SCHEDULING STATUS: S4

1 NAME OF THE MEDICINE

AMOXICILLIN 125 mg/5 ml SUSPENSION UNIMED

AMOXICILLIN 250 mg/5 ml SUSPENSION UNIMED

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Amoxicillin 125 mg/5 ml Suspension Unimed

Each 5 ml contains:

Amoxicillin trihydrate equivalent to amoxicillin anhydrous	125 mg
Contains sugar: Sorbitol	730 mg
Contains sweetener: Saccharin sodium	9 mg

Amoxicillin 250 mg/5 ml Suspension Unimed

Each 5 ml contains:

Amoxicillin trihydrate equivalent to amoxicillin anhydrous	250 mg
Contains sugar: Sorbitol	580 mg
Contains sweetener: Saccharin sodium	9 mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for Suspension

AMOXICILLIN 125 MG/5 ML SUSPENSION UNIMED

White to off-white powder forming an orange suspension on reconstitution with water.

The resulting suspension has a characteristic flavour.

AMOXICILLIN 250 MG/5 ML SUSPENSION UNIMED

White to off-white powder forming an orange suspension on reconstitution with water.

The resulting suspension has a characteristic flavour.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

AMOXICILLIN SUSPENSION UNIMED is indicated in the treatment of infections due to susceptible non-penicillinase producing strains of the following:

- Infections of the ear, nose and throat due to streptococci, pneumococci, nonpenicillinase-producing staphylococci and *H. influenzae*.
- Infections of the genitourinary tract due to *E. coli, Proteus mirabilis* and *Streptococcus faecalis*.
- Infections of the skin and soft-tissues due to streptococci, susceptible staphylococci and *E. coli*.
- Infections of the lower respiratory tract due to streptococci, pneumococci, non-penicillinase producing staphylococci and *H. influenzae*.
- Gonorrhea, acute uncomplicated ano-genital and urethral infections due to *N. gonorrhoea* (males and females).

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Posology

Paediatric dose:

Infants up to 6 kg body weight:	25-50 mg every eight hours.
Infants 6 to 8 kg body weight:	50-100 mg every eight hours.
Infants and children 8-20 kg body weight:	6,7-13,3 mg per kg body weight every eight hours.
Children 20 kg of body weight and over:	250-500 mg every eight hours.

Adults who are not able to take capsules may be given AMOXICILLIN SUSPENSION UNIMED.

Usual Adult dose: 250-500 mg every eight hours.

Maximum dose up to 4,5 g a day.

Method of administration

AMOXICILLIN SUSPENSION UNIMED is for oral use.

For instructions on reconstitution of the medicine before administration, see section 6.6.

4.3 CONTRAINDICATIONS:

Hypersensitivity to amoxicillin, to any of the penicillins or to any of the other excipients (see section 6.1)

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).
Patients with infectious mononucleosis since they are especially susceptible to amoxycillin-induced skin rashes.
It is contra-indicated in babies born to mothers hypersensitive to amoxicillin or any other penicillins, and in the neonatal period.
Patients with lymphatic leukemia and patients with hyperuricaemia being treated with allopurinol may also be at an increased risk of developing skin rashes.

4.4 SPECIAL WARNINGS and SPECIAL PRECAUTIONS FOR USE:

Life support, epinephrine (adrenaline), corticosteroids and
antihistamines should be used to treat anaphylaxis.

Hypersensitivity reactions

Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens beta-lactam medicines (see sections 4.3 and 4.8). Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If any allergic reaction occurs, appropriate therapy should be instituted and AMOXICILLIN SUSPENSION UNIMED therapy must be discontinued.

Non-susceptible microorganisms

Amoxicillin Suspension Unimed 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 A**moxicillin Suspension Unimed** (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.

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 according to the degree of impairment. Care should be taken when high doses are given to patients with renal impairment (because of the risk of neurotoxicity) or congestive heart failure.

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 (AGEP, see section 4.8). This reaction requires AMOXICILLIN SUSPENSION UNIMED discontinuation and contraindicates any subsequent administration. AMOXICILLIN SUSPENSION UNIMED 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. Patients with lymphatic leukaemia or possibly HIV infection may also be at increased risk of developing skin rashes.

Overgrowth of non-susceptible microorganisms

Pseudomembranous colitis has been reported.

The possibility of superinfections with mycotic or bacterial pathogens should be kept in

mind during therapy. It is important to consider this diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. If superinfections occur (usually involving *Enterobacter, Pseudomonas* or *Candida*), AMOXICILLIN SUSPENSION UNIMED should be discontinued and/or appropriate therapy instituted. Antiperistaltic medicines are contraindicated in this situation.

Jarisch-Herxheimer reaction

Care should be taken when treating patients with syphilis, as the Jarisch-Herxheimer reaction may occur shortly after starting treatment. This reaction, manifesting as fever, chills, headache and reactions at the site of the lesion, can be dangerous in cardiovascular syphilis or where there is a serious risk of increased local damage such as with optic atrophy.

The Jarisch-Herxheimer reaction has been reported 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.

Prolonged therapy

Periodic assessment of renal, hepatic and hematopoetic function should be made during prolonged therapy with AMOXICILLIN SUSPENSION UNIMED. Elevated liver enzymes and changes in blood count have been reported (see section 4.8)

Crystalluria

Caution must be exercised when treating patients with dehydration or oliguria because of the possibility of crystalluria.

During the administration of high doses of AMOXICILLIN SUSPENSION UNIMED, 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).

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).

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 SUSPENSION UNIMED treatment, enzymatic glucose oxidase methods should be used.

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

AMOXICILLIN SUSPENSION UNIMED contains sorbitol

Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION:

Probenecid

Probenecid can delay the excretion of AMOXICILLIN SUSPENSION UNIMED when given concurrently. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol

Concomitant use of allopurinol during treatment with AMOXICILLIN SUSPENSION UNIMED can increase the likelihood of allergic skin reactions.

Tetracyclines

Tetracyclines and other bacteriostatic medicines may interfere with the bactericidal effects of AMOXICILLIN SUSPENSION UNIMED.

Oral anticoagulants

There is a possibility of a prolonged bleeding time (increase in INR) after oral treatment with Amoxicillin Suspension Unimed in patients receiving anticoagulants such as warfarin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of AMOXICILLIN SUSPENSION UNIMED.
Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

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

Oral contraceptives

AMOXICILLIN SUSPENSION UNIMED may decrease the efficacy of oral contraceptives and may cause increased breakthrough bleeding.

Diagnostic tests

AMOXICILLIN SUSPENSION UNIMED may interfere with some diagnostics tests such as for urinary glucose using copper sulphate, direct antiglobulin (Coomb') tests for urinary or serum proteins. AMOXICILLIN SUSPENSION UNIMED may interfere with tests that use bacteria, for example the Guthrie test for phenylketonuria using *Bacillus subtilis* organisms.

Amoxicillin Suspension Unimed may affect the absorption of other medicines due to its effect on the gastro-intestinal flora.

4.6 FERTILITY, PREGNANCY AND LACTATION:

Animal reproduction studies have failed to demonstrate a risk to the foetus and there are no adequate and well controlled studies in pregnant women.

Breastfeeding

Amoxicillin is excreted into breast milk in small quantities with the possible risk of sensitisation. Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breastfed infant, so that breastfeeding might have to be discontinued.

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:

AMOXICILLIN SUSPENSION UNIMED may cause dizziness or confusion. Caution is advised for patients to not drive or use machines, until their individual susceptibility to the effects of AMOXICILLIN SUSPENSION UNIMED is known.

4.8 UNDESIRABLE EFFECTS:

a. Summary of the safety profile

The most commonly reported adverse reactions (ADRs) are diarrhoea, nausea and skin rash.

b) Tabulated summary of adverse reactions

The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below.

MedDRA system organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Less frequent	Mucocutaneous candidiasis

Blood and lymphatic system disorders	Less frequent	Reversible leukopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia, thrombocytopenic purpura, eosinophilia and granulocytopenia, prolongation of bleeding time and prothrombin time (see section 4.4).
Immune system disorders	Less frequent	Severe allergic reactions, including angioedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4).
	Frequency unknown	Jarisch-Herxheimer reaction (see section 4.4)

Nervous system disorders	Less frequent	Reversible hyperactivity, agitation, anxiety, insomnia, confusion, behavioural changes, dizziness, convulsions (see section 4.4)
Vascular disorders	Less frequent	Vasculitis
Gastrointestinal disorders	Frequent	Nausea, heartburn and diarrhoea.
	Less frequent	Vomiting, antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis (see section 4.4). A sore mouth or tongue and a black hairy tongue
Hepato-biliary disorders	Less frequent	Hepatitis and cholestatic jaundice, a moderate rise in AST and/or ALT
Skin and subcutaneous tissue disorders	Frequent	Skin rash

	Less frequent	Urticaria, pruritus, erythematous maculopapular rashes such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) (see section 4.4), drug reaction with eosinophilia and systemic symptoms (DRESS)
	Frequency unknown	Linear IgA disease
Renal and urinary disorders	Less frequent	Nephropathy and interstitial nephritis, crystalluria (see sections 4.4 and 4.9)
Cardiac disorders	Frequency unknown	Kounis syndrome (see section 4.4)

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 OVERDOSE

Symptoms

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balances 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

Treatment is symptomatic and supportive. The water/electrolyte balance should be monitored.

In the event of overdosage, AMOXICILLIN SUSPENSION UNIMED can be removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

Pharmacological classification: A 20.1.2 Penicillins

Pharmacotherapeutic group: penicillins with extended spectrum

ATC code: J01CA04

5.1 Pharmacodynamic properties:

Amoxicillin trihydrate is a semisynthetic penicillinase susceptible penicillin, an analogue

of ampicillin, with a broad spectrum of *in-vitro* bactericidal activity against many Gram-positive and Gram-negative micro-organisms.
In vitro sensitivity does not necessarily imply *in-vivo* efficacy.
Resistant strains: *Enterobacter, Pseudomonas, Klebsiella, Serratia, Acinetobacter* and indole-positive *Proteus*.

5.2 Pharmacokinetic properties:

Absorption

Amoxicillin is resistant to inactivation by gastric acid and may be given without regard to meals. It is well absorbed after oral administration. Orally administered doses of 250 mg and 500 mg amoxicillin result in average peak blood levels one to two hours after administration in the range of 3,5 µg/ml to 5,0 µg/ml and 5,5 µg/ml to 7,5 µg/ml respectively.

Detectable serum levels are observed up to 8 hours after an orally administered dose of amoxicillin.

Distribution

Amoxicillin is not highly protein-bound. It diffuses readily into most body tissues and fluids, with the exception of brain and spinal fluid, except when meninges are inflamed.

Elimination

The half-life of amoxicillin is 1 to 1,5 hours. Approximately 60 percent of an orally administered dose is excreted unchanged in the urine within six to eight hours by glomerular filtration and tubular secretion. Amoxicillin is removed by haemodialysis. High concentrations have been reported in bile; some may be excreted in faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica, sodium citrate, xanthan gum, sorbitol, saccharin sodium,

sunset yellow supra, tutti frutti flavour.

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

Dry powder: 2 years

Reconstituted suspension: 14 days when stored in a refrigerator (2 - 8°C)

6.4 Special precautions for storage

Store at or below 25 °C, protect from moisture.

After reconstitution the product must be stored at 2 – 8 °C in a refrigerator.

The prepared suspension should be consumed within 14 days of preparation.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Amoxicillin 125 mg/5 ml Suspension Unimed

White, translucent HDPE bottle for 100 ml pack

White, translucent HDPE bottle for 75 ml pack

Amoxicillin 250 mg/5 ml Suspension Unimed

White, translucent HDPE bottle for 100 ml pack

6.6 Special Precautions for disposal

No special requirements.

STORAGE INSTRUCTIONS:

Store at or below 25 °C, protect from moisture.

After reconstitution the product must be stored at 2 – 8 °C in a refrigerator.

The prepared suspension should be consumed within 14 days of preparation.

KEEP OUT OF REACH OF CHILDREN.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

UNIMED HEALTHCARE (PTY) LTD

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Anchorville,

Lenasia, 1827
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8. REGISTRATION NUMBERS:

Amoxicillin 125 mg/5 ml Suspension Unimed: 35/20.1.2/0212

Amoxicillin 250 mg/5 ml Suspension Unimed: 35/20.1.2/0213

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

First Authorisation: 06 June 2003

10. DATE OF REVISION OF THE TEXT:

31 March 2025