in adults, for the short-term treatment of upper and lower respiratory tract infections when caused by susceptible pathogens (sensitivity test is recommended):

- **Acute sinusitis** due to *Haemophilus influenzae (ß-lactamase and non-ß-lactamase producing strains)*, *Streptococcus pneumoniae*, methicillin sensitive *Staphylococcus aureus (penicillinase and non-penicillinase producing strains)*, *Moraxella catarrhalis*, *(Branhamella catarrhalis) (ß-lactamase and non-ß-lactamase producing strains)* and *Haemophilus parainfluenza (ß-lactamase and non-ß-lactamase producing strains).*
- **Pharyngitis and tonsillitis** due to *Streptococci of* Groups A (*S. pyogenes*), C and G.
- **Acute bronchitis, relapses or exacerbation of chronic bronchitis** due to *Haemophilus influenzae (ß-lactamase and non-ß-lactamase producing strains)*, *Streptococcus pneumoniae*, methicillin sensitive *Staphylococcus aureus (penicillinase and non-penicillinase producing strains)*, *Moraxella catarrhalis*, *(Branhamella catarrhalis) (ß-lactamase and non-ß-lactamase producing strains)* and *Haemophilus parainfluenza (ß-lactamase and non-ß-lactamase producing strains)*.
- **Bacterial pneumonia and community acquired pneumoniae** due to *Haemophilus influenzae (ß-lactamase and non-ß-lactamase producing strains)*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *(Branhamella catarrhalis) (ß-lactamase and non-ß-*

lactamase producing strains) and *Haemophilus parainfluenza (ß-lactamase and non-ß-lactamase producing strains).*

4.2 Posology and method of administration

Posology:

Adults:

Each film-coated tablet contains 100 mg or 200 mg of cefpodoxime. The dosage depends on the condition being treated.

Tonsillitis, pharyngitis and acute bronchitis:

One **Cefpodoxime 100 mg Alkem** tablet every 12 hours with meals (200 mg/ day).

A therapeutic dose must be administered for at least 10 days.

Acute sinusitis, acute exacerbations of chronic bronchitis, pneumonia:

One **Cefpodoxime 200 mg Alkem** tablet every 12 hours with meals (400 mg/day).

Special populations

Elderly patients:

Where renal function is normal, it is not necessary to adjust the dose.

Hepatic insufficiency in adults and children*:*

No dosage adjustment necessary.

Renal insufficiency in adults and children:

When the creatinine clearance is above 40 ml/min, it is not necessary to adjust the dose. For values below 40 ml/min, the daily dosage regimen should be reduced by half and administered as a single daily dose for values 10 - 39 ml/min, every second day for values below 10 ml/min and after each dialysis session for haemodialysis patients.

Method of administration:

Route of administration: oral administration.

The tablets should be taken with food for optimum absorption.

4.3 Contraindications

- Hypersensitivity to cefpodoxime, any other cephalosporins or to any of the excipients of **Cefpodoxime Alkem** listed in section 6.1.
- Previous history of immediate and / or severe hypersensitivity reaction (anaphylaxis) to penicillin or other beta-lactam antibiotic.
- Safety of use in pregnancy and lactation has not been established (see section 4.6).
- Children below 1 year of age.

4.4 Special warnings and precautions for use

Cefpodoxime Alkem is not a preferred antibiotic for the treatment of staphylococcal pneumonia and should not be used in the treatment of atypical pneumonia caused by organisms such as Legionella, Mycoplasma and Chlamydia.

Cefpodoxime Alkem is not recommended for the treatment of pneumonia due to S. pneumoniae (see section 5.1).

Serious and occasionally fatal hypersensitivity reactions have been reported with beta-lactam antibacterial medicines. In case of severe hypersensitivity reactions, treatment with cefpodoxime must be discontinued immediately and adequate emergency measures must be initiated. Before beginning treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to cefpodoxime, to other cephalosporins or to any other type of beta-lactam medicine. Caution should be used if cefpodoxime is given to patients with a history of non-severe hypersensitivity to other beta-lactam medicines.

In cases of severe renal insufficiency, it may be necessary to reduce the dosage regimen dependent on the creatinine clearance (see section 4.2).

Antibacterial medicine-associated colitis and pseudo-membranous colitis have been reported with nearly all anti-bacterial medicines, including cefpodoxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of **Cefpodoxime Alkem** (see section 4.8).

Discontinuation of therapy with **Cefpodoxime Alkem** and the administration of specific treatment for Clostridium difficile should be considered. Medicines that inhibit peristalsis should not be given. **Cefpodoxime Alkem** should always be prescribed with caution in patients with a history of gastrointestinal disease, particularly colitis. Neutropenia and more less frequently agranulocytosis may develop particularly during extended treatment. For cases of treatment lasting longer than 10 days, the blood count should be monitored and treatment discontinued if neutropenia is found.

Cephalosporins may be absorbed onto the surface of red cell membranes and react with antibodies directed against the medicine. This can produce a positive Coomb's test and less frequently, haemolytic anaemia. Cross-reactivity may occur with penicillin for this reaction.

Changes in renal function have been observed with cephalosporin antibiotics, particularly when given concurrently with potentially nephrotoxic medicines such as aminoglycosides and/or potential diuretics. In such cases, renal function should be monitored.

Prolonged use of cefpodoxime may result in the overgrowth of non-susceptible organisms (*candida and Clostridium difficile*), which may require interruption of treatment.

Interaction 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.

Colourants in product may cause allergic reactions.

Cefpodoxime Alkem contains lactose.

Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Probenecid:

Probenecid reduces the excretion of cephalosporins.

Oestrogens:

Cephalosporins potentially reduce the contraceptive effect of oestrogens.

Oral anticoagulants:

Cephalosporins potentially enhance the anticoagulant effect of coumarins. Simultaneous administration of **Cefpodoxime Alkem** with warfarin may augment its anti-coagulant effects. Patients receiving antibacterial medicines may experience increases in oral anticoagulant activity. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of the cephalosporins to the increase in INR (international normalised ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after co-administration of cefpodoxime with an oral anti-coagulant medicine.

Antacids and H_2-blockers:

Histamine H_2-antagonists and antacids reduce the bioavailability of **Cefpodoxime Alkem**. Bioavailability could decrease by approximately 30 % when **Cefpodoxime Alkem** is administered with medicines which neutralise gastric pH or inhibit acid secretions. Therefore, such medicines as antacids of the mineral type and H_2 blockers such as ranitidine, which can cause an increase in gastric pH, should be taken 2 to 3 hours after **Cefpodoxime Alkem** administration.

Positive Coombs test may occur during treatment with cephalosporins. Urinary glucose testing with non-specific reducing medicines, may yield a false-positive reaction in patients treated with cefpodoxime proxetil. This phenomenon is not seen when a glucose-oxydase specific method is used.

4.6 Fertility, pregnancy and lactation

Pregnancy:

The safety and efficacy have not been established in pregnancy.

Breastfeeding:

The safety and efficacy have not been established in breastfeeding.

4.7 Effects on ability to drive and use machines

Dizziness has been reported during treatment with **Cefpodoxime Alkem** and may affect the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: Frequent, less frequent, frequency unknown.

Blood and lymphatic system disorders:

Frequent: Eosinophilia

Less frequent: Haematological disorders such as reduction in haemoglobin, thrombocytosis, thrombocytopenia, leucopenia, and haemolytic anaemia.

Frequency unknown: Neutropenia, agranulocytosis

Nervous system disorders:

Less frequent: Headache, paraesthesia, dizziness

Ear and labyrinth disorders:

Less frequent: Tinnitus.

Gastrointestinal disorders:

Frequent: Gastric pressure, nausea, vomiting, abdominal pain, flatulence, diarrhoea.

Less frequent: Bloody diarrhoea can occur as a symptom of enterocolitis. The possibility of pseudomembranous enterocolitis should be considered if severe or persistent diarrhoea occurs during or after treatment (see section 4.4).

Metabolism and nutrition disorders:

Frequent: Loss of appetite

Immune system disorders:

Frequent: Hypersensitivity reactions of all degrees of severity have been observed (see section 4.4).

Less frequent: anaphylactic reactions, bronchospasm, purpura and angioedema.

Renal and urinary disorders:

Less frequent: Slight increases in blood urea and creatinine.

Hepato-biliary disorders:

Less frequent: Transient moderate elevations of AST, ALT and alkaline phosphatase and/or bilirubin. These laboratory abnormalities which may be explained by the infection, may rarely exceed twice the upper limit of the named range and elicit a pattern of liver injury, usually cholestatic and most often asymptomatic and liver damage.

Skin and subcutaneous tissue disorders:

Less frequent: Hypersensitivity mucocutaneous reactions, rash, urticaria, pruritis, Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme.

Infections and infestations:

Less frequent: There can be multiplication of non-sensitive micro-organisms (see section 4.4).

General disorders and administration site conditions:

Less frequent: Asthenia or malaise.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8 Alternatively all adverse events can be reported to Alkem Laboratories vial the e-mail: pharmacist.rsa@alkem.com.

4.9 Overdose

In the event of overdosage with cefpodoxime, supportive and symptomatic therapy is indicated.

In cases of overdosage, particularly in patients with renal insufficiency, encephalopathy may occur. The encephalopathy is usually reversible once cefpodoxime plasma levels have fallen. Convulsions have also been reported with high doses of Cefpodoxime in renally-impaired patients.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta-lactam antibacterial, a 3rd generation cephalosporin.

ATC Code: J01DD13

Pharmacological Classification: A 20.1.1 Broad and medium spectrum antibiotics

Cefpodoxime proxetil is a semisynthetic ß-lactam antibiotic belonging to the third generation oral cephalosporin group. Cefpodoxime proxetil is the prodrug of the bactericidal antibiotic cefpodoxime.

Cefpodoxime possess in vitro bacterial activity against broad spectrum gram negative and gram positive bacteria.

Cefpodoxime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

5.2 Pharmacokinetic properties

Absorption:

Cefpodoxime proxetil is taken up in the intestine and is hydrolysed to the active metabolite cefpodoxime. Cefpodoxime is absorbed rapidly when administered orally as a tablet and absorption is increased by food intake.

Distribution:

The peak plasma levels of cefpodoxime are achieved within 2 to 3 hours after dosing. The maximum plasma concentration of about 1 mg/L and 1.2 mg/L after doses of 100 mg and 200 mg respectively. Following administration of 100 mg and 200 mg twice daily over 14.5 days, the plasma pharmacokinetic parameters of cefpodoxime remain unchanged. Approximately 40 % of Cefpodoxime is bound to plasma proteins (albumin). This binding is non saturable in type.

Diffusion in fluids and tissues:

Concentrations of cefpodoxime in excess of the minimum inhibitory levels (MIC) for common pathogens can be achieved in lung parenchyma, bronchial mucosa, pleural fluid, tonsils, interstitial fluid and prostate tissue.

Elimination:

The main route of excretion of Cefpodoxime is renal, 80 % is excreted unchanged in the urine, and the elimination half-life is approximately 2.4 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Carboxymethyl cellulose calcium

Colloidal silicon dioxide

Crospovidone (Type B)

Low-substituted hydroxy propyl cellulose

Lactose monohydrate

Magnesium stearate

Sodium lauryl sulfate

Tablet coating

Hypromellose

Macrogol (PEG)

FD&C Yellow #5 (E102)

FD&C Yellow #6 (E110)

Red iron oxide (E172)

Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at or below 25 °C.

Do not remove strip from carton until required for use.

Keep bottle tightly closed. Store in the original package in order to protect from moisture.

Store all medicine out of reach of children.

6.5 Nature and contents of container

Cefpodoxime 100 mg Alkem and **Cefpodoxime 200 mg Alkem** are packed Aluminium/ aluminium foil blister strip of 6 tablets (inserted in a printed cardboard carton) and in HDPE bottles.

Pack sizes: 6's tablets for blisters and 20's, 100's and 500's tablets for HDPE bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Ascend Laboratories (Pty) Ltd.

R21 Corporate Park

121 Sovereign Drive

Block A, Office 202

Irene Ext.30, Centurion, 0157

8 MARKETING AUTHORISATION NUMBER(S)

To be allocated by authority.

9 DATE OF REVISION OF THE TEXT

To be allocated by authority.