SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ADCO-AMOXYCILLIN 125 mg/5 ml (SUSPENSION)

ADCO-AMOXYCILLIN 250 mg/5 ml (SUSPENSION)

ADCO-AMOXYCILLIN 250 mg (CAPSULES)

ADCO-AMOXYCILLIN 500 mg (CAPSULES)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Capsules:

Each capsule contains amoxicillin trihydrate equivalent to 250 mg amoxicillin or 500 mg amoxicillin.

Sugar free.

Powder for oral suspension:

The powder contains amoxicillin trihydrate equivalent to 125 mg or 250 mg amoxicillin per 5 ml.

Excipient(s) with known effect:

Sodium methyl hydroxybenzoate 0,08 % *m/v* as preservative when reconstituted.

Contains sugar: Sucrose 3,05 g per 5 ml (for the 125 mg/5 ml suspension).

Contains sugar: Sucrose 3,15 g per 5 ml (for the 250 mg/5 ml suspension).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension:

A cream-coloured free flowing granular powder with a characteristic odour. Reconstitution with water as per label instructions, produces a lime-coloured suspension.

Capsules:

250 mg and 500 mg: Hard gelatin capsules with an opaque maroon cap and opaque maroon body: overprinted with "ADCO 250" or "ADCO 500".

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Infections caused by non-penicillinase-producing organisms including:

- Upper respiratory tract infections
- Lower respiratory tract infections
- Otitis media
- Typhoid fever
- Upper urinary tract infections
- Lower urinary tract infections
- Skin and soft tissue infections
- Gastro-intestinal tract infections
- Gonorrhoea
- Non-specific urethritis

4.2 Posology and method of administration

Posology

Adults:

- The average adult dose for ADCO-AMOXYCILLIN is 750 mg - 1,5 g/day, but in serious infections up to 6 g daily has been administered.
- 250 mg (1 x 250 mg capsule or 5 ml of 250 mg/5 ml suspension) three times a day.

Special populations

Paediatric population

- ***Children 2 - 10 years:**
  125 mg (5 ml of 125 mg/5 ml suspension) three times a day.
- ***Children 6 months - 2 years:**
  125 mg (5 ml of 125 mg/5 ml suspension) three times a day.
- ***Infants 0 - 6 months:**
  62,5 mg (2,5 ml of 125 mg/5 ml suspension) three times a day.
- **Premature infants 1,0 - 2,5 kg:**
  30,0 - 62,5 mg (quarter to half medicine measure of 125 mg/5 ml suspension) once daily for the first 1 - 2 weeks depending on the size and maturity of the infant, thereafter the dose may be given 2 – 3 times daily.

***In severe infections these dosages may be increased.**

Renal impairment

- Patients with renal insufficiency may possibly require a reduced dose.

During treatment with high doses of ADCO-AMOXYCILLIN, an adequate fluid intake and urinary output must be maintained (see section 4.4).

In-dwelling catheters should be checked regularly for potency since at room temperature high urinary concentration of ADCO-AMOXYCILLIN may precipitate out of solution *(see section 4.4).*

Specific dosages:

Indications	Daily Dosages		Duration
	Adults	**Children**	
Gastro-intestinal tract infections	1 - 2 g	-	4 - 5 days
Acute typhoid fever	4 g	- 100 mg/kg	14 days 21 days
Gonorrhoea	2 - 3 g	-	Stat

Method of administration

For oral use.

The presence of food does not interfere with the absorption of ADCO-AMOXYCILLIN.

ADCO-AMOXYCILLIN may, therefore, be taken with meals.

4.3 Contraindications

- Hypersensitivity to the penicillins or any of the cephalosporins or to any of the excipients listed in section 6.1.
- Amoxicillin as contained in ADCO-AMOXYCILLIN is penicillin and should not be given to patients with a history of hypersensitivity to β-lactam antibiotics (e.g. carbapenem or monobactam). Potential cross allergy to other beta-lactams such as cephalosporins should be taken into account.

4.4 Special warnings and precautions for use

Hypersensitivity reactions:

- Serious and occasionally fatal hypersensitivity (anaphylactoid) 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.
- Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8).

- Before commencing therapy with any penicillin as contained in ADCO-AMOXYCILLIN, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergies (see section 4.3).
- If an allergic reaction occurs, appropriate therapy should be instituted and ADCO-AMOXYCILLIN therapy discontinued.
- Drug-induced enterocolitis syndrome (DIES) has been reported mainly in children receiving amoxicillin (see section 4.8). DIES is an allergic reaction with the leading symptom of protracted vomiting (1-4 hours after medicine intake) in the absence of allergic skin or respiratory symptoms. Further symptoms could comprise abdominal pain, diarrhoea, hypotension or leucocytosis with neutrophilia. There have been severe cases including progression to shock.

Skin reactions:

- ADCO-AMOXYCILLIN should be avoided if infectious mononucleosis and glandular fever is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Lymphatic leukaemia:

- ADCO-AMOXYCILLIN should preferably not be used in patients with lymphatic leukaemia, since they are especially susceptible to ampicillin-induced skin rashes.
- The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP). This reaction requires ADCO-AMOXYCILLIN discontinuation and contraindicates any subsequent administration.

Overgrowth of non-susceptible microorganisms:

- Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.
- Antibiotic associated Pseudomembranous colitis has been reported. The severity of the colitis may range from mild to life-threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with ADCO-AMOXYCILLIN use (this may occur up to several weeks after cessation of ADCO-AMOXYCILLIN therapy). If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment with ADCO-AMOXYCILLIN should be discontinued immediately.
- Anti-peristaltic medicines are contraindicated in this situation.

Anticoagulants:

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

Hepatic impairment:

- ADCO-AMOXYCILLIN should be used with caution in patients with evidence of hepatic dysfunction.
- Changes in liver function tests have been observed in some patients receiving amoxicillin.
- Transient hepatitis and cholestatic jaundice have been reported.

Renal impairment:

- The dose should be reduced in patients with renal failure.

Prolonged therapy:

- Periodic assessment of renal, hepatic, and haematopoietic functions should be made during prolonged therapy.
- The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur ADCO-AMOXYCILLIN should be discontinued and/or appropriate therapy instituted.

Jarisch-Herxheimer reaction:

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

Crystalluria:

- In patients with reduced urine output, crystalluria (including acute renal injury) has been observed. The presence of high urinary concentrations of amoxicillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals. When high doses are administered, adequate fluid intake and urinary output must be maintained (see section 4.8 and 4.9).

Convulsions:

- Convulsions may occur in patients with impaired renal function, 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).

Non-susceptible microorganisms:

- The use of ADCO-AMOXYCILLIN may lead to the appearance of resistant strains of organisms and sensitivity testing should therefore be carried out wherever possible, to ensure the appropriateness of the therapy.
- ADCO-AMOXYCILLIN 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 ADCO-AMOXYCILLIN. This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.
- Amoxicillin, an aminopenicillin, 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 (see sub-header 'Skin reactions').

Hereditary intolerances to sugars

- Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Interference with laboratory tests

- Since high urine concentrations of amoxicillin as contained in ADCO-AMOXYCILLIN may result in false positive reactions when testing for the presence of glucose in urine, it is recommended that glucose tests based on enzyme-based glucose oxidase reactions be used (see section 4.5).
- The amoxicillin may distort assay results for oestriol in pregnant women.

Use in lactation

- ADCO-AMOXYCILLIN is excreted in breast milk and should be used with caution when administered to lactating women (see section 4.6).

Paediatric population

A moderate rise in serum glutamic oxaloacetic transaminase (SGOT) has been noted particularly in infants but the significance of this finding is unknown.

On account of the slow physiological renal development in newborns, amoxicillin is excreted slowly in infants aged between two and three weeks.

4.5 Interaction with other medicines and other forms of interaction

Anticoagulants:

- Concomitant administration of ADCO-AMOXYCILLIN and anticoagulants, e.g. coumarin may prolong the bleeding time.
- A dose adjustment of anticoagulants may be necessary (see section 4.4). If coadministration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of ADCO-AMOXYCILLIN.

Probenecid:

- Concomitant administration of probenecid and ADCO-AMOXYCILLIN is not recommended. Probenecid decreases the renal tubular secretion of ADCO-AMOXYCILLIN.
- Concomitant use with ADCO-AMOXYCILLIN may result in increased and prolonged blood concentrations of ADCO-AMOXYCILLIN.

Allopurinol:

- The concurrent administration of allopurinol during treatment with ADCO-AMOXYCILLIN can increase the incidence of allergic skin reactions.

Tetracyclines:

- Tetracyclines and other bacteriostatic medicines may interfere with the bactericidal effects of ADCO-AMOXYCILLIN.

Methotrexate:

- ADCO-AMOXYCILLIN may reduce the renal excretion of methotrexate causing potential increase in toxicity.
- Serum methotrexate levels should be closely monitored in patients who receive ADCO-AMOXYCILLIN and methotrexate simultaneously (see section 4.4).

Oral hormonal contraceptives:

- ADCO-AMOXYCILLIN may decrease the efficacy of oestrogen-containing oral contraceptives and patients must be warned accordingly.
- ADCO-AMOXYCILLIN may affect the absorption of other medicines due to its effect on the gastrointestinal flora.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females

ADCO-AMOXYCILLIN may reduce the efficacy of oral contraceptives and patients should be warned accordingly (see section 4.5).

Pregnancy

Safety and efficacy in pregnancy and lactation have not been established.

Breastfeeding

ADCO-AMOXYCILLIN is excreted in breast milk and should be used with caution when administered to lactating women.

4.7 Effects on ability to drive and use machines

ADCO-AMOXYCILLIN may cause allergic reactions, dizziness or convulsions and may thus have an effect on mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse side effects are diarrhoea, nausea, vomiting, indigestion, abdominal pain, skin rashes, urticaria and erythema multiforme, vaginitis, abnormal taste, headache, dizziness, tiredness and hot flushes.

Tabulated list of adverse reactions

System Organ Class	Frequent	Less frequent	Frequency not known
Infections and infestations		Mucocutaneous candidiasis	
Blood and the lymphatic system disorders			Reversible leucopenia (including severe neutropenia and agranulocytosis), Reversible thrombocytopenia, Thrombocytopenic purpura,

			Eosinophilia, Haemolytic anaemia, Prolongation of bleeding time and prothrombin time (see section 4.4)
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		Hyperkinesia, Dizziness, Convulsions (see section 4.4)	Aseptic meningitis
Cardiac disorders			Kounis syndrome (see section 4.4)
Gastrointestinal disorders	Diarrhoea, Nausea	Vomiting, Gastritis Stomatitis, Glossitis, Enterocolitis, Black hairy tongue, Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) (see section 4.4), Superficial tooth discolouration	
Hepato-biliary disorders		Hepatitis and cholestatic jaundice	Rises in Aspartate aminotransferase (AST) and/or Alanine

			aminotransferase (ALT)
Skin and subcutaneous tissue disorders	Skin rash	Erythematous maculopapular rash, Pruritis, Urticaria, Erythema multiforme, Bullous exfoliative dermatitis, Toxic epidermal necrolysis, Stevens-Johnson syndrome, Acute generalised pustulosis, Lyell's syndrome, Acute generalised exanthemous pustulosis (AGEP) (see section 4.4), Drug reaction with eosinophilia and systemic symptoms (DRESS)	Linear IgA disease
Renal and urinary disorders		Interstitial nephritis	Crystalluria (including acute renal injury) (see section 4.9)

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 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.

You may also report to Adcock Ingram Limited using the following e-mail address: Adcock.AEReports@adcock.com.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

Symptoms:

- Oral administration can cause gastro-intestinal symptoms such as transient diarrhoea, nausea and colic which are dose-related and a result of local irritation and not toxicity.

Treatment:

- If encountered, gastro-intestinal symptoms and disturbances of the fluid and electrolyte balance may be evident.
- They may be treated symptomatically and supportive with attention to the water/electrolyte balance.
- In the absence of an adequate fluid intake and urinary output, crystalluria, in some cases leading to renal failure, is a possibility.
- Amoxicillin may be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.1.2 Antimicrobial agents – penicillins

Pharmacotherapeutic group: Penicillins with extended spectrum, ATC code: J01CA04

Mechanism of action

Amoxicillin is a semi-synthetic, broad-spectrum penicillin derived from the 6-amino-penicillanic acid nucleus. Chemically, it is 6-[D(-)-α-amino-p-hydroxyphenyl -acetamido] penicillanic acid trihydrate.

Amoxicillin is a penicillinase-susceptible penicillin. Amoxicillin exhibits in vitro bactericidal activity against a wide range of Gram-negative and Gram-positive organisms

Pharmacodynamic effects

Amoxicillin does not resist destruction by penicillinase and is thus not effective against penicillinase-producing bacteria, particularly resistant staphylococci. All strains of Pseudomonas and most strains of Klebsiella, indole-positive Proteus, Serratia, Acinetobacter and Enterobacter are resistant to amoxicillin.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin is rapidly and well absorbed orally. A single 250 mg oral dose achieves an average peak serum level virtually equal to that achieved by IM injection viz. 5,38 µg/ml oral and 5,6 µg/ml IM. The peak serum level is achieved within 1,5 - 2 hours after oral and 15 minutes after IM or IV (18,2 µg/ml) administration.

After oral administration, there is no significant difference between the peak serum levels in fasting and non-fasting subjects. The presence of food does not interfere with the absorption of amoxicillin. ADCO-AMOXYCILLIN may, therefore, be taken with meals. There is a linear/dose response in peak serum levels after both oral and parenteral administration.

Distribution

(i) Sputum:

The concentration of amoxicillin in sputum does not decrease as occurs with ampicillin as purulence subsides.

(ii) Bile:

Amoxicillin is present in bile obtained from a common bile duct drain of a healthy gallbladder, however, biliary levels are lower when the gallbladder is diseased and absent in the presence of biliary tract obstruction.

(iii) Urine:

The average concentration of amoxicillin in urine collected during the first six hours after 250 mg oral dose is 580 µg/ml.

Excretion

(i) Renal:

Approximately 60 % of an oral dose of amoxicillin is excreted unchanged in the active form into the urine within six hours. Approximately 70 % - 80 % of an intramuscular dose and 90 % of an intravenous dose is excreted unchanged in the active form, into the urine within 12 hours.

(ii) Biliary:

A variable percentage of amoxicillin is excreted into the bile.

Probenecid

Even higher amoxicillin serum levels may be achieved after oral administration to patients with normal renal function, by the simultaneous administration of a renal blocking medicine such as probenecid. Probenecid should not be given in the presence of abnormal renal function. No data on the effect of probenecid on parenteral amoxicillin are yet available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ADCO-AMOXYCILLIN (Capsules)

Colloidal anhydrous silica

Magnesium stearate

Composition of Hard Empty Gelatin Capsule:

Cap and Body:

Brilliant Blue FCF

Erythrosine BS

Titanium dioxide (CI No. 77891)

Sunset Yellow

Sodium lauryl sulphate

Gelatin

Composition of Imprinting White Ink

Titanium dioxide (CI No. 77891)

Shellac

Isopropyl alcohol

Alcohol

Tween 80

ADCO-AMOXYCILLIN (Suspension)

Quinoline yellow supra (CI No. 47005)

Lemon dry flavour

Apricot dry flavour

Sodium methyl hydroxybenzoate

Carmellose sodium

Sodium citrate

Colloidal anhydrous silica

Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Capsules: 36 months

Suspensions: 24 months

In-use shelf-life:

The potency of reconstituted suspensions will be maintained for one week at temperatures not exceeding 25 °C and for two weeks under refrigeration (2 °C - 8°C).

6.4 Special precautions for storage

Capsules and powders:

Store below 25 °C. Protect from moisture.

For storage conditions after reconstitution of the medicine, see section 6.3.

6.5 Nature and contents of container

Powders for oral suspension:

Powder for oral suspension is available in clear glass and white HDPE bottles providing 100 ml or 75 ml of the suspension when reconstituted.

Capsules:

The 250 mg capsules are packed in containers of 15, 100, 500 and 1 000 capsules.

The 500 mg capsules are packed in containers of 15, 100 and 1 000 capsules, and blister packs of 15 and 100 capsules.

Not all pack sizes/types are necessarily marketed.

6.6 Special precautions for disposal and other handling

Reconstitution of powders:

The 125 mg/5 ml powder is reconstituted with 60 ml of water to yield 100 ml of suspension or with 44 ml of water to yield 75 ml of suspension.

The 250 mg/5 ml powder is reconstituted with 57 ml of water to yield 100 ml of suspension.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER(S)

ADCO-AMOXYCILLIN 125 mg/5 ml: X/20.1.2/198

ADCO-AMOXYCILLIN 250 mg/5 ml: X/20.1.2/199

ADCO-AMOXYCILLIN 250 mg: X/20.1.2/196

ADCO-AMOXYCILLIN 500 mg: X/20.1.2/197

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

ADCO-AMOXYCILLIN 500 mg: 11 April 1990

10. DATE OF REVISION OF THE TEXT

31 March 2025