APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

AURO AMOXYCILLIN SUSPENSION 125 mg/5 ml (Powder for Suspension)

AURO AMOXYCILLIN SUSPENSION 250 mg/5 ml (Powder for Suspension)

COMPOSITION:

AURO AMOXYCILLIN SUSPENSION 125 mg/5 ml:

Each 5 ml of reconstituted suspension contains Amoxicillin Trihydrate equivalent to Amoxicillin 125 mg.

AURO AMOXYCILLIN SUSPENSION 250 mg/5 ml:

Each 5 ml of reconstituted suspension contains Amoxicillin Trihydrate equivalent to Amoxicillin 250 mg.

Sugar Free.

Preservative: Sodium benzoate…….0.07 % m/v

AURO AMOXYCILLIN SUSPENSION contains the following excipients: saccharin sodium, sodium benzoate, disodium edetate, xanthan gum, silica, colloidal anhydrous, sorbitol, citron, strawberry guarana flavour, silicon dioxide.

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.2 Penicillins

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Amoxicillin is a semisynthetic penicillinase-susceptible penicillin of the beta-lactam group of antibiotics. It has a broad spectrum of antibacterial activity against non-penicillinase producing Gram positive, and Gram negative microorganisms, acting through the inhibition of biosynthesis of cell wall mucopeptide. The spectrum of activity does not include those organisms that produce beta-lactamases, namely resistant staphylococci, and all strains of *Pseudomonas, Klebsiella* and *Enterobacter.*

Strains of the following organisms are generally sensitive to the bactericidal action of amoxicillin *in vitro*:

Gram-positive bacteria: *Staphylococcus aureus* (penicillin-sensitive)*, *Streptococcus pyogenes, Streptococcus viridans*, Streptococcus faecalis*, Streptococcus pneumoniae*, Corynebacterium* species*, *Clostridium* species*, *Bacillus anthracis*, Listeria monocytogenes.*

Gram-negative bacteria: *Neisseria gonorrhoeae*, Neisseria meningitides, Haemophilus influenza***, *Bordetella pertussis, Escherichia coli*, Salmonella* species*, Shigella* species*, Proteus mirabilis, Pasteurella multocida, Helicobacter pylori, Leptospira* spp.*, Fusobacterium* spp.

Other: *Borrelia burgdorferi*

*Sensitivity tests must be performed

**except type b strains causing meningitis in children

<u>Pharmacokinetic properties</u>:

Absorption:

Amoxicillin is rapidly absorbed from the gut to an extent of 72-93 %.

Food does not interfere with the absorption of amoxicillin.

Distribution:

Approximately 18 % of the total plasma amoxicillin content is protein bound. Amoxicillin diffuses readily into most body tissues with the exception of the brain and spinal fluid. Inflammation generally increases the permeability of the meninges to penicillins and this may apply to amoxicillin.

Excretion:

The elimination half-life is approximately 1 hour. Amoxicillin is primarily excreted via the kidneys.

Small amounts of the drug are also excreted in the faeces and bile.

Amoxicillin crosses the placenta and is distributed into breast milk.

INDICATIONS:

AURO AMOXYCILLIN SUSPENSION is indicated for the treatment of mild to moderately severe infections at the following sites, when caused by sensitive organisms (refer to **"PHARMACOLOGICAL ACTION"**):

- Upper Respiratory tract infections such as sinusitis, otitis media, tonsillitis
- Lower respiratory tract infections such as acute exacerbations of chronic bronchitis, lobar and bronchopneumonia
- Gastro-intestinal infections such as typhoid fever
- Genitourinary infections such as cystitis, pyelonephritis, bacteriuria in pregnancy, uncomplicated gonococcal infections.
- Other infections including Borreliosis (Lyme disease)
- As part of combination therapy in established *Helicobacter pylori* infection, associated with duodenal ulceration.
- Prophylaxis of endocarditis

CONTRA-INDICATIONS:

Hypersensitivity to penicillins or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

WARNINGS AND SPECIAL PRECAUTIONS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with **AURO AMOXYCILLIN SUSPENSION**, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity, who have experienced severe reactions when treated with cephalosporins.

If an allergic reaction occurs, **AURO AMOXYCILLIN SUSPENSION** should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation may also be required.

AURO AMOXYCILLIN SUSPENSION should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of

amoxicillin.

Prolonged use may result in overgrowth of non-susceptible organisms. Pseudomembranous enterocolitis has been reported.

Prolongation of prothrombin time has been reported rarely in patients receiving **AURO AMOXYCILLIN SUSPENSION**. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Periodic assessment of organ function, including renal, hepatic and hematopoietic functions, is advisable during prolonged therapy.

Transient hepatitis and cholestatic jaundice has been reported. **AURO AMOXYCILLIN SUSPENSION** should be used with caution in patients with evidence of hepatic dysfunction.

Caution is needed when administering amoxicillin to patients with syphilis, as the Jarisch-Herxheimer reaction may occur in these patients.

When high doses are administered, adequate fluid intake and urinary output must be maintained.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic **function,** is advisable during prolonged therapy. Since **AURO AMOXYCILLIN SUSPENSION contains** amoxicillin, an aminopenicillin, it is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infectious mononucleosis, in the presence of which there is a high incidence of rash if amoxicillin is used. **AURO AMOXYCILLIN SUSPENSION** should be given with caution to patients with lymphatic leukemia since they are especially susceptible to amoxicillin induced skin rashes.

The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur, the agent should be discontinued and/or appropriate therapy instituted.

Impaired hepatic function:

Changes in liver function tests have been observed in some patients receiving **AURO AMOXYCILLIN SUSPENSION.** It should be used with care in patients with evidence of severe hepatic dysfunction. The events may be severe, and occur predominantly in adult or elderly patients. Signs and symptoms usually occur during or shortly after treatment, but in some cases may not become apparent until several weeks after treatment has ceased. The hepatic effects are usually reversible. However, in

extremely rare circumstances, death has been reported. These have almost always been cases associated with serious underlying disease or concomitant medication.

Impaired renal function:

In patients with moderate or severe renal impairment **AURO AMOXYCILLIN SUSPENSION** dosage should be adjusted. (See **"DOSAGE AND DIRECTIONS FOR USE")**

The use of **AURO AMOXYCILLIN SUSPENSION** may lead to the selection of resistant strains of organisms and sensitivity testing should, therefore, be carried out whenever possible, to demonstrate the appropriateness of therapy.

AURO AMOXYCILLIN SUSPENSION may cause gastro-intestinal reactions. This may be reduced by taking **AURO AMOXYCILLIN SUSPENSION** at the start of a meal.

Superficial tooth discolouration has been reported especially with the suspension and chewable tablet formulations. It can usually be removed by brushing.

The safety of **AURO AMOXYCILLIN SUSPENSION** in pregnancy has not been established.

Amoxicillin is excreted in the milk. Mothers on **AURO AMOXYCILLIN SUSPENSION** should not breastfeed their infants.

Treatment with **AURO AMOXYCILLIN SUSPENSION** is not known to affect your ability to drive and use machines.

INTERACTIONS:

AURO AMOXYCILLIN SUSPENSION may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

The concomitant administration of allopurinol and ampicillin substantially increases the incidence of skin rashes in patients receiving both agents as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricaemia present in these patients.

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of **AURO AMOXYCILLIN SUSPENSION**.

Interaction with Laboratory tests:

It is recommended that when testing for the presence of glucose in urine during **AURO AMOXYCILLIN SUSPENSION** treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of **AURO AMOXYCILLIN SUSPENSION**, false positive readings are common with chemical methods.

PREGNANCY AND LACTATION:

Use in pregnancy:

The safety of **AURO AMOXYCILLIN SUSPENSION** in pregnancy has not been established.

Reproduction studies have been performed in mice and rats at doses up to ten times the human dose and these studies have revealed no evidence of impaired fertility or harm to the foetus due to amoxicillin. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment

Use in lactation:

AURO AMOXYCILLIN SUSPENSION is distributed into breast milk. The use of **AURO AMOXYCILLIN SUSPENSION** by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant. Mothers on **AURO AMOXYCILLIN SUSPENSION** should not breastfeed their infants.

DOSAGE AND DIRECTIONS FOR USE:

The total daily dose as below is administered in divided doses. The most common regimen is 8 hourly.

ORAL ADMINISTRATION

Treatment should be continued for 48 to 72 hours beyond the time that a clinical response has been obtained.

It is recommended that at least 10 days treatment be given for any infection caused by beta-haemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.

The absorption of **AURO AMOXYCILLIN SUSPENSION** is not affected significantly when taken with food.

<u>Adults and children over 40 kg</u>

Total daily dosage of 750 mg to 3 g administered in divided doses. Maximum recommended dose: 6

g/day in divided doses.

Respiratory tract infections: 500 mg administered 8 hourly.

Lyme disease: 4 g/day in isolated erythema chronicum migrans and 6 g/day in the case of generalised manifestations, both for a minimum of 12 days.

Eradication of Helicobacter pylori: 750 mg - 1 g in combination treatment given 12 hourly for the eradication of established H pylori infection associated with duodenal ulceration for seven days.

Children under 40 kg:

20 - 50 mg/kg/day in divided doses.

Maximum recommended dose: 150 mg/kg/day in divided doses.

Lyme disease: 25 - 50 mg/kg/day in isolated erythema chronicum migrans and 100 mg/kg/day in the case of generalised manifestations, both for a minimum of 12 days.

Usual total daily dosages of paediatric suspension given in divided doses, except for lower respiratory tract infections are:

< 6 kg = 150 mg

6 - 8 kg = 600 mg

For lower respiratory tract infections

< 6 kg = 300 mg

6 - 8 kg = 600 mg

Elderly

No adjustment needed: as for adults unless there is evidence of severe renal impairment (see below).

Renal impairment

Glomerular filtration rate > 30 ml/min: No adjustment needed.

Glomerular filtration rate 10 - 30 ml/min: Maximum 500 mg 12 hourly.

Glomerular filtration rate < 10 ml/min: Maximum 500 mg daily.

In patients receiving peritoneal dialysis: Maximum 500 mg daily

PROPHYLAXIS OF ENDOCARDITIS

Prophylaxis with alternative antibiotics should be considered if the patient has received a penicillin

within the previous month or is allergic to penicillin.

1. For dental, oral or upper respiratory tract procedures:

Prophylaxis for patients undergoing dental extraction, scaling or surgery involving gingival tissues, tonsillectomy, adenoidectomy, bronchoscopy with a rigid bronchoscope and surgical procedures that involve respiratory mucosa.

For patients NOT having a general anaesthetic:

Adults: 2 g orally, 1 hour before the procedure

Children: 50 mg/kg, 1 hour before the procedure

Children's dose not to exceed the adult dose.

RECONSTITUTION INSTRUCTIONS:

AURO AMOXYCILLIN SUSPENSION 125 mg/5 ml:

For reconstitution to 100 ml, add 91 ml water, invert the bottle and shake well until all the powder is dispersed.

AURO AMOXYCILLIN SUSPENSION 250 mg/5 ml:

For reconstitution to 100 ml, add 90 ml water, invert the bottle and shake well until all the powder is dispersed.

SIDE-EFFECTS:

The following adverse reactions have been reported and may occur with **AURO AMOXYCILLIN SUSPENSION.**

Blood and the lymphatic system disorders:

Less Frequent: Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leucopenia and agranulocytosis. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.

Immune system disorders:

Less Frequent: Skin rashes, pruritus and urticaria, serum sickness-syndrome, erythema multiforme, rare cases of Stevens-Johnson syndrome, hypersensitivity vasculitis and less frequently bullous

exfoliative dermatitis and toxic epidermal necrolysis

Nervous System Disorders:

Frequent: Headache

Less frequent: CNS effects have been seen rarely. These include reversible hyperactivity, dizziness and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.

Vascular Disorders

Less frequent: Hot flushes

Gastrointestinal disorders:

Frequent: Nausea, vomiting, diarrhoea

Less frequent: gastritis, stomatitis, glossitis, black 'hairy' tongue, enterocolitis, mucocutaneous candidiasis and antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis). Indigestion, abdominal pain, abnormal taste, superficial tooth discolouration.

Hepato-biliary disorders:

Less frequent: Hepatitis and cholestatic jaundice.

Renal and Urinary Disorders

Less frequent: Interstitial nephritis, crystalluria

Reproductive system and Breast Disorders

Less frequent: Vaginitis

Investigations:

A moderate raise in Aspartate transaminase (AST) and/or Alanine transaminase (ALT) has been noted in patients treated with **AURO AMOXYCILLIN SUSPENSION**, but the significance of these findings is unknown.

General Disorders

Less frequent: Tiredness

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Overdosage with **AURO AMOXYCILLIN SUSPENSION** is usually asymptomatic. However, gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and symptoms of water and electrolyte imbalance should be treated symptomatically.

Adequate fluid intake and urinary output must be maintained to minimize the possibility of crystalluria.

AURO AMOXYCILLIN SUSPENSION may be removed from the circulation by haemodialysis.

IDENTIFICATION:

AURO AMOXYCILLIN SUSPENSION 125 mg/5 ml:

For Dry Powder: White to off white granular powder.

For Reconstituted Suspension: White to off white suspension with citrus flavour.

AURO AMOXYCILLIN SUSPENSION 250 mg/5 ml:

For Dry Powder: White to off white granular powder.

For Reconstituted Suspension: White to off white suspension with citrus flavour.

PRESENTATION:

AURO AMOXYCILLIN SUSPENSION 125 mg/5 ml:

The granular powders are packed in a 150 ml plastic translucent, round bottle with a 28 mm white propylene neck closed with a 28 mm screw cap with induction sealing wad.

(100 ml of suspension after reconstitution).

Pack size: One 150 ml plastic translucent, round bottle closed with a white propylene screw cap with an induction sealing wad, packed in a printed carton with a package insert.

AURO AMOXYCILLIN SUSPENSION 250 mg/5 ml:

The granular powders are packed in a 150 ml plastic translucent, round bottle with a 28 mm white propylene neck closed with a 28 mm screw cap with induction sealing wad.

(100 ml of suspension after reconstitution).

Pack size: One 150 ml plastic translucent, round bottle closed with a white propylene screw cap with

an induction sealing wad, packed in a printed carton with a package insert.

STORAGE CONDITIONS:

Store at or below 30 °C.

Storage for Reconstituted Suspension:

Once reconstituted, the suspension should be kept in a refrigerator

(2 to 8 °C) and used within 14 days. Shake well before use.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:

AURO AMOXYCILLIN SUSPENSION 125 mg/5 ml: 42/20.1.1/0337

AURO AMOXYCILLIN SUSPENSION 250 mg/5 ml: 42/20.1.1/0338

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

Aurogen South Africa (Pty) Ltd

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