Approved Professional Information for Medicines for Human Use: Amyn S 125, Amyn SF 250

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

AMYN S 125 powder for suspension

AMYN SF 250 powder for suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

AMYN S 125: Each 5 mL suspension contains amoxicillin trihydrate equivalent to 125 mg amoxicillin and 4 mg sodium benzoate as preservative (0,08 % m/v).

Contains sugar (sucrose: 1796,26 mg per 5 mL).

AMYN SF 250: Each 5 mL suspension contains amoxicillin trihydrate equivalent to 250 mg amoxicillin and 4 mg sodium benzoate as preservative (0,08 % m/v).

Contains sugar (sucrose: 1784,35 mg per 5 mL).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for suspension.

AMYN S 125 - Off white free flowing powder without any visible foreign particles which on reconstitution gives white to off white flavoured suspension.

AMYN SF 250 - Off white free flowing powder without any visible foreign particles which on reconstitution gives white to off white flavoured suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AMYN S 125 and AMYN SF 250 formulations are indicated for the treatment of mild to moderately severe infections caused by susceptible organisms:

- upper respiratory tract infections such as sinusitis, otitis media, tonsillitis
- lower respiratory tract infections such as bronchitis, lobar and bronchopneumonia
- gastro-intestinal tract infections such as typhoid fever
- other infections including Borreliosis (Lyme disease)
- in the following infections, amoxicillin therapy should be initiated only if there is microbiological evidence that the causative organism Is sensitive to amoxicillin:

  Skin and soft tissue infections

  Urinary tract infections: cystitis, urethritis, pyelonephritis, bacteriuria in pregnancy.
- as part of combination therapy in established *Helicobacter pylori* infection, associated with duodenal ulceration
- prophylaxis of endocarditis.

4.2 Posology and method of administration

Posology

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

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 AMYN S 125 or AMYN SF 250 is not affected significantly when taken with food.

Adults and children over 40 kg:

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.

Gonorrhoea: 3 g with 1 g probenecid.

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.

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.

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.

Special populations

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 every 12 hours.

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

In patients receiving peritoneal dialysis: Maximum 500 mg daily.

Paediatric population

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

Method of administration

AMYN S 125 and AMYN SF 250 are for oral use.

4.3 Contraindications

- Hypersensitivity to amoxicillin or to any of the excipients listed in section 6.1.

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

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Before initiating therapy with amoxicillin, such as in AMYN S 125 and AMYN SF 250, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam medicines (see section 4.3 and 4.8). Serious and fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. 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 in atopic individuals. 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, AMYN S 125 or AMYN SF 250 therapy must be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation, may also be required.

Non-susceptible microorganism

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin (see section 5.1). This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat. Sensitivity testing should, therefore, be carried out whenever possible, to demonstrate the appropriateness of therapy.

Convulsions

Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. history of seizures, treated epilepsy or meningeal disorders (see section 4.8).

Renal impairment

In patients with renal impairment the dose should be adjusted accordingly to the degree of impairment (see section 4.2).

Skin reactions

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AEGP, see section 4.8). This reaction requires amoxicillin discontinuation and contraindicates any subsequent administration.

Amoxicillin, such as in AMYN S 125 and AMYN SF 250 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.AMYN S 125 or AMYN SF 250 should be given with caution to patients with lymphatic leukaemia since they are especially susceptible to amoxicillin induced skin rashes.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease (see section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms

Prolonged use may also occasionally result in overgrowth of non-susceptible organisms. Antibiotic-associated colitis has been reported with nearly all antibacterial medicines and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, AMYN S 125 or AMYN SF 250 should immediately be discontinued, a doctor consulted, and appropriate therapy initiated. Anti-peristaltic medicines are contraindicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported (see section 4.8).

Anticoagulants

Prolongation of prothrombin time has been reported in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section 4.5 and 4.8).

Crystalluria

In patients with reduced urine output, crystalluria has been observed, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.8 and 4.9).

Interference with diagnostic tests

Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used.

The presence of amoxicillin may distort assay results for estriol in pregnant women.

Impaired hepatic function

Transient hepatitis and cholestatic jaundice has been reported. AMYN S 125 or AMYN SF 250 should be used with caution in patients with evidence of hepatic dysfunction.

Changes in liver function tests have been observed in some patients receiving AMYN S 125 or AMYN SF 250. It should be used with care in patients with evidence of severe hepatic dysfunction.

Important Information about excipients

AMYN S 125 and AMYN SF 250 contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take AMYN S 125 or AMYN SF 250.

AMYN S 125 and AMYN SF 250 contain sodium benzoate (E211). Increase in bilirubinaemia following its displacement from albumin may increase neonatal jaundice which may develop into kernicterus (non-conjugated bilirubin deposits in the brain tissue.

The sodium content must be taken into account in patients on a sodium-restricted diet if the administration of high doses is necessary.

4.5 Interaction with other medicines and other forms of interaction

Probenecid

Probenecid decreases the renal tubular secretion of AMYN S 125 or AMYN SF 250. Concurrent use of probenecid with AMYN S 125 or AMYN SF 250 may result in increased and prolonged blood concentrations of AMYN S 125 and AMYN SF 250.

Allopurinol

The concomitant administration of allopurinol and ampicillin substantially increases the incidence of skin rashes in patients receiving both medicines 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.

Oral contraceptives

AMYN S 125 or AMYN SF 250 may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Tetracyclines

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of AMYN S 125 or AMYN SF 250.

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Oral typhoid vaccine

The oral typhoid vaccine is inactivated by antibacterials.

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Interaction with laboratory tests

It is recommended that when testing for the presence of glucose in urine during AMYN S 125 or AMYN SF 250 treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of AMYN S 125 or AMYN SF 250, false positive readings are common with chemical methods

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of AMYN S 125 or AMYN SF 250 in pregnancy has not been established.

Breastfeeding

AMYN S 125 and AMYN SF 250 are distributed into breast milk. Although significant problems in humans have not been documented, the use of AMYN S 125 or AMYN SF 250 by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant.

Fertility

There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals have shown no teratogenic effects on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive or use machines (see section 4.8).

4.8 Undesirable effects

Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarketing spontaneous reports with amoxicillin.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations		Mucocutaneous candidiasis	
Blood and lymphatic system disorders		Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leucopenia (including severe neutropenia and	

		agranulocytosis) (see section 4.4). Prolongation of bleeding time and prothrombin time.	
Immune system disorders		Severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4).	Jarisch-Herxheimer reaction (see section 4.4).
Nervous system disorders	Headache	Reversible hyperactivity, hyperkinesia, dizziness, and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses (see section 4.4).	

Vascular disorders		Hot flushes
Gastrointestinal disorders	Diarrhoea, nausea, vomiting	Gastritis, stomatitis, glossitis, black ‘hairy’ tongue, enterocolitis, antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) (see section 4.4), indigestion, abdominal pain, abnormal taste, superficial tooth discolouration#.
Hepatobiliary disorders		Hepatitis, cholestatic jaundice.
Skin and subcutaneous tissue disorders	Skin rash	Pruritus, urticaria, serum sickness syndrome, erythema multiforme, bullous exfoliative

	dermatitis and toxic epidermal necrolysis, Stevens-Johnson syndrome, acute generalised exanthematous pustulosis (AGEP) (see section 4.4) and drug reaction with eosinophilia and systemic symptoms (DRESS).
Renal and urinary disorders	Crystalluria (see section 4.4 and 4.9 Overdose), interstitial nephritis
Reproductive system and breast disorders	Vaginitis
General disorders and administration site conditions	Tiredness

Investigations	A moderate rise in aspartate transaminase (AST) and/or alanine tranferase (ALT) has been noted in patients treated with AMYN, but the significance of these findings is unknown.

#Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

Description of selected adverse events

Skin and subcutaneous disorders

Whenever such skin and subcutaneous tissue disorders occur, AMYN S 125 or AMYN SF 250 should be discontinued. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see section 4.4).

Gastrointestinal disorders

If gastrointestinal disorders are evident, they may be reduced by taking AMYN S 125 or AMYN SF 250 at the start of a meal.

Hepatobiliary disorders

The hepatobiliary disorders 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 some circumstances, death has been reported. These have almost always been cases associated with serious underlying disease or concomitant medication.**

Haematological effects

Haematological effects are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1 % of patients treated with, AMYN S 125 or AMYN SF 250. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

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 Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Signs and symptoms

Overdosage with AMYN S 125 or AMYN SF 250 is usually asymptomatic. However, gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident.

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses (see sections 4.4 and 4.8).

Treatment

Symptoms of water and electrolyte imbalance should be treated symptomatically. Adequate fluid intake and urinary output must be maintained to minimise the possibility of crystalluria. AMYN S 125 or AMYN SF 250 may be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 20.1.2 Penicillins

Pharmacotherapeutic group: penicillins with extended spectrum

ATC Code: J01CA04.

Mechanism of action

Amoxicillin is a semi-synthetic beta-lactamase-susceptible penicillin, which has *in vitro* bactericidal activity against broad spectrum of non beta-lactamase-producing Gram-positive and Gram-negative organisms. The spectrum of activity does not include those organisms that

produce beta lactamases, namely resistant staphylococci, and all strains of *Pseudomonas, Klebsiella* and *Enterobacter.*

5.2 Pharmacokinetic properties

Absorption

Amoxicillin is stable in the presence of acidic gastric secretions. Peak blood levels are achieved 1-2 hours after administration. There is a linear dose response in peak serum levels. 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.

Elimination

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Sodium benzoate

Sodium citrate

Carboxy methyl cellulose sodium

Citric acid monohydrate

Colloidal silicon dioxide

Essence Pineapple DC 106

Essence DC Casparoma Vanilla 110

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Dry powder for suspension: 3 years.

Reconstituted suspension: use within 14 days if stored in a refrigerator (2 to 8 °C) or within 7 days if stored at or below 25 °C.

6.4 Special precautions for storage

Dry powder for suspension: Store tightly closed in a dry place at or below 25 °C and protect from light.

Reconstituted suspension: The reconstituted suspension must be used within 14 days if stored in a refrigerator (2 to 8 °C) or within 7 days if stored at or below 25 °C. Shake the suspension before use.

6.5 Nature and contents of container

AMYN S 125:

White coloured, round HDPE translucent 100 mL bottle containing powder for reconstitution to 75 mL or 100 mL of AMYN S 125 mg / 5 mL suspension. The HDPE bottle is fitted with a plain white aluminium or polypropylene cap.

AMYN SF 250:

White coloured, round HDPE translucent 100 mL bottle containing powder for reconstitution to 100 mL of AMYN SF 250mg / 5 mL suspension. The HDPE bottle is fitted with a plain white aluminium or polypropylene cap.

6.6 Special precautions for disposal and other handling

RECONSTITUTION INSTRUCTIONS:

AMYN S 125: To reconstitute the pack size of 75 mL suspension, add 56 mL distilled water or previously boiled and cooled water; and for the 100 mL suspension, add 74 mL distilled water or previously boiled and cooled water. Invert the bottle and shake until all the powder is dispersed.

AMYN SF 250: To reconstitute the pack size of 100 mL suspension, add 71 mL distilled water or previously boiled and cooled water. Invert the bottle and shake until all the powder is dispersed.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Shanur Healthcare (Pty) Ltd.,

Loch House Unit 003,

3A Eton Road,

Parktown,

Johannesburg 2193

8. REGISTRATION NUMBER(S)

AMYN S 125: 41/20.1.2/0261

AMYN SF 250: A40/20.1.2/0563

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

AMYN S 125: 10 August 2007

AMYN SF 250: 6 October 2006

10. DATE OF REVISION OF THE TEXT

5 December 2022