FINAL PACKAGE INSERT 26 October 2018

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

CO-AFARIS PAED 75/50/150 (dispersible tablet)

COMPOSITION

CO-AFARIS PAED 75/50/150

Each dispersible tablet contains rifampicin 75 mg, isoniazid 50 mg pyrazinamide 150 mg.

The other ingredients are microcrystalline cellulose, crospovidone, povidone, bleached shellac, croscarmellose sodium, strawberry flavour, magnesium stearate.

Contains aspartame. Sugar free.

PHARMACOLOGICAL CLASSIFICATION

A 20.2.3 Tuberculostatic

PHARMACOLOGICAL ACTION

Antimicrobial medicine.

Pharmacodynamic properties:

CO-AFARIS PAED 75/50/150 is a combination of three medicines used in the treatment of tuberculosis. Rifampicin and pyrazinamide are bactericidal anti-tuberculosis medicines. Isoniazid is bactericidal for rapidly dividing micro-organisms and bacteriostatic for resting bacilli.

Rifampicin

Rifampicin inhibits the growth of *Mycobacterium tuberculosis*. Rifampicin binds to the β subunit of DNA-dependent RNA polymerase (*rpoB*) to form a stable medicine-enzyme complex. Rifampicin binding suppresses chain formation in RNA synthesis.

Isoniazid

Isoniazid is bactericidal and the mechanism of action is by entering the bacilli through passive diffusion. Isoniazid then inhibits the biosynthesis of mycolic acids which are essential

components of the cell wall of *Mycobacterium tuberculosis,* leading to bacterial cell death.

Pyrazinamide

Pyrazinamide is the pyrazine analogue of nicotinamide. The mechanism of action is unknown, however, three mechanisms have been proposed:

- Inhibition of fatty acid synthase type I leading to interference with mycolic acid synthesis
- Reduction of intracellular pH
- Disruption of membrane transport by HPOA (protonated pyrazinoic acid).

Pharmacokinetic properties:

Rifampicin

Absorption

Rifampicin is readily absorbed from the gastrointestinal tract with an oral bioavailability of 68 % for a 150 mg dose, C_{max} of approximately 2,1 µg/mL and t_{max} of 1,5 – 2,0 hours. Absorption of rifampicin is reduced by about 30 % when ingested with food.

Distribution

Rifampicin is widely distributed throughout the body and has good penetration into many tissues, but levels in CNS reach only approximately 5 % of those in plasma. Rifampicin is about 85 % protein bound.

Metabolism

Rifampicin is metabolised by microsomal β-esterases and cholinesterases that remove the acetyl group at position 25, resulting in 25-*O*-desacetyl rifampicin. Rifampicin is also metabolised by hydrolysis to 3-formyl rifampicin. A major pathway for rifampicin elimination is CYP3A. Due to autoinduction, rifampicin reduces its own area under concentration-time curve (AUC) with repeated administration.

Elimination

The half-life of rifampicin ranges from 2 – 5 hours. Rifampicin and its metabolites are excreted by bile and eliminated via faeces, with urine elimination accounting for one–third and less of metabolites.

Isoniazid

Absorption

Isoniazid is readily absorbed from the gastrointestinal tract with an oral bioavailability of 100 % for a 300 mg dose; C_{max} of 3,4 – 7,4 µg/mL for rapid acetylators and C_{max} of 5,2 – 9 µg/mL for slow acetylators; t_{max} of 1,1 ± 0,5 hours for rapid acetylators and 1,1 ± 0,6 hours for slow acetylators . Absorption of isoniazid is decreased by food and antacids.

Distribution

The ratio of isoniazid in the epithelial lining fluid to that in plasma is 1 – 2 and for CSF is 0,9. Approximately 10 % of isoniazid is protein bound.

Metabolism

Isoniazid is metabolised by hepatic arylamine *N*-acetyltransferase type 2 (NAT2). Isoniazid is N-acetylated to N-acetylisoniazid in reactions that uses acetyl-coA. Acetylisoniazid is excreted by the kidney; acetylisoniazid can also be converted to acetylhydrazine and then to hepatoxic metabolites by CYP2E1. Alternatively, acetylhydrazine may be further acetylated by NAT2 to diacetylhydrazine, which is non-toxic.

Isoniazid clearance in patients is classified as one of two phenotypic groups: “slow” acetylators and “fast” acetylators. Rapid acetylators will remove acetylhydrazine while slower acetylators or induction of CYP2E1 will lead to more toxic metabolites.

Elimination

The half-life of isoniazid ranges from 1,1 ± 0,1 hours for rapid acetylators and 3,1 ± 1,1 for slow acetylators. From 75 – 95 % of a dose of isoniazid is excreted in the urine within 24 hours, mostly as acetylisoniazid and isonicotinic acid.

Pyrazinamide

Absorption

Pyrazinamide oral bioavailability is > 90 % for a 500 mg dose; C_{max} of approximately 12 to 14 µg/mL; t_{max} of 1,6 ± 0,94 hours.

Distribution

Pyrazinamide is concentrated 20-fold in the lung epithelial lining fluid. Approximately 10 % of pyrazinamide is protein bound.

Metabolism

Pyrazinamide is metabolised by microsomal deamidase to pyrazinoic acid (POA) and subsequently hydroxylated to 5-hydroxy-POA, which is then excreted by the kidneys.

Elimination

Cℓ (clearance) and V_d (volume of distribution) increase with patient mass (0,5 ℓ/hour and 4,3 ℓ for every 10 kg above 50 kg and V_d is large in males (by 45 ℓ). The $t_{½}$ of pyrazinamide will vary based on weight and gender. Pyrazinamide clearance is reduced in renal failure, therefore, the dosing frequency is reduced to three times a week in at low glomerular filtration rates. Haemodialysis, removed pyrazinamide, therefore, re-dosing is required after each session of haemodialysis.

INDICATIONS

CO-AFARIS PAED 75/50/150 is indicated for pulmonary tuberculosis in children.

CONTRAINDICATIONS

CO-AFARIS PAED 75/50/150 is contraindicated in patients with a history of hypersensitivity to rifamycins or isoniazid or pyrazinamide and other chemically related medicines or to any of the excipients of **CO-AFARIS PAED 75/50/150**.

It is contraindicated in the presence of jaundice or in patients with hepatic impairment.

Pregnancy and lactation (see **HUMAN REPRODUCTION**).

CO-AFARIS PAED 75/50/150 is contraindicated in patients with moderate to severe renal or hepatic impairment, diabetes mellitus, chronic alcoholism, a history of gout, patients suffering from convulsive disorders and porphyria.

The concomitant use of **CO-AFARIS PAED 75/50/150** and nevirapine, saquinavir, ritonavir is contraindicated.

WARNINGS AND SPECIAL PRECAUTIONS

Rifampicin:

Patients with impaired liver function should not be given **CO-AFARIS PAED 75/50/150**. Should **CO-AFARIS PAED 75/50/150** be the only treatment option in these patients, careful monitoring of liver function, especially serum glutamic pyruvic transaminase ALT and serum glutamic oxaloacetic transaminase AST, should be carried out prior to therapy and repeated every two to

four weeks during therapy. If signs of hepatocellular damage occur, **CO-AFARIS PAED 75/50/150** should be withdrawn (see **CONTRAINDICATIONS**).

A report showing a moderate rise in bilirubin and/or transaminase level in itself is not an indication for interruption of treatment. This decision should rather be made after repeating the tests, noting trends in the levels and considering them in conjunction with the patient's clinical condition.

Liver function should be checked before and during treatment with **CO-AFARIS PAED 75/50/150** and special care should be taken in alcoholic patients or those with pre-existing liver disease should **CO-AFARIS PAED 75/50/150** be the only treatment option (see **CONTRAINDICATIONS**). Dosage adjustment is necessary where there is evidence of hepatic function impairment and treatment may need to be changed where there is more serious liver toxicity. Blood counts should be monitored during prolonged treatment and in patients with hepatic disorders. If other serious complications arise, e.g. renal failure or haemolytic anaemia, **CO-AFARIS PAED 75/50/150** should be stopped and never restarted.

Patients should be advised that discolouration of the urine, faeces, saliva, sputum, sweat and tears may occur. Patients should be further advised that soft contact lenses may be permanently stained.

Rifampicin has enzyme induction properties that can enhance the metabolism of endogeneous substrates including adrenal hormones, thyroid hormones and vitamin D.

Isoniazid:

Use of isoniazid as contained in **CO-AFARIS PAED 75/50/150** is contraindicated in patients with chronic liver disease or renal dysfunction. Should **CO-AFARIS PAED 75/50/150** be the only treatment option, these patients should be carefully monitored. Severe and sometimes fatal hepatitis associated with isoniazid therapy may occur and may even develop after many months of treatment. The risk of developing hepatitis is age related. Patients should be monitored for prodromal symptoms of hepatitis, such as fatigue, weakness, malaise, anorexia, nausea or vomiting. If these symptoms appear or if signs suggestive of hepatic damage are detected,

treatment should be discontinued promptly. Continued use of **CO-AFARIS PAED 75/50/150** in these cases may cause a more severe form of liver damage (see **CONTRAINDICATIONS**).

Liver function should be checked before and during treatment with **CO-AFARIS PAED 75/50/150** and special care should be taken in alcoholic patients or those with pre-existing liver disease should **CO-AFARIS PAED 75/50/150** be the only treatment option (see **CONTRAINDICATIONS**).

Periodic eye examinations during **CO-AFARIS PAED 75/50/150** treatment have been suggested.

Vitamin B_6 in a dose of 15 to 50 mg per day should be administered with isoniazid therapy to minimise adverse reactions in malnourished patients and those predisposed to neuropathy.

Use of isoniazid should be carefully monitored in patients with slow acetylators status (see Pharmacokinetic properties), history of psychosis, history of peripheral neuropathy and HIV infection.

Pyrazinamide:

Pyrazinamide as contained in **CO-AFARIS PAED 75/50/150** should be used with caution in patients with a history of gout. If hyperuricaemia accompanied by an acute gouty arthritis occurs, the patient should be transferred to a regimen not containing pyrazinamide.

Liver function should be assessed before and regularly during treatment in all patients. Caution should be observed in patients with impaired renal function.

Diabetes mellitus may become difficult to control in patients who are receiving **CO-AFARIS PAED 75/50/150**.

Effects on ability to drive and use machines

CO-AFARIS PAED 75/50/150 may cause dizziness, impaired concentration, and/or drowsiness. Patients should be instructed that if they experience these symptoms they should avoid potentially hazardous tasks such as driving or operating machinery.

Phenylketonurics:

Phenylketonuric patients should be advised that **CO-AFARIS PAED 75/50/150** contain phenylalanine (a component of aspartame).

INTERACTIONS

Rifampicin:

The concomitant use of **CO-AFARIS PAED 75/50/150** and nevirapine is contraindicated.

When **CO-AFARIS PAED 75/50/150** is given concomitantly with the combination of saquinavir/ritonavir the potential for hepatotoxicity is increased. Therefore, concomitant use of saquinavir/ritonavir is contraindicated.

Halogenated inhalation anaesthetics, when given concomitantly with rifampicin has been reported to increase the hepatotoxicity of both rifampicin and isoniazid.

Ketoconazole has been reported to diminish the serum concentrations of both medicines when given concomitantly.

Rifampicin has liver-enzyme inducing properties and may reduce the activity of azathioprine, chloramphenicol, cimetidine, clofibrate, corticosteroids, coumarin anticoagulants, ciclosporin, dapsone, diazepam, doxycycline, fluconazole, haloperidol, hexobarbitone, itraconazole, ketoconazole, methadone, oral hypoglycaemic medicines, phenytoin, quinine, sulphasalazine, thyroid hormones, theophylline, zidovudine, and several cardiovascular medicines including beta-adrenoceptor blocking medicines, digoxin, and antidysrhythmic medicines such as disopyramide, lorcainide, mexiletine, propafenone, quinidine, tocainide, and verapamil and other calcium-channel blocking medicines, oral contraceptives, narcotics, analgesics and barbiturates. It may be necessary to adjust the dosage of these medicines if they are given concurrently with **CO-AFARIS PAED 75/50/150.** Patients using oral contraceptives should be advised to change to non-hormonal methods of birth control during therapy with **CO-AFARIS PAED 75/50/150**.

Magnesium trisilicate, aluminium hydroxide or sodium bicarbonate reduce the bioavailability of **CO-AFARIS PAED 75/50/150**.

Alcohol

Concurrent daily consumption of alcohol may increase the risk of rifampicin-induced hepatotoxicity and increased the metabolism of rifampicin. Dosage adjustments of rifampicin may be necessary and patients should be monitored closely for signs of hepatotoxicity.

Corticosteroids

Concurrent use with rifampicin may enhance the metabolism of corticosteroids by induction of hepatic microsomal enzymes, resulting in a decrease in corticosteroid plasma concentration. Dosage adjustment of the corticosteroid may be required.

Anti-retroviral medicines

Rifampicin as contained in **CO-AFARIS PAED 75/50/150** can induce the metabolism of zidovudine, the NNRTI's delavirdine, efavirenz and nevirapine (see **CONTRAINDICATIONS**) and the HIV-protease inhibitors, resulting in subtherapeutic plasma concentrations. Furthermore, HIV-protease inhibitors inhibit the metabolism of rifampicin resulting in elevated plasma-rifampicin concentrations and an increased incidence of adverse effects.

Rifampicin as contained in **CO-AFARIS PAED 75/50/150** decreases the concentration of efavirenz and it is recommended that the dose of efavirenz be increased in patients weighing more than 60 kg; no dose modification is required for rifampicin as contained in **CO-AFARIS PAED 75/50/150**.

Isoniazid:

Isoniazid is known to inhibit and rifampicin to induce certain cytochrome P-450 enzymes. In general, the impact of the competing effects of rifampicin and isoniazid on the metabolism of medicines that undergo biotransformation through the affected pathways is unknown. Therefore, caution should be used when prescribing **CO-AFARIS PAED 75/50/150** with medicines metabolised by cytochrome P-450. To maintain optimum therapeutic blood levels, the dosages of these medicines metabolised by these enzymes may require adjustment when starting or stopping **CO-AFARIS PAED 75/50/150**.

As isoniazid is an inhibitor of hepatic metabolism of medicines it may therefore enhance the effects of some medicines taken concomitantly.

Adverse reactions have occurred when isoniazid has been given with phenytoin, primidone, carbamazepine, ethosuximide, benzodiazepines such as diazepam or triazolam and warfarin. Appropriate adjustments of the doses of the anticonvulsants should be made.

Theophylline plasma concentrations can be increased.

Increased central nervous system adverse effects have occurred when isoniazid is given with cycloserine and disulfiram.

Isoniazid can be affected by compounds such as alcohol, alfentanil, aminosalicylic acid, corticosteroids, ketoconazole, propranolol and large doses of pyridoxine.

Oral absorption of isoniazid as contained in **CO-AFARIS PAED 75/50/150** is reduced by aluminium-containing antacids; **CO-AFARIS PAED 75/50/150** should be given at least 1 hour before the antacid.

Concurrent use of **CO-AFARIS PAED 75/50/150** with chronically used paracetamol, alcohol and other hepatotoxic medicines may increase the potential for isoniazid induced hepatotoxicity.

Anti-retroviral medicines

The clearance of isoniazid is approximately doubled when given concomitantly with zalcitabine.

CO-AFARIS PAED 75/50/150 should be used with caution with stavudine and zalcitabine as stavudine, zalcitabine and isoniazid have been associated with causing peripheral neuropathy. The use of **CO-AFARIS PAED 75/50/150** with stavudine has been reported to increase the incidence of peripheral neuropathy.

Food interactions:

Due to some monoamine oxidase inhibiting activity of isoniazid, an interaction with tyramine-containing foods (cheese, red wine) may occur. Diamine oxidase may also be inhibited, causing exaggerated response (e.g. headache, sweating, palpitations, flushing, hypotension) to foods containing histamine (e.g. skipjack, tuna, other tropical fish). Tyramine- and histamine-containing foods should be avoided by patients receiving **CO-AFARIS PAED 75/50/150**.

Pyrazinamide:

Combinations containing any of the following medicines may also interact with pyrazinamide as contained in **CO-AFARIS PAED 75/50/150:**

Sulfinpyrazone, allopurinol, colchicine and probenecid*:*

Pyrazinamide may increase serum uric acid concentrations and decrease the efficacy of the gout therapy of allopurinol, colchicine, probenecid or sulfinpyrazone. Dosage adjustments of these medicines may be necessary to control hyperuricaemia and gout when antigout medicines are used concurrently with **CO-AFARIS PAED 75/50/150**.

Ciclosporin:

Concurrent use with **CO-AFARIS PAED 75/50/150** may decrease the serum concentrations of ciclosporin, leading to inadequate immunosuppression. Ciclosporin serum concentrations should be monitored when used concurrently with **CO-AFARIS PAED 75/50/150**.

HUMAN REPRODUCTION

Safety during pregnancy and lactation has not been established.

Rifampicin, isoniazid and pyrazinamide cross the placenta and all three active ingredients are excreted in breastmilk.

DOSAGE AND DIRECTIONS FOR USE

The South African TB control programme defines daily dosage as 5 days per week.

CO-AFARIS PAED 75/50/150 is recommended in the initial intensive phase of the short course treatment of pulmonary tuberculosis. During this phase, which lasts for 2 months, **CO-AFARIS PAED 75/50/150** should be administered on a continuous daily basis. When indicated, other antituberculosis medicines such as streptomycin may be added.

The total dosage requirement is as follows:

	Daily	Maximum daily dose
Rifampicin	15 mg/kg (10 to 20)	600 mg
Isoniazid	10 mg/kg (7 to 15)	300 mg

Pyrazinamide	35 mg/kg (30-40) ,	2 g

The daily dosage is calculated from the recommended daily requirement given above and to closely regulate dosage according to body mass.

Table 1: Dosage calculation

Number of tablets	**For infants/children with body mass (kg)**
1 tablet	4 - 7
2 tablets	8 - 11
3 tablets	12 - 15
4 tablets	16 - 24
Adult dosages recommended	25 +

The tablets can either be dispersed in as little as 5 ml of water, or chewed, and should preferably be taken on an empty stomach as a single dosage.

Chemoprophylaxis: Children less than 5 years of age in close household contact with a smear positive case of pulmonary TB should be treated with rifampicin/isoniazid for a period of 3 months. Routine chemoprophylaxis of those older than 5 years is not recommended.

CO-AFARIS PAED 75/50/150 should be taken at least 1 hour before aluminium containing antacids are used.

SIDE EFFECTS

RIFAMPICIN

Blood and lymphatic system disorders:

Less frequent: Blood dyscrasias, unusual bleeding or bruising, thrombocytopenia, purpura, haemolysis, eosinophilia, leucopenia, haemolytic anaemia.

Immune system disorders:

Frequency not known: Anaphylaxis and shock.

Nervous system disorders:

Less frequent: Confusion, drowsiness, headache, ataxia, dizziness, peripheral neuropathy and generalised numbness.

Eye disorders:

Less frequent: Blurred vision, eye irritation.

Ear and labyrinth disorders:

Less frequent: Transient hearing loss.

Respiratory, thoracic and mediastinal disorders:

Frequency not known: Pulmonary fibrosis, pneumonitis, shortness of breath and wheezing.

Gastrointestinal disorders:

Frequent: Nausea, vomiting, anorexia, diarrhoea and epigastric distress.

Less frequent: Pseudomembranous colitis.

Frequency not known: Ulcerative colitis, gastrointestinal bleeding.

Hepato-biliary disorders:

Less frequent: Hepatitis (which may be fatal), hepatitis prodromal symptoms which include loss of appetite, nausea or vomiting, unusual tiredness or weakness. A rise in serum transaminase levels.

Skin and subcutaneous tissue disorders:

Frequent: Cutaneous reactions, which typically consist of flushing and itching, with or without a rash.

Less frequent: More serious hypersensitivity cutaneous reactions, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme including Stevens-Johnson syndrome and vasculitis drug reaction with eosinophilia system symptoms (DRESS).

Musculoskeletal and connective tissue disorders:

Frequent: Muscle weakness and myopathy.

Renal and urinary disorders:

Less frequent: Interstitial nephritis, renal failure.

Reproductive system and breast disorders:

Less frequent: Disturbances of the menstrual cycle, reduction of effectiveness of oral contraceptives.

General disorders and administrative site conditions:

Frequent: Reddish-orange to reddish-brown discolouration of the urine, faeces, saliva, sputum, sweat and tears. Soft contact lenses may be permanently stained.

Less frequent: Intermittent, interrupted or repeated treatment of rifampicin may increase the chance of a patient developing flu syndrome, a febrile reaction with influenza-like symptoms, fungal overgrowth i.e. sore mouth or tongue.

ISONIAZID:

Blood and lymphatic system disorders:

Less frequent: Various haematological disturbances including eosinophilia, agranulocytosis, thrombocytopenia and various anaemias.

Immune system disorders:

Less frequent: Hypersensitivity reactions including various skin eruptions, fever, lymphadenopathy and vasculitis, lupus-like reactions.

Metabolism and nutrition disorders:

Less frequent: Hyperglycaemia, metabolic acidosis.

Psychiatric disorders:

Less frequent: Psychotic reactions (characterised by delusions, hallucinations and confusion), memory impairment.

Nervous system disorders:

Frequent: Peripheral neuropathy.

Less frequent: Polyneuritis associated with paraesthesia, muscle weakness, loss of tendon reflexes, convulsions, increase in frequency of fits in epileptic patients, ataxia.

Eye disorders:

Less frequent: Optic neuritis (blurred vision or loss of vision, with or without eye pain).

Ear and labyrinth disorders:

Less frequent: Vertigo.

Gastrointestinal disorders:

Frequent: Diarrhoea, nausea and vomiting, stomach pain, constipation, dry mouth, pancreatitis.

Hepato-biliary disorders:

Frequent: Hepatitis (sometimes fatal), hepatitis prodromal symptoms (loss of appetite, nausea or vomiting, unusual tiredness or weakness), transient increase in liver enzymes.

Skin and subcutaneous tissue disorders:

Less frequent: Skin reactions, pellagra, acne, Steven-Johnsons syndrome, exfoliative dermatitis.

Frequency not known: Alopecia, urticaria.

Musculoskeletal and connective tissue disorders:

Frequency unknown: A rheumatic syndrome, hyperreflexia.

Renal and urinary disorders:

Less frequent: Urinary retention.

Reproductive system and breast disorders:

Less frequent: Gynaecomastia.

Pyrazinamide:

Blood and lymphatic disorders:

Less frequent: Sideroblastic anaemia, thrombocytopenia.

Immune system disorders:

Less frequent: Hypersensitivity reaction.

Metabolism and nutrition disorders:

Less frequent: Pellagra.

Gastrointestinal disorders:

Less frequent: Anorexia, nausea, vomiting, aggravation of peptic ulcer.

Hepato-biliary disorders:

Frequent: Hepatotoxicity (frequency appears to be dose related).

Skin and subcutaneous tissue disorders:

Less frequent: Photosensitivity, skin rash, pruritus.

Musculoskeletal, connective tissue and bone disorders:

Frequent: Arthralgia, which is related to hyperuricaemia.

Less frequent: Gouty arthritis.

Renal and urinary disorders:

Less frequent: Dysuria.

General disorders and administrative site conditions:

Less frequent: Malaise, fever.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Rifampicin: Acute overdosage with rifampicin has produced a characteristic bright-red discolouration of the skin and mucous membranes, sometimes referred to as “the red-man syndrome”, mental obtundation, periorbital or facial oedema and generalised pruritus.

Isoniazid: Symptoms are more likely to be related to isoniazid. These include hyperglycaemia and metabolic acidosis, slurred speech, convulsions, coma, hallucinations, respiratory distress, central nervous system depression; fatalities can occur.

Pyrazinamide

Symptoms may be the exacerbation of side effects.

General: In case of overdosage with **CO-AFARIS PAED 75/50/150** activated charcoal slurry into the stomach may help absorb any remaining medicine from the gastrointestinal tract. Antiemetic medication may be required to control severe nausea and vomiting. Intensive supportive measures should be instituted and individual symptoms treated as they arise. Further treatment is symptomatic and supportive.

If acute overdose is suspected, even in asymptomatic patients, the administration of intravenous pyridoxine (vitamin B6) should be considered. In patients with seizures not controlled with pyridoxine, anticonvulsant therapy should be administered. Sodium bicarbonate should be given to control metabolic acidosis. Haemodialysis is advised for refractory cases: if this is not available, peritoneal dialysis can be used along with forced diuresis.

IDENTIFICATION

CO-AFARIS PAED 75/50/150

Brick red mottled, 11,0 mm circular, uncoated biconvex tablets having deep score on one side and plain surface on other side.

PRESENTATION

CO-AFARIS PAED 75/50/150

HDPE Container:

Tablets are packed in a transparent, self-sealing LDPE polybag and further packed in a silver coloured triple laminated aluminium sachet (LDP/PET/AL), kept in a white plastic container

(HDPE), which is sealed at the mouth with an aluminium tagger and is closed with a white HDPE screw-on lid. Pack sizes include 100 tablets.

Alu-alu strip pack:

Tablets are packed in silver-metallic coloured aluminium foil (soft tempered) laminated with low density polyethylene film as the lidding and forming material. The blister is packed in a pre-printed carton. Pack sizes include 28, 56, 84, 100 and 112 tablets.

STORAGE INSTRUCTIONS

Store at or below 30 °C. Protect from moisture and light.

Keep the aluminium sachet in the HDPE container until required for use.

Keep the blister in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

52/20.2.3/0306

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

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