Averroes pharma for pharmaceutical industries

Averobios 642.9/5 ml powder for oral suspension

Averobios 1062.5 mg extended release tablets

To reduce the development of drug-resistant bacteria and maintain the effectiveness of AVEROBIOS (amoxicillin/clavulanate potassium) and other antibacterial drugs, AVEROBIOS should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

AVEROBIOS is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the β-lactamase inhibitor clavulanate potassium (the potassium salt of clavulanic acid). Amoxicillin is an analog of ampicillin, derived from the basic penicillin nucleus 6-aminopenicillanic acid. The amoxicillin trihydrate molecular formula is $C_{16}H_{19}N_3O_5S \cdot 3H_2O$, and the molecular weight is 419.45. Chemically, amoxicillin trihydrate is (2S,5R ,6R)-6-[(R)-(-)-2-Amino-2-(p-hydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate

Clavulanic acid is produced by the fermentation of Streptomyces clavuligerus. It is a β-lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of β-lactamases by blocking the active sites of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-mediated β-lactamases frequently responsible for transferred drug resistance to penicillins and cephalosporins. The clavulanate potassium molecular formula is $C_8H_8KNO_5$, and the molecular weight is 237.25. Chemically, clavulanate potassium is potassium (Z)-(2R ,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]-heptane-2-carboxylate,

AVEROBIOS XR only contains also

The amoxicillin sodium molecular formula is $C_{16}H_{18}N_3NaO_5S$, and the molecular weight is 387.39. Chemically, amoxicillin sodium is [2S-[2α,5α,6β(S *)]]-6-[[Amino(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid monosodium salt

Inactive Ingredients:

AVEROBIOS powder for oral suspension:

carboxy methyl cellulose sodium , xanthan gum , microcrystalline cellulose RC 591 , colloidal silicon dioxide (Aerosil 200) , orange flavor powder , sodium citrate , Citric acid anhydrous , aspartame , sucrose , purified water .

Averobios XR :

Hydroxypropyl methyl cellulose(Methocel K15 M), Pregelatinized maize starch (Starch 1500), Citric acid anhydrous , Microcrystalline cellulose (Avicel pH 302),magnesium stearate,hydrophobic silicon dioxide, Hydroxypropyl methyl cellulose(Methocel E5) , ethyl cellulose , triacetin , titanium dioxide, talc purified.

CLINICAL PHARMACOLOGY

AVEROBIOS XR:

Amoxicillin and clavulanate potassium are well absorbed from the gastrointestinal tract after oral administration of AVEROBIOS.

AVEROBIOS is an extended-release formulation which provides sustained plasma concentrations of amoxicillin. Amoxicillin systemic exposure achieved with AVEROBIOS is similar to that produced by the oral administration of equivalent doses of amoxicillin alone. In a study of healthy adult volunteers, the pharmacokinetics of AVEROBIOS were compared when administered in a fasted state, at the start of a standardized meal (612 kcal, 89.3 g carb, 24.9 g fat, and 14.0 g protein), or 30 minutes after a high-fat meal. When the systemic exposure to both amoxicillin and clavulanate is taken into consideration, AVEROBIOS is optimally administered at the start of a standardized meal. Absorption of amoxicillin is decreased in the fasted state. AVEROBIOS is not recommended to be taken with a high-fat meal, because clavulanate absorption is decreased.

Clearance of amoxicillin is predominantly renal, with approximately 60% to 80% of the dose being excreted unchanged in urine, whereas clearance of clavulanate has both a renal (30% to 50%) and a non-renal component.

Concurrent administration of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanate.

Neither component in AVEROBIOS is highly protein-bound; clavulanate has been found to be approximately 25% bound to human serum and amoxicillin approximately 18% bound.

Amoxicillin diffuses readily into most body tissues and fluids, with the exception of the brain and spinal fluid. The results of experiments involving the administration of clavulanic acid to animals suggest that this compound, like amoxicillin, is well distributed in body tissues.

Microbiology:

Amoxicillin is a semisynthetic antibiotic with a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Amoxicillin is, however, susceptible to degradation by β-lactamases, and therefore, its spectrum of activity does not include organisms which produce these enzymes. Clavulanic acid is a β-lactam, structurally related to penicillin, which possesses the ability to inactivate a wide range of β-lactamase enzymes commonly found in microorganisms resistant to penicillins and cephalosporins. In particular, it has good activity against the clinically important plasmid-mediated β-lactamases frequently found responsible for transferred drug resistance.

The clavulanic acid component of AVEROBIOS protects amoxicillin from degradation by β-lactamase enzymes and effectively extends the antibiotic spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other β-lactam antibiotics.

Amoxicillin/clavulanic acid has been shown to be active against most isolates of the following microorganisms, both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section.

Aerobic Gram-Positive Microorganisms:

Streptococcus pneumoniae (including isolates with penicillin MICs ≤ 2 mcg/mL)

Staphylococcus aureus (including β-lactamase−producing isolates)

NOTE: *Staphylococci* which are resistant to methicillin/oxacillin must be considered resistant to amoxicillin/clavulanic acid.

Aerobic Gram-Negative Microorganisms:

Haemophilus influenzae (including β-lactamase−producing isolates)

Moraxella catarrhalis (including β-lactamase−producing isolates)

Haemophilus parainfluenzae (including β-lactamase−producing isolates)

Klebsiella pneumoniae (all known isolates are β-lactamase−producing)

The following in vitro data are available, but their clinical significance is unknown.

At least 90% of the following microorganisms exhibit in vitro minimum inhibitory concentrations (MICs) less than or equal to the susceptible breakpoint for amoxicillin/clavulanic acid.1,2 However, the safety and efficacy of amoxicillin/clavulanic acid in treating infections due to these microorganisms have not been established in adequate and well-controlled trials.

Aerobic Gram-Positive Microorganisms:

Streptococcus pyogenes

Anaerobic Microorganisms:

Bacteroides fragilis (including β-lactamase−producing isolates)

Fusobacterium nucleatum (including β-lactamase−producing isolates)

Peptostreptococcus magnus

Peptostreptococcus micros

NOTE: *S. pyogenes, P. magnus, and P. micros* do not produce β-lactamase, and therefore, are susceptible to amoxicillin alone. Adequate and well-controlled clinical trials have established the effectiveness of amoxicillin alone in treating certain clinical infections due to S. pyogenes.

INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectiveness of AVEROBIOS and other antibacterial drugs, AVEROBIOS should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

AVEROBIOS Extended Release Tablets:

indicated for the treatment of patients with community-acquired pneumonia or acute bacterial sinusitis due to confirmed, or suspected β-lactamase−producing pathogens (i.e., H. influenzae, M. catarrhalis, H. parainfluenzae, K. pneumoniae, or methicillin-susceptible S. aureus) and S. pneumoniae with reduced susceptibility to penicillin (i.e., penicillin MICs = 2 mcg/mL). AVEROBIOS is not indicated for the treatment of infections due to S. pneumoniae with penicillin MICs ≥ 4 mcg/mL. Data are limited with regard to infections due to S. pneumonia with penicillin MICs ≥ 4 mcg/mL .

Of the common epidemiological risk factors for patients with resistant pneumococcal infections, only age > 65 years was studied. Patients with other common risk factors for resistant pneumococcal infections (e.g., alcoholism, immune-suppressive illness, and presence of multiple co-morbid conditions) were not studied.

In patients with community-acquired pneumonia in whom penicillin-resistant S. pneumoniae is suspected, bacteriological studies should be performed to determine the causative organisms and their susceptibility when AVEROBIOS is prescribed.

Acute bacterial sinusitis or community-acquired pneumonia due to a penicillin-susceptible strain of S. pneumoniae plus a β-lactamase−producing pathogen can be treated with another AVEROBIOS (amoxicillin/clavulanate potassium) product containing lower daily doses of amoxicillin (i.e., 500 mg every 8 hours or 875 mg every 12 hours). Acute bacterial sinusitis or community-acquired pneumonia due to S. pneumoniae alone can be treated with amoxicillin.

Averobios powder for oral suspension:

indicated for the treatment of pediatric patients with recurrent or persistent acute otitis media due to *S. pneumoniae* (penicillin MICs ≤2 mcg/mL), *H. influenzae* (including β-lactamase–producing strains), or *M. catarrhalis* (including β-lactamase–producing strains) characterized by the following risk factors:
• antibiotic exposure for acute otitis media within the preceding 3 months, and either of the following:
• age ≤2 years
• daycare attendance [See CLINICAL PHARMACOLOGY, Microbiology.] **NOTE:** Acute otitis media due to *S. pneumoniae* alone can be treated with amoxicillin.

not indicated for the treatment of acute otitis media due to *S. pneumoniae* with penicillin MIC ≥4 mcg/mL.

Therapy may be instituted prior to obtaining the results from bacteriological studies when there is reason to believe the infection may involve both *S. pneumoniae* (penicillin MIC ≤2 mcg/mL) and the β-lactamase–producing organisms listed above.

CONTRAINDICATIONS

AVEROBIOS is contraindicated in patients with a history of allergic reactions to any penicillin. It is also contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with treatment with amoxicillin/clavulanate potassium.

AVEROBIOS is contraindicated in patients with severe renal impairment (creatinine clearance < 30 mL/min.) and in hemodialysis patients.

WARNINGS

Averobios powder for oral suspension contain aspartame which is source of phenyl alanine may be harmful for people with phenyl ketone urea

SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTIC) REACTIONS HAVE BEEN REPORTED IN PATIENTS ON PENICILLIN THERAPY. 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. BEFORE INITIATING THERAPY WITH AVEROBIOS, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OR OTHER ALLERGENS. IF AN ALLERGIC REACTION OCCURS, AVEROBIOS SHOULD BE DISCONTINUED AND THE APPROPRIATE THERAPY INSTITUTED. SERIOUS ANAPHYLACTIC REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, SHOULD ALSO BE ADMINISTERED AS INDICATED.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including AVEROBIOS, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

AVEROBIOS should be used with caution in patients with evidence of hepatic dysfunction. Hepatic toxicity associated with the use of amoxicillin/clavulanate potassium is usually reversible. On rare occasions, deaths have been reported (less than 1 death reported per estimated 4 million prescriptions worldwide). These have generally been cases associated with serious underlying diseases or concomitant medications (see CONTRAINDICATIONS and ADVERSE REACTIONS—Liver).

PRECAUTIONS

General:

While amoxicillin/clavulanate potassium possesses the characteristic low toxicity of the penicillin group of antibiotics, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic function, is advisable if therapy is for longer than the drug is approved for administration.

A high percentage of patients with mononucleosis who receive ampicillin develop an erythematous skin rash. Thus, ampicillin-class antibiotics should not be administered to patients with mononucleosis.

The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving Pseudomonas spp. or Candida spp.), the drug should be discontinued and/or appropriate therapy instituted.

Prescribing AVEROBIOS in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients:

AVEROBIOS should be taken every 12 hours with a meal or snack to reduce the possibility of gastrointestinal upset. If diarrhea develops and is severe or lasts more than 2 or 3 days, call your doctor.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Patients should be counseled that antibacterial drugs, including AVEROBIOS, should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When AVEROBIOS is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate treatment, and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by AVEROBIOS or other antibacterial drugs in the future. Discard any unused medicine.

Averobios powder for oral suspension:

Keep suspension refrigerated. Shake well before using. When dosing a child with the suspension (liquid) of Averobios, use a dosing spoon. Be sure to rinse the spoon. Bottles of suspension of Averobios may contain more liquid than required. Follow your doctor’s instructions about the amount to use and the days of treatment your child requires. Discard any unused medicine.

Drug Interactions:

Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with AVEROBIOS may result in increased and prolonged blood levels of amoxicillin. Coadministration of probenecid cannot be recommended.

Abnormal prolongation of prothrombin time (increased international normalized ratio [INR]) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricemia present in these patients. In controlled clinical trials of Averobios, 25 patients received concomitant allopurinol and Averobios. No rashes were reported in these patients. However, this sample size is too small to allow for any conclusions to be drawn regarding the risk of rashes with concomitant AVEROBIOS and allopurinol use.
In common with other broad-spectrum antibiotics, AVEROBIOS may reduce the efficacy of oral contraceptives.

Drug/Laboratory Test Interactions:

Oral administration of AVEROBIOS will result in high urine concentrations of amoxicillin. High urine concentrations of ampicillin may result in false-positive reactions when testing for the presence of glucose in urine using CLINITEST®, Benedict's Solution, or Fehling's Solution. Since this effect may also occur with amoxicillin and therefore Averobios, it is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as CLINISTIX®) be used.

Following administration of ampicillin to pregnant women, a transient decrease in plasma concentration of total conjugated estriol, estriol-glucuronide, conjugated estrone, and estradiol has been noted. This effect may also occur with amoxicillin, and therefore, Averobios.

Pregnancy:

Teratogenic Effects:

Averobios XR:

Pregnancy Category B. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Averobios powder for oral suspension:

No adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed

Nursing Mothers:

Ampicillin-class antibiotics are excreted in the milk; therefore, caution should be exercised when AVEROBIOS is administered to a nursing woman.

Pediatric Use:

Averobios XR:

The safety and effectiveness of AVEROBIOS have been established for pediatric patients weighing ≥ 40 kg who are able to swallow tablets.

The adverse event profile in 44 pediatric patients who received at least one dose of AVEROBIOS was consistent with the established adverse event profile for the product in adults.

Averobios powder for oral suspension:

Safety and efficacy of Averobios in infants younger than 3 months have not been established. Safety and efficacy of Averobios have been demonstrated for treatment of acute otitis media in infants and children 3 months to 12 years.

The safety and effectiveness of Averobios have been established for the treatment of pediatric patients (3 months to 12 years) with acute bacterial sinusitis. This use is supported by evidence from adequate and well-controlled studies of Averobios XR™ Extended Release Tablets in adults with acute bacterial sinusitis, studies of Averobios in pediatric patients with acute otitis media, and by similar pharmacokinetics of amoxicillin and clavulanate in pediatric patients taking Averobios (see CLINICAL PHARMACOLOGY) and adults taking Averobios XR.

Geriatric Use for Averobios XR :

No overall differences in safety and effectiveness were observed between these subjects and younger subjects, and other clinical experience has not reported differences in responses between the elderly and younger patients, but a greater sensitivity of some older individuals cannot be ruled out.

This drug is known to be substantially excreted by the kidney, and the risk of dose-dependent toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

Each tablet of AVEROBIOS contains 29.3 mg (1.27 mEq) of sodium.

ADVERSE REACTIONS

The most frequently reported adverse effects which were suspected or probably drug-related were diarrhea, vaginal mycosis , nausea , and loose stools. AVEROBIOS had a higher rate of diarrhea which required corrective therapy.

The following adverse reactions have been reported for ampicillin-class antibiotics:

Gastrointestinal:

Diarrhea, nausea, vomiting, indigestion, gastritis, stomatitis, glossitis, black “hairy” tongue, mucocutaneous candidiasis, enterocolitis, and hemorrhagic/pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).

Hypersensitivity Reactions:

Skin rashes, pruritus, urticaria, angioedema, serum sickness-like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia, and frequently fever), erythema multiforme (rarely Stevens-Johnson syndrome), acute generalized exanthematous pustulosis, hypersensitivity vasculitis, and an occasional case of exfoliative dermatitis (including toxic epidermal necrolysis) have been reported. Whenever such reactions occur, the drug should be discontinued, unless the opinion of the physician dictates otherwise. Serious and occasional fatal hypersensitivity (anaphylactic) reactions can occur with oral penicillin (see WARNINGS).

Liver:

A moderate rise in AST (SGOT) and/or ALT (SGPT) has been noted in patients treated with ampicillin-class antibiotics, but the significance of these findings is unknown. Hepatic dysfunction, including hepatitis and cholestatic jaundice, (see CONTRAINDICATIONS), increases in serum transaminases (AST and/or ALT),

serum bilirubin, and/or alkaline phosphatase, has been infrequently reported with Averobios or Averobios XR. It has been reported more commonly in the elderly, in males, or in patients on prolonged treatment. The histologic findings on liver biopsy have consisted of predominantly cholestatic, hepatocellular, or mixed cholestatic-hepatocellular changes. The onset of signs/symptoms of hepatic dysfunction may occur during or several weeks after therapy has been discontinued. The hepatic dysfunction, which may be severe, is usually reversible. On rare occasions, deaths have been reported (less than 1 death reported per estimated 4 million prescriptions worldwide). These have generally been cases associated with serious underlying diseases or concomitant medications.

Renal:

Interstitial nephritis and hematuria have been reported rarely. Crystalluria has also been reported (see OVERDOSAGE).

Hemic and Lymphatic Systems:

Anemia, including hemolytic anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, and agranulocytosis have been reported during therapy with penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. There have been reports of increased prothrombin time in patients receiving Averobios and anticoagulant therapy concomitantly.

Central Nervous System:

Agitation, anxiety, behavioral changes, confusion, convulsions, dizziness, headache, insomnia, and reversible hyperactivity have been reported rarely.

Miscellaneous:

Tooth discoloration (brown, yellow, or gray staining) has been rarely reported. Most reports occurred in pediatric patients. Discoloration was reduced or eliminated with brushing or dental cleaning in most cases.

OVERDOSAGE

Following overdosage, patients have experienced primarily gastrointestinal symptoms including stomach and abdominal pain, vomiting, and diarrhea. Rash, hyperactivity, or drowsiness have also been observed in a small number of patients.

In the case of overdosage, discontinue Averobios, treat symptomatically, and institute supportive measures as required. If the overdosage is very recent and there is no contraindication, an attempt at emesis or other means of removal of drug from the stomach may be performed. A prospective study of 51 pediatric patients at a poison control center suggested that overdosages of less than 250 mg/kg of amoxicillin are not associated with significant clinical symptoms and do not require gastric emptying.5

Interstitial nephritis resulting in oliguric renal failure has been reported in a small number of patients after overdosage with amoxicillin.

Crystalluria, in some cases leading to renal failure, has also been reported after amoxicillin overdosage in adult and pediatric patients. In case of overdosage, adequate fluid intake and diuresis should be maintained to reduce the risk of amoxicillin crystalluria.

Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of both amoxicillin and clavulanate. Both amoxicillin and clavulanate are removed from the circulation by hemodialysis (see DOSAGE AND ADMINISTRATION).

DOSAGE AND ADMINISTRATION

AVEROBIOS XR:

AVEROBIOS should be taken at the start of a meal to enhance the absorption of amoxicillin and to minimize the potential for gastrointestinal intolerance. Absorption of the amoxicillin component is decreased when AVEROBIOS is taken on an empty stomach (see CLINICAL PHARMACOLOGY).

The recommended dose of AVEROBIOS XR is 4,000 mg/250 mg daily according to the following table:

Indication	Dose	Duration
Acute bacterial sinusitis	2 tablets q12h	10 days
Community-acquired pneumonia	2 tablets q12h	7-10 days

Renally Impaired Patients:

The pharmacokinetics of AVEROBIOS have not been studied in patients with renal impairment. AVEROBIOS is contraindicated in patients with a creatinine clearance of < 30 mL/min. and in hemodialysis patients (see CONTRAINDICATIONS).

Hepatically Impaired Patients:

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals (see WARNINGS).

Pediatric Use:

Pediatric patients who weigh 40 kg or more and can swallow tablets should receive the adult dose.

Geriatric Use:

No dosage adjustment is required for the elderly (see PRECAUTIONS, Geriatric Use).

Averobios powder for oral suspension:

Dosage: ***Pediatric patients 3 months and older:*** Based on the amoxicillin component (600 mg/5 mL), the recommended dose of Averobios is 90 mg/kg/day divided every 12 hours, administered for 10 days (see chart below).

Body Weight (kg)	Volume of Averobios providing 90 mg/kg/day
8	3.0 mL twice daily
12	4.5 mL twice daily
16	6.0 mL twice daily
20	7.5 mL twice daily
24	9.0 mL twice daily
28	10.5 mL twice daily
32	12.0 mL twice daily
36	13.5 mL twice daily

Pediatric patients weighing 40 kg and more: Experience with Averobios (600 mg/5 mL formulation) in this group is not available.

Adults: Experience with Averobios (600 mg/5 mL formulation) in adults is not available and adults who have difficulty swallowing should not be given Averobios (600 mg/5 mL) in place of the 500-mg or 875-mg tablet of Averobios.

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals. (See WARNINGS.)

Directions for Mixing Oral Suspension: Prepare a suspension at time of dispensing as follows: Tap bottle until all the powder flows freely. Add approximately 2/3 of the total amount of water for reconstitution (see table below) and shake vigorously to suspend powder. Add remainder of the water and again shake vigorously.
Averobios **(600 mg/5 mL Suspension)**
Each teaspoonful (5 mL) will contain 600 mg amoxicillin as the trihydrate and 42.9 mg of clavulanic acid as the potassium salt.

NOTE: SHAKE ORAL SUSPENSION WELL BEFORE USING.

HOW SUPPLIED

AVEROBIOS Extended Release Tablets:

Carton box containing one Al/Al strip of 10 tablets + inner leaflet

Averobios powder for oral suspension:

Carton box containing amber glass (type III) bottle with plastic closure cap made of high density poly ethylene with powder to make 60 ml after reconstitution and an inner leaflet.

STORAGE

AVEROBIOS Extended Release Tablets:

Store tablets at temperature not exceeding 30°C.

Keep out of reach of children

Averobios powder for oral suspension:

Store powder at temperature not exceeding 30°C in dry place

After reconistitution keep the bottle at temperature (2-8) °C for 10 days

Keep out of reach of children

(THIS IS A MEDICAMENT)

-Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.

-Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

-Do not by yourself interrupt the period of treatment prescribed.

-Do not repeat the same prescription without consulting your doctor.

Averobios powder for oral suspension produced by sigmatec pharmaceutical industries for Averroes pharma for pharmaceutical industries

Averobios XR tablet produced by sigmatec pharmaceutical industries for Averroes pharma for pharmaceutical industries