1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Annmox Powder for Oral Suspension

(Amoxicillin Powder for Oral Suspension 125 mg/5 ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:

Amoxicillin Trihydrate BP

Eq. To anhydrous Amoxicillin 125 mg

3. PHARMACEUTICAL FORM

Dosage Form: Powder for oral Suspension

A white powder filled in HDPE bottle which turns yellow suspension on reconstitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Annmox is indicated for the treatment of bacterial infections; Billiary Tract Infections, Bronchitis, Endocarditis, Gastro – Enteritis (including E.coli Enteritis, Salmonella Enteritis, but not shigellosis), Otitis media, Mouth Infections, Pneumonia, Typhoid and paratyphoid fever, Urinary tract infections, Bone and Joint infections and Skin and Soft tissue infections.

4.2 Posology and method of administration

Always take Annmox suspension exactly as your doctor has told you and always read the label. Your doctor will decide on the appropriate dose to suit your condition. Ask your doctor or pharmacist if you are not sure.

The powder should be reconstituted immediately before use, by adding freshly boiled and cooled water to the mark of the bottle (For Annmox neonatal drops) and 70 ml of freshly boiled and cooled water to the powder (For Annmox suspension) respectively. The contents should be mixed thoroughly to produce a uniform suspension.

Shake the bottle well before the administration of each dose of the medicine. Take the suspension an hour before or two hours after a meal.

Once reconstituted, the suspension should be used within seven (7) days.

Doses

Neonates: Use the calibrated dropper provided.

≤ 3 months; 30 mg/kg per day given every 12 hours.

Administer 0.6-1.0 ml, every 4-6 hours, half to one hour prior to feeding.

Children:

For Bacterial Infections:

≥ 3 months; 20-40 mg/kg per day given every 8 hours OR 25-45 mg/kg per day given every 12 hours.

2 years-10 years: 5-10 ml (1-2 Teaspoonful), every 8 hours.

1 month-2 years: 2.5-5 ml (Half-One Teaspoonful), every 8 hours.

4.3 Contraindications:

Annmox should not be given to patients with known hypersensitivity to penicillin or cephalosporin. Cases of cross sensitivity have been reported. It should not be given to babies born of hypersensitive mothers in the neonatal period.

It should not be given to patients with infectious mononucleosis, lymphatic leukaemia, HIV infection or myasthenia gravis. It should be given with care to patients with poor renal function.

4.4 Special warnings and precautions for use:

Special care must be taken with Annmox suspension, especially in patients taking other antibacterial which are bacteriostatic in mode of action.

Annmox should not be administered concomitantly with other antibacterial drugs that are bacteriostatic in nature.

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

Renal and haematological systems should be monitored during prolonged and high dose therapy.

Warnings: Annmox may cause anaphylactic reactions inpatients intolerant to penicillin.

Do not administer to babies and children who are allergic to penicillin or cephalosporin.

Important information about some of the ingredients of ANNMOX (Amoxicillin) suspension.

Sucrose: This should be taken into account in patients with diabetes mellitus.

4.5 Interaction with other medicinal products and other forms of interaction

Annmox interacts with certain drugs such as birth control pills, Probenecid, Warfarin, other antibiotics such as Doxycycline and Tetracycline.

4.6 Pregnancy and lactation

Pregnancy

Annmox suspension is a drug that is administered to neonates. Its use in pregnancy therefore may be considered to be safe.

Breast-feeding

Annmox suspension is a drug that is administered to neonates. Its use in breast feeding mothers therefore may be considered to be safe.

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 and use machines.

4.8 Undesirable effects

Like all medicines, Annmox suspension can cause side effects, although not everybody gets them. Do not be alarmed by this list of possible side effects. You may not form experience any of them.

Common side effects include nausea, vomiting and diarrhoea.

Severe side effects include.

- Bloody or watery stools with or without stomach cramps.
- Severe allergic reaction with symptoms such as swelling of the tongue and throat, difficult breathing, swelling of hands, feet and other body parts.
- Severe skin rash.
- Yellowing of the child's skin and the whites of the eyes. This can be a sign of liver problems.
- Brown, yellow or grey staining of the child's teeth.
- Unusual bleeding and bruising.

4.9 Overdose

Taking an overdose of the suspension can be harmful. See side effects and precautions:

1. Tell your doctor, pharmacist or nearest hospital casualty department immediately.
2. Take the bottle and any remaining suspension with you so that people can see what you have taken.
3. Do this even if the patients feels well.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC-Code: J01CA04

Pharmacotherapeutic group: Beta-lactam antibacterials, Penicillins with extended spectrum.

Mode of action

Amoxicillin is an aminobenzyl penicillin that has a bactericidal action due to its inhibition of the synthesis of the bacterial cell wall.

PK/PD relationship

For amoxicillin, time above MIC (T>MIC) is the key pharmacodynamic parameter in predicting a successful clinical and bacteriological outcome.

Mechanism of resistance

Bacteria may be resistant to amoxicillin due to production of beta-lactamases which hydrolyse aminopenicillins, due to alteration in penicillin-binding proteins, due to impermeability to the drug, or due to drug efflux pumps. One or more of these mechanisms may co-exist in the same organism, leading to a variable and unpredictable cross-resistance to other beta-lactams and to antibacterial drugs of other classes.

***Breakpoints* (EUCAST)**

Organism	Susceptibility Breakpoints (µg/ml)		
	Susceptible	Intermediate	Resistant
Haemophilus influenzae	≤ 1	-	> 1
Moraxella catharrhalis	≤ 1	-	> 1
Enterococcus	≤ 4	8	> 8
Streptococcus A, B, C, G[1]	≤ 0.25	-	> 0.25
Streptococcus pneumoniae[2]	≤ 0.5	1-2	> 2

Enterobacteriaceae[3]	-	-	> 8
Gram-negative anaerobes	≤ 0.5	-	> 2
Gram-positive Anaerobes	≤ 4	8	> 8
Non-species related breakpoints	≤ 2	4-8	> 8

[1] Breakpoint values in the table are based on Benzylpenicillin breakpoints.

[2] Breakpoint values in the table are based on ampicillin breakpoints.

[3] The resistant breakpoint of R>8 mg/L ensures that all isolates with resistance mechanisms are reported resistant.

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Aerobic Gram-positive *Corynebactierum diphteriae* *Enterococcus faecalis* [$] *Listeria monocytogenes* *Streptococcus agalactiae* *Streptococcus bovis* *Streptococcus pyogenes* * Aerobic Gram-negative *Helicobacter pylori* Anaerobes *Peptostreptococci* Others *Borrelia*
Species for which acquired resistance may be a problem
Aerobic Gram-positive *Corynebacterium spp* *Enterococcus faecium* [$]

Streptococcus pneumoniae * +
Streptococcus viridans
Aerobic Gram-negative
Escherichia coli +
Haemophilus influenzae *
Haemophilus para-influenzae *
Moraxella catarrhalis +
Proteus mirabilis
Anaerobes
Prevotella
Fusobacterium spp
Inherently resistant organisms
Aerobic Gram-positive
Staphylococcus aureus
Aerobic Gram-negative
Acinetobacter spp
Citrobacter spp
Enterobacter spp
Klebsiella spp
Legionella
Morganella morganii
Proteus vulgaris
Providencia spp
Pseudomonas spp
Serratia spp
Anaerobes
Bacteroides fragilis
Others
Chlamydia
Mycoplasma
Rickettsia

* Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications

+ pathogens resistance prevalence is > 50%

$ Naturally intermediate species

5.2 Pharmacokinetic properties

Absorption:

The absolute bioavailability of amoxicillin depends on the dose and ranges between 75 and 90%. In the dose range between 250 mg and 1000 mg the bioavailability (parameters: AUC and Cmax) is linearly proportional to the dose. At higher doses the extent of absorption decreases. The absorption is not affected by concomitant food intake. Oral administration of a single dose of 500 mg amoxicillin results in plasma concentrations of 6 - 11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasma concentrations reach 27 mg/l. Peak plasma concentrations are present about 1-2 hours after administration.

Distribution:

Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine. In healthy meninges amoxicillin diffuses badly in liquor cerebrospinalis. Amoxicillin crosses the placenta and a small percentage is excreted into the breast milk.

Biotransformation and elimination:

The main route of excretion of amoxicillin is the kidney. About 60-80% of an oral dose of amoxicillin are excreted in unchanged active form in the urine within 6 hours of administration, and a small fraction is excreted in the bile. Approximately 7 - 25% of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is approximately 1 – 1,5 hour. In patients with end-stage renal failure the half-life ranges between 5 to 20 hours. The substance is haemodialysable.

Pediatric population

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75 – 2 ml/min, very similar to the inulin clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the decreased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished by decreased bioavailability when given orally.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6. Pharmaceutical particulars

6.1 List of excipients

Aerosil 200
Citric Acid
Methyl Paraben
Propyl Paraben
Sodium Citrate
Sodium CMC (MVP)
Sugar Pharmagrade
Colour Tatrazine Supra
Dry Flavour Pineapple
Dry Flavour Raspberry

6.2 Incompatibilities

None

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in cool and dry place, Temperature below 30^0C. Protect from Moisture.

6.5 Nature and contents of container

100 ml HDPE White Bottle

7. MARKETING AUTHORISATION HOLDER

ANNIE PHARMA LIMITED

Plot 6 Abimbola Street, Isolo Industrial Estate, Isolo, Lagos, Nigeria

E-mail: contactus@jawasil.com

8. MANUFACTURED BY:

JAWA INTERNATIONAL LIMITED

Plot 6 Abimbola Street, Isolo Industrial Estate, Isolo, Lagos, Nigeria

Phone: +2348073894283. E-mail: contactus@jawasil.com

9.MARKETING AUTHORISATION NUMBER(S)

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10. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

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11. DATE OF REVISION OF THE TEXT

July 25, 2018

Legal Classification

POM: Prescription Only Medicine

Not to be sold without the prescription of a Registered Medical Practitioner.