ANPRODROXIL GRANULES FOR ORAL SUSPENSION 125mg/5ml

NAME AND STRENGTH OF ACTIVE SUBSTANCE:
Each 5ml of reconstituted suspension contains Cefadroxil (base) 125mg

PRODUCT DESCRIPTION:
Red granules with raspberry & strawberry flavour and sweet taste.
When reconstituted with water, the product is converted into palatable suspension for oral administration.

PHARMACODYNAMICS :
Cefadroxil belongs to the first generation cephalosporins. It is broad spectrum in activity. It is active *in vitro* against many Gram-positive aerobic cocci but has limited activity against Gram-negative bacteria. The beta-lactam ring of the structure is the chemical group associated with antibacterial activity. The final reaction in bacterial cell-wall synthesis is a cross-linking of adjacent peptidoglycan strands by transpeptidation reaction. This reaction involves cleavage of the terminal alanine from the penta-peptide attached to N-acetylglucosamine. A pentapeptide bridge is then added between the remaining D-alanine on one linear peptide and L-lysine on another linear peptide, thus completing the cross-linking of the adjacent peptidoglycan polymers. The cephalosporins are structurally similar to the terminal D-alanyl-D-alanine portion and, therefore can compete for and bind to proteins (enzymes) that catalyse transpeptidation and cross-linking. These proteins are called penicillin-binding proteins (PBPs) and consists of transpeptidases, transglycosylases and D-alanine carboxykinases. The transpeptidases have different function in the cells, and selective inactivation of each transpeptidases results in different effect on the bacterial cells. Interference with the PBPs responsible for the cross-linking of the peptidoglycan polymers results in the formation of a structurally weakened cell wall and, ultimately, cell death.

PHARMACOKINETICS:
Cefadroxil is acid-stable and rapidly and almost completely absorbed from the gastro-intestinal tract. The rate of absorption and peak plasma concentrations are not affected when administered with food. Peak plasma concentrations are reached within 1 – 2 hours and average about 10 – 18µg/ml following oral administration of a single 500mg dose in normal healthy adults with normal renal function. In children of 13 months to 12 years old (with normal renal function), the peak plasma concentrations were attained within 1 hour, averaged 13.7µg/ml after a single oral dose of 15mg/kg.
The plasma half-life of cefadroxil is about 1.5 hours and is prolonged in patients with impaired renal function. More than 90% of a dose of cefadroxil is excreted unchanged in urine, normally within 24 hours by glomerular filtration and tubular secretion. Cefadroxil is removed by hemodialysis. It is also widely distributed to the body tissue and fluids. It crosses placenta and appears in breast milk.

INDICATION:
For the treatment of group A β-hemolytic streptococcal pharyngitis and tonsilitis. It is also used in the treatment of skin and skin structure infections caused by susceptible staphylococci or streptococci and urinary tract infections caused by susceptible organisms (e.g. *E.coli, Proteus mirabilis, Klebsiella*).

RECOMMENDED DOSAGE:
To be taken orally.

i) Adults: 1 – 2 g daily given as a single dose or in 2 equally divided doses.
Uncomplicated lower UTI (i.e. cystitis) : 1 or 2g per day in single or 2 equally divided doses.
All other UTIs : 2g per day in 2 equally divided doses.
Skin & skin structure infections : 1g daily given in a single dose or in 2 equally divided doses.
Group A β-hemolytic streptococcal pharyngitis or tonsilitis : 1g daily as a single dose or in 2 equally divided doses.

ii) Paediatric Dosage : Above 6 years : 500mg (20ml) twice daily.
1 to 6 years : 250mg (10ml) twice daily
infant under 1 year : 25 mg (1ml) / kg daily in divided doses.

Doses should be reduced in patients with impaired renal function, usually when the creatinine clearance is 50ml or less per minute. The following dosage intervals are recommended based on the patient's creatinine clearance :

Creatinine Clearance (ml/min)	*Dosage Interval*
25 – 50	every 12 hours
10 – 25	every 24 hours
0 – 10	every 36 hours

ROUTE OF ADMINISTRATION:
Oral route.

CONTRAINDICATIONS:
Known hypersensitivity to penicillin or with known history of allergy to any of the cephalosporins. Cefadroxil was considered to be unsafe in patients with acute porphyria.

WARNINGS AND PRECAUTIONS:

1. Prolonged use results in overgrowth of resistant organisms.
2. Reduced dosage is recommended in patients with impaired kidney function.
3. Patients who have experienced severe or immediate hypersensitivity reactions to a penicillin should not be given cephalosporin because there is cross-reactivity in 4 – 5% of persons.
4. Caution in individual with a history of gastro-intestinal disease, particularly colitis.

INTERACTIONS WITH OTHER MEDICAMENTS:

1. The urine of patients taking cefadroxil may give a false positive reaction for glucose with copper-reduction reagents.
2. Positive results to the Coomb's test have been reported with cefadroxil.
3. Probenecid delays urinary excretion.
4. Combined use of a cephalosporin with an aminoglycoside enhances the renal toxicity of each.

PREGNANCY AND LACTATION:

1. The safety in pregnancy has not been established.
2. Care should be taken in nursing mothers as small quantities are found in milk of nursing mothers.

SIDE EFFECTS:

1. Hypersensitivity reaction: Allergies (in the form of rash, urticaria, angioedema, and pruritis) have been observed. These reactions usually subside upon discontinuation of the drug. Anaphylaxis has also been reported.
2. Gastrointestinal : nausea, vomiting and diarrhoea and abdominal discomfort.
3. Hematologic : rises in serum aminotransferases have been noted. Eosinophilia and neutropenia have occurred in a few patients.
4. Renal : nephrotoxicity occurs but is usually reversible.
5. Others : superinfection with resistant microorganisms particularly *Candida*, may follow treatment.
6. Pseudomembranous colitis has been reported.

SYMPTOMS AND TREATMENT OF OVERDOSE:

Symptoms : Convulsions and other signs of CNS toxicity have been associated with high doses, especially in patients with renal failure.

Treatment : Symptomatic treatment as there is no specific antidote available.
Absorption of drug from the gastro-intestinal tract may be decreased by giving activated charcoal, which in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric or charcoal. Forced diuresis, peritoneal dialysis, or charcoal hemoperfusion have not been established as beneficial for an overdose of Cefadroxil; however, it would be extremely unlikely that one of these procedures would be indicated.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not applicable

PRECLINICAL SAFETY DATA

Not applicable

INSTRUCTION FOR USE

Directions for Reconstitution/Mixing of Oral Suspensions:

Add sufficient water (about 30ml distilled or boiled water, cooled to room temperature), close bottle and shake vigorously, and make up volume to 60ml mark with water. Shake well before each dose.

DOSAGE FORMS AND PACKAGING AVAILABLE:

Dosage Form : Granules for Oral Suspension
Pack size : 60ml in plastic bottle (after reconstitution)

NAME AND ADDRESS OF MANUFACTURER / PRODUCT REGISTRATION HOLDER:

MALAYSIAN PHARMACEUTICAL INDUSTRIES SDN BHD (101323-U)
Plot 14, Lebuhraya Kampung Jawa,11900 Bayan Lepas,
Pulau Pinang, Malaysia.

DATE OF REVISION:

19/09/2019