APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

AMRO 250 mg (Capsule)

AMRO 500 mg (Capsule)

COMPOSITION:

AMRO 250 mg:

Each capsule contains Amoxycillin Trihydrate equivalent to anhydrous Amoxycillin 250 mg.

AMRO 500 mg:

Each capsule contains Amoxycillin Trihydrate equivalent to Anhydrous Amoxycillin 500 mg.

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.2 Penicillins

PHARMACOLOGICAL ACTION:

Amoxycillin is semisynthetic 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.*

The following organisms are generally sensitive to the bactericidal action of amoxycillin in vitro. In vitro sensitivity does not mean in vivo efficacy [(*) denotes sensitivity tests must be performed]

Gram positive bacteria

Staphylococcus aureus (penicillin sensitive)*

Streptococcus pyoenes

*Streptococcus viridans**

*Streptococcus faecalis**

*Streptococcus pneumomae**

*Corynebacterium species**

*Clostridium species**

*Bacillus anthracis**

Listeria monocytogenes

Gram negative bacteria

Neisseria meningitidis *(except the carrier state)

*Neisseria gonorrhoeae**

*Haemophilus influenza**

Bordetella pertussis

*Escherichia coli**

*Salmonella species**

*Shigella species**

*Proteus mirabilis**

*Pasteurella multocida**

*Fusabacterium species**

Helicobacter pylori

Leptospira species

PHARMACOKINETICS:

Absorption:

Amoxycillin is stable in the presence of acidic gastric secretions. Peak blood levels are achieved 1 -2hr after administration, There is a Linear dose response in peak serum levels.

Food does not interfere with the absorption of amoxycillin.

Distribution:

Approximately 18 % of the total plasma amoxycillin content is protein bound. Amoxycillin 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 amoxycillin.

Excretion:

The elimination half-Life is approximately 1 hour. Amoxycillin is primarily excreted via the kidneys. Small amounts of the drug are also excreted in the faeces and bile.

Amoxycillin crosses the placenta and is distributed into breast milk.

INDICATIONS:

AMRO formulations are indicated for the treatment of mild to moderately severe infections caused by susceptible organisms:

1 Upper Respiratory tract infections such as sinusitis, otitis media, tonsillitis

2 Lower respiratory tract infections such as bronchitis, lobar and bronchopneumonia

3 Gastro-intestinal infections such as typhoid fever

4. Other infections including Borreliosis (Lyme disease)

5 In the following infections, amoxycillin 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

6 "As part of combination therapy in established Helicobacter pylori infection, associated with duodenal ulceration. "

7. Prophylaxis of endocarditis

CONTRA-INDICATIONS:

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

WARNINGS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with **AMRO**, 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 cephalosporin.

If an allergic reaction occurs, **AMRO** 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.

AMRO 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 amoxycillin.

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 **AMRO**. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

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

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

INTERACTIONS:

Probenecid decreases the renal tubular secretion of **AMRO**. Concurrent use with **AMRO** may result in increased and prolonged blood concentrations of **AMRO.**

AMRO 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 **AMRO**.

Interaction with Laboratory tests:

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

PREGNANCY AND LACTATION:

Use in pregnancy:

The safety of **AMRO** in pregnancy has not been established.

Use in lactation:

AMRO is distributed into breast milk. Although significant problems in humans have not been documented, the use of **AMRO** by nursing mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant.

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 **AMRO** 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.

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 chrionicum migrans and 100 mg/kg/day in the case of generalised manifestations, both for a minimum of 12 days

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/mm:	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 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

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side effects

Gastrointestinal disorders:

Frequent: Diarrhoea, nausea, vomiting, indigestion, abdominal pain, abnormal taste.

Frequency unknown: Gastritis, stomatitis, glossitis, black 'hairy' tongue, enterocolitis, mucocutaneous candidiasis and antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis). If gastro-intestinal reactions are evident, they may be reduced by taking **AMRO** 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.

Skin and subcutaneous tissue disorders:

Frequent: Skin rashes, urticaria and erythema multiforme, pruritus, serum sickness-like syndrome. *Less* frequent: Stevens-Johnson syndrome, hypersensitivity vasculitis and bullous exfoliative dermatitis and toxic epidermal necrolysis.

Whenever such reactions occur, **AMRO** should be discontinued. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see Warnings).

Nervous system disorders

Frequent: Headache, dizziness.

Less frequent: Reversible hyperactivity and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.

Reproductive system and breast disorders

Frequent: Vaginitis

Endocrine disorders:

Frequent: Tiredness and hot flushes.

Renal and urinary disorders:

Less frequent: Interstitial nephritis, crystalluria.

Hepato-biliary disorders:

Less frequent: Hepatitis and cholestatic jaundice have been reported. 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.

Investigations:

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

Blood and the lymphatic system disorders:

Frequency unknown: Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leucopenia and agranulocytosis have been reported. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.

Less frequent: A slight thrombocytosis was noted in less than 1% of the patients treated with **AMRO**. Prolongation of bleeding time and prothrombin time have also been reported less frequently. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

Special Precautions

Caution is needed when administering amoxycillin 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.

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

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function, is advisable during prolonged therapy. Since **AMRO** contains amoxycillin, 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 infections mononucleosis, in the presence of which there is a high incidence of rash if amoxycillin is used.

AMRO should be given with caution to patients with lymphatic leukemia since they are especially susceptible to amoxycillin 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 **AMRO**. It should be used with care in patients with evidence of severe hepatic dysfunction.

Impaired renal function:

In patients with moderate or severe renal impairment **AMRO** dosage should be adjusted. (See Dosage and administration.)

Use in Lactation:

Amoxycillin is excreted in the milk. Therefore, caution should be exercised when **AMRO** is administered to a nursing woman.

The use of **AMRO** 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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Overdosage with **AMRO** 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.

AMRO may be removed from the circulation by haemodialysis

IDENTIFICATION:

AMRO 250 mg:

Maroon/yellow size "1" hard gelatin capsule filled with white to off white granular powder and imprinted with A" on maroon cap and "85" on yellow body with black ink.

AMRO 500 mg:

Maroon/yellow size "0EL" hard gelatin capsule filled with white to off white granular powder and imprinted with "A" on maroon cap and "86" on yellow body with black ink.

PRESENTATION:

1. Blisters:

Both **AMRO 250 mg** and **AMRO 500 mg**:

1. PVC/ACLAR-Aluminium Blister Packaging:

Capsules are packed in 250 Micron white opaque PVC laminated with 23 Micron Aclar (Width 127 mm) as the forming material and 25 microns Aluminium foil (Width 123 mm) as the lidding material. Each blister contains 15 capsules.

Pack size: 15's: Each carton contains 1 blister of 15 capsules.

2. Triple Laminate: PVC/PE/PVdC- Aluminium Blister Packaging:

Capsules are packed in Triple Laminate: 250 Micron white opaque PVC / 25 micron PE film coated with 60 GSM PVdC (width 127 mm) as the forming material and 25 microns Aluminium Foil (Width 123 mm) as the lidding material. Each blister contains 15 capsules.

Pack size: 15's: Each carton contains 1 blister of 15 capsules.

2. HDPE Containers:

AMRO 250 mg:

Tablets are packed in a HDPE container with a child resistant closure and induction sealing wad, in the following pack sizes:

Pack size: 100's

Tablets are packed in a HDPE container with a stock ribbed closure and induction sealing wad, in the following pack sizes:

Pack size: 500's

AMRO 500 mg:

Tablets are packed in a HDPE container with a child resistant closure and induction sealing wad, in the following pack sizes:

Pack size: 100's

STORAGE CONDITIONS:

Store in a cool, dry place below 25°C.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

AMRO 250 mg: 41/20.1.2/0055

AMRO 500 mg: 41/20.1.2/0056

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

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