1.3.1.1 Professional Information for Medicines for Human Use

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

XENARA ORAL SUSPENSION 125mg/5ml, 125mg/5ml (powder for oral suspension)

XENARA ORAL SUSPENSION 250mg/5ml, 250mg/5ml (powder for oral suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

XENARA ORAL SUSPENSION 125mg/5ml

Each 5 mL reconstituted suspension contains cephalexin monohydrate equivalent to cephalexin 125 mg. Contains sucrose: 2550,066 mg/5 mL and sodium benzoate: 2,200 mg/5 mL.

For full list of excipients, see section 6.1.

XENARA ORAL SUSPENSION 250mg/5ml

Each 5 mL reconstituted suspension contains cephalexin monohydrate equivalent to cephalexin 250 mg. Contains sucrose: 2418,590 mg/5 mL and Sodium benzoate: 2,200 mg/5 mL.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

XENARA ORAL SUSPENSION 125mg/5ml *(powder for oral suspension)*

XENARA ORAL SUSPENSION 250mg/5ml *(powder for oral suspension)*

Dry Powder:

Off-white to pale yellow coloured powder.

Reconstituted Suspension:

Off-white to light pink suspension with Cherry flavour

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

XENARA ORAL SUSPENSION is indicated for the treatment of the following Infections caused by susceptible micro-organisms:

- **Respiratory tract infections** caused by *Streptococcus pneumoniae and group A β-haemolytic streptococci.*
- **Otitis media** due to *Streptococcus pneumoniae, H. influenzae, staphylococci, streptococci and N. catarrhalis.*
- Skin and soft tissue infections, caused by *staphylococci and/or streptococci.*
- **Genito-urinary tract infections**, including acute prostatitis caused by *E. coli, P. mirabilis and Klebsiella.*
- **Dental infections** caused by staphylococci and/or *streptococci.*

Appropriate culture and susceptibility studies, should be performed to determine susceptibility of causative organism to cephalexin. 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** dosage 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.

Adults who are not able to take capsules may be given **XENARA ORAL SUSPENSION**.

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

Special Population:

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

Paediatric Population:

The usual recommended dosage for children is 25 mg/kg/day to 50 mg/kg/day in divided doses every six hours.

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

Method of administration

XENARA ORAL SUSPENSION is administered orally.

Cephalexin is acid stable and may be given without regard to meals.

For instructions on reconstitution of **XENARA ORAL SUSPENSION**, see section 6.6.

4.3. Contraindications

XENARA ORAL SUSPENSION is contraindicated:

- Patients with known allergy to the cephalosporin group of antibiotics. (See section 4.4).
- Patients with hypersensitivity to cephalexin or any of the excipients of **XENARA ORAL SUSPENSION**. (See section 4.4).
- Pregnancy and lactation (see section 4.6).

4.4. Special warnings and precautions for use

Hypersensitivity reactions

Before therapy with **XENARA ORAL SUSPENSION** is started, careful enquiry should be made concerning previous hyper-sensitivity reactions to cephalosporins, penicillins or other medicine. **XENARA ORAL SUSPENSION** should be administered with caution to penicillin-sensitive patients. There is evidence of cross allergencity between the penicillins and cephalosporin's. Patients have been reported to have had severe reactions (including anaphylaxis) to both.

Allergic reactions in the form of rash, urticaria, angioedema, anaphylaxis, erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis have been reported with the use of cephalexin. If an allergic reaction to cephalexin as contained in **XENARA ORAL SUSPENSION** occurs, discontinue the medicine and institute appropriate treatment.

Pseudomembranous colitis

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 **XENARA ORAL SUSPENSION.**

Laboratory investigations

XENARA ORAL SUSPENSION may interfere with the Jaffe method of measuring creatinine concentrations and may produce falsely high values; this should be borne in mind when measuring renal function.

Positive direct Coombs' (antiglobulin) have been reported during treatment with the cephalosporin antibiotics and these can interfere with blood cross matching.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets.

Elderly Use

This medicine is substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection

Prolonged Prothrombin Time with Renal or Hepatic Impairment

Cephalosporin's may be associated with prolonged prothrombin time. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antibacterial therapy, and patients receiving anticoagulant therapy. Monitor prothrombin time in patients at risk and manage as indicated.

Renal Impairment

Cephalexin should be administered with caution in the presence of impaired renal function (creatinine clearance < 30 mL/min, with or without dialysis). Under such conditions, careful clinical observation and laboratory studies renal function monitoring should be conducted because safe dosage may be lower than that usually recommended.

Dosage reduction may be necessary. Renal and haematological status should be monitored especially during prolonged and high-dose therapy.

***Clostridium difficile* – Associated Diarrhoea**

Clostridium difficile-associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including cephalexin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C.difficile*.

C. difficile produces toxins A and B, which contribute to the development of CDAD. Hypertoxin-producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can

be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Seizure Potential

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures occur, discontinue cephalexin. Anticonvulsant therapy can be given if clinically indicated.

Development of Drug-Resistant Bacteria

Prescribing cephalexin in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Prolonged use of cephalexin 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.

Fructose intolerance

XENARA ORAL SUSPENSION contains sugar (Sucrose). Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take **XENARA ORAL SUSPENSION**.

4.5 Interaction with other medicinal products and other forms of interaction

- The concomitant use of nephrotoxic medicines such as the aminoglycosides gentamicin and tobramycin may increase the risk of kidney damage with **XENARA ORAL SUSPENSION**.
- There is also evidence for enhanced nephrotoxicity with the loop diuretic furosemide.
- The renal excretion of **XENARA ORAL SUSPENSION** is inhibited by probenecid. Co-administration of probenecid with cephalexin is not recommended.
- There may be antagonism between **XENARA ORAL SUSPENSION** and bacteriostatic anti-bacterials.
- Administration of cephalexin with metformin results in increased plasma metformin concentrations and decreased renal clearance of metformin. Careful patient monitoring and dose adjustment of metformin is recommended in patients concomitantly taking cephalexin and metformin.
- **XENARA ORAL SUSPENSION** may decrease the efficacy of oestrogen containing contraceptives.
- Interaction with laboratory or diagnostic testing – A false-positive reaction may occur when testing for the presence of glucose in the urine using Benedict's solution or Fehling's solution.

4.6 Fertility, Pregnancy and Lactation

Pregnancy and lactation:

The safety in pregnancy and lactation has not been established.

XENARA ORAL SUSPENSION is contraindicated during pregnancy (see section 4.3).

Breastfeeding:

Cephalexin is excreted in human milk.

XENARA ORAL SUSPENSION is contraindicated during lactation (see section 4.3).

Effects on fertility:

No human data on the effect of Cephalexin on fertility are available.

Reproduction studies have been performed on mice and rats using oral doses of cephalexin monohydrate 0.6 and 1.5 times the maximum daily human dose (66 mg/kg/day) based upon body surface area basis, and have revealed no evidence of impaired fertility or harm to the foetus.

4.7 Effects on ability to drive and use machines

XENARA ORAL SUSPENSION may cause dizziness or drowsiness. Patients should therefore be advised not to drive or operate machinery until their individual susceptibility is known.

4.8 Undesirable effects

Blood and the lymphatic system disorders:

Frequent: Eosinophilia

Less frequent:, haemolytic anaemia, neutropenia or thrombocytopenia

Immune system disorders:

Less frequent: Hypersensitivity reactions, including skin rashes, urticaria, eosinophilia, fever, allergic reactions, reactions resembling serum sickness-like reactions, and anaphylaxis

Nervous system disorders:

Frequent: Headache

Less frequent: Dizziness and drowsiness. Convulsions and confusion have been associated with high doses, especially in patients *with renal impairment.*

Gastro-intestinal disorders:

Frequent: Nausea, vomiting and diarrhoea

Less frequent: Abdominal cramps. Pseudomembranous colitis and overgrowth of non-susceptible organisms have been reported.

Hepato-biliary disorders:

Less frequent: Hepatitis and cholestatic jaundice

Renal and urinary disorders:

Less frequent: Nephrotoxicity, acute renal tubular necrosis, acute Interstitial nephritis.

Reproductive system and breast disorders:

Less frequent: Vulval candidiasis.

General disorders and administration site conditions:

Less frequent: Fatigue

Investigations:

Less frequent: Positive response to the Coombs' test (antiglobulin), transient increases in liver enzyme values.

Paediatric population

Not specific

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via

The '6.04 Adverse Drug Reactions Reporting Form'. Found under SAHPRA's publications:

https://www/sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms

Symptoms of oral overdose may include nausea, vomiting, epigastric distress, diarrhoea, and haematuria. In the event of an overdose, institute general supportive measures.

Treatment is symptomatic and supportive. Cephalexin is removed by haemodialysis and peritoneal

dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.20.1.1 Broad and medium spectrum antibiotics

Pharmacotherapeutic group: Antibacterial for systemic use

ATC code: J01DB01

Mechanism of action

Cephalexin is a broad spectrum bactericidal antibiotic. It acts by inhibiting bacterial cell-wall synthesis. Cephalexin is active against Gram positive and Gram negative organisms in vitro.

Gram-positive bacteria

Staphylococcus aureus (methicillin-susceptible isolates only) Streptococcus pneumoniae (penicillin-susceptible isolates) Streptococcus pyogenes

Gram-negative bacteria

Escherichia coli

Haemophilus influenzae

Klebsiella pneumoniae

Moraxella catarrhalis

Proteus mirabilis

Resistance

Methicillin-resistant st*aphylococci and* most isolates of enterococci are resistant to cephalexin. Cephalexin is not active against most isolates of *Enterobacter spp., Morganella morganii, and Proteus vulgaris*. Cephalexin has no activity against *Pseudomonas spp., Herellea* species. or *Acinetobacter calcoaceticus*. *Penicillin-resistant Streptococcus pneumonia*e is usually cross-

resistant to *betalactam* antibacterial drugs.

5.2 Pharmacokinetic properties

Absorption

Cephalexin is acid stable and may be given without regard to meals.

It is rapidly absorbed from the upper gastro-intestinal tract, giving peak levels at 1 hour and following food at 2 hours. Following doses of 250 mg and 500 mg in adults average serum levels of about 9 and 18 µg per ml respectively were obtained at one hour.

Distribution:

Cephalexin is approximately 10% to 15% bound to plasma proteins.

Excretion:

Cephalexin is excreted in the urine by glomerular filtration and tubular secretion. Studies showed that over 90% of the drug was excreted unchanged in the urine within 8 hours. During this period, peak urine concentrations following the 250 mg, 500 mg, and 1 g doses were approximately 1000, 2200, and 5000 mcg/mL respectively. In uremic patients the half-life may increase to 5 – 30 hours.

Special Populations

Patients with renal impairment

The elderly and patients with impaired renal function: As for adults. Reduce dosage if renal function is markedly impaired. Renal and haematological status should be monitored especially during prolonged and high-dose therapy.

5.3 Preclinical safety data

Not applicable

Environmental Risk Assessment

Not Applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sucrose USNF (40/80)
- Silicon Dioxide USNF (Syloid AL-1-FP)
- Sodium Benzoate USNF
- Xanthan Gum USNF (Xantural 75)
- Art Cherry Flavour IHS (SD #594)
- FD&C Red No. 40 HIS

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

For Dry powder:

Store between at or below 25 °C (15 °C to 25 °C).

Protect from light.

For Reconstituted suspension:

The reconstituted suspension is stable for 14 days under refrigeration (2 – 8°C)

Discard any unused reconstituted suspension after 14 days. Keep the bottle in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

HDPE Container Pack:

100 mL pack:

XENARA ORAL SUSPENSION is a dry powder filled in heavy weight translucent round 150 ml HDPE container with 28 mm neck finish closed with white polypropylene 28 mm - 400 child resistant closure with universal induction sealing wad.

These Cephalexin for Oral Suspension USP HDPE bottles shall be further packed in pre-printed carton with a packaging leaflet.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

Directions for mixing

Add 67 ml water in two portions to the dry mixture in the bottle.

Shake well after each addition.

7 NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

AUROGEN SA (Pty) Ltd

Woodhill Office Park, Building 1, First Floor

53 Phillip Engelbrecht Avenue

Meyersdal, Ext. 12, 1448

Johannesburg

8 REGISTRATION NUMBER

9 DATE OF FIRST AUTHORISATION

10 DATE OF REVISION OF TEXT