AFARIS PAED 75/50
PM03052701

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM
AFARIS PAED 75/50 (dispersible tablet)

COMPOSITION
AFARIS PAED 75/50
Each dispersible tablet contains rifampicin 75 mg and isoniazid 50 mg.
The other ingredients are microcrystalline cellulose, crospovidone, povidone, bleached shellac, croscarmellose sodium, raspberry flavour, magnesium stearate.
Contains aspartame. Sugar free.

PHARMACOLOGICAL CLASSIFICATION
A 20.2.3 Tuberculostatic

PHARMACOLOGICAL ACTION
Antimicrobial medicine.
Pharmacodynamic properties
Rifampicin and isoniazid are bactericidal antituberculosis medicines which both act against tuberculosis. 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.

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 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 use 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.

INDICATIONS
AFARIS PAED 75/50 is indicated for pulmonary tuberculosis in children.

CONTRAINDICATIONS
AFARIS PAED 75/50 is contraindicated in patients with a history of hypersensitivity to rifamycins, other rifamycins or isoniazid and other chemically related medicines or to any of the excipients of **AFARIS PAED 75/50**.
It is contraindicated in the presence of jaundice or in patients with hepatic impairment.
AFARIS PAED 75/50 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 **AFARIS PAED 75/50** and nevirapine is contraindicated.
AFARIS PAED 75/50 is contraindicated when given concurrently with the combination of saquinavir/ritonavir (see Interactions).
Pregnancy and lactation (see **HUMAN REPRODUCTION**).

WARNINGS AND SPECIAL PRECAUTIONS
Rifampicin:
Patients with impaired liver function should not be given **AFARIS PAED 75/50**. Should **AFARIS PAED 75/50** 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, **AFARIS PAED 75/50** 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 **AFARIS PAED 75/50** and special care should be taken in alcoholic patients or those with pre-existing liver disease should **AFARIS PAED 75/50** 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. (see **CONTRAINDICATIONS**).
If other serious complications arise e.g. renal failure or haemolytic anaemia, **AFARIS PAED 75/50** should be stopped and never restarted.

Because of the possibility of immunological reactions including anaphylaxis occurring with intermittent therapy (less than 2 to 3 times per week) patients should be closely monitored. Patients should be cautioned against interruption of dosage regimens since these reactions may occur.

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 **AFARIS PAED 75/50** is contraindicated in patients with chronic liver disease or renal dysfunction. Should **AFARIS PAED 75/50** 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 **AFARIS PAED 75/50** in these cases may cause a more severe form of liver damage (see **CONTRAINDICATIONS**).

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

Periodic eye examinations during **AFARIS PAED 75/50** 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.

Effects on ability to drive and use machines
AFARIS PAED 75/50 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 **AFARIS PAED 75/50** contain phenylalanine (a component of aspartame).

INTERACTIONS
Rifampicin:
The concomitant use of **AFARIS PAED 75/50** and nevirapine is contraindicated.
When **AFARIS PAED 75/50** is given concomitantly with the combination of saquinavir/ritonavir, the potential for hepatotoxicity is increased. Therefore, concomitant use of **AFARIS PAED 75/50** with saquinavir/ritonavir is contraindicated.
Halogenated inhalation anaesthetics, when given concomitantly with rifampicin have 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 **AFARIS PAED 75/50**. Patients using oral contraceptives should be advised to change to non-hormonal methods of birth control during therapy with **AFARIS PAED 75/50**.
Magnesium trisilicate, aluminium hydroxide or sodium bicarbonate reduce the bioavailability of **AFARIS PAED 75/50**.

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 **AFARIS PAED 75/50** 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 **AFARIS PAED 75/50** 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 **AFARIS PAED 75/50**.

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 **AFARIS PAED 75/50** 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 **AFARIS PAED 75/50**.
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 **AFARIS PAED 75/50** is reduced by aluminium-containing antacids; **AFARIS PAED 75/50** should be given at least 1 hour before the antacid.
Concurrent use of **AFARIS PAED 75/50** 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.
AFARIS PAED 75/50 should be used with caution with stavudine and zalcitabine as stavudine, zalcitabine and isoniazid have been associated with causing peripheral neuropathy. The use of **AFARIS PAED 75/50** 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 **AFARIS PAED 75/50**.

HUMAN REPRODUCTION
Safety during pregnancy and lactation has not been established.
Rifampicin and isoniazid cross the placenta and both are excreted in breastmilk.

DOSAGE AND DIRECTIONS FOR USE
AFARIS PAED 75/50 is recommended in the continuation phase of the treatment of pulmonary tuberculosis. During this phase **AFARIS PAED 75/50** should be administered on a continuous daily basis.
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

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.

AFARIS PAED 75/50 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. Arise 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 and 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.
Frequency not known: Oedema.

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 increases in liver enzymes.

Skin and subcutaneous tissue disorders:
Less frequent: Skin reactions, pellagra, acne, Stevens-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.

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.
General: In cases of overdosage with **AFARIS PAED 75/50** 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
AFARIS PAED 75/50
Brick red mottled, 9,5 mm circular, uncoated biconvex tablets having deep score on one side and plain surface on other side.

PRESENTATION
AFARIS PAED 75/50
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 and 100 tablets.

STORAGE INSTRUCTIONS
Store at or below 25 °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
51/20.2.3/0852

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
MACLEODS PHARMACEUTICALS SA (PTY) LTD
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SCHEDULING STATUS

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM
AFARIS PAED 75/50 (dispersible tablet)
Rifampicin 75 mg and isoniazid 50 mg

READ ALL OF THIS LEAFLET CAREFULLY BEFORE YOU START GIVING AFARIS PAED 75/50
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **AFARIS PAED 75/50** has been prescribed for your child personally and you should not share your child's medicine with other people. It may harm them, even if their symptoms are the same as your child's.

WHAT AFARIS PAED 75/50 CONTAINS
AFARIS PAED 75/50 contains the active substances rifampicin 75 mg and isoniazid 50 mg.
The other ingredients are microcrystalline cellulose, crospovidone, povidone, bleached shellac, croscarmellose sodium, raspberry flavour, magnesium stearate.
Contains aspartame. Sugar free.

WHAT AFARIS PAED 75/50 IS USED FOR
AFARIS PAED 75/50 is an antimicrobial medicine used in the treatment of pulmonary tuberculosis (TB infection in the lungs) in children.

BEFORE YOU GIVE AFARIS PAED 75/50
Do not give AFARIS PAED 75/50 if your child suffers from any of the conditions mentioned below:
- If your child is hypersensitive (allergic) to rifamycins including rifampicin, isoniazid or other chemically-related medicines such as ethionamide, pyrazinamide, niacin or to any of the ingredients contained in **AFARIS PAED 75/50**.
- If your child has any kind of liver disease or jaundice (yellowing of the eyes and skin).
- **AFARIS PAED 75/50** should not be given with nevirapine, saquinavir and ritonavir (used in HIV treatment).
- Your child has any kidney disease.
- Your child has porphyria.
- Your child has a history of gout.
- Your child is diabetic.
- Your child has epilepsy.
- If your child developed thrombocytopenia and purpura while taking **AFARIS PAED 75/50** (bruising, nosebleeds or bleeding in the mouth and gums, rash with pinpoint red spots).
- If your child is pregnant or breastfeeding her child.

If your child develops itching with swelling or skin rash or difficulty breathing, or if the skin and eyes turn yellow while taking **AFARIS PAED 75/50**, do not give any more **AFARIS PAED 75/50** and tell your doctor immediately.

Take special care with AFARIS PAED 75/50
- Before you give **AFARIS PAED 75/50**, tell your doctor if your child has epilepsy.
- **AFARIS PAED 75/50** should not be given to children whose liver is not functioning normally, however, in cases where there are no other treatment options your doctor will monitor your child's liver function before treatment and every two to four weeks during treatment with **AFARIS PAED 75/50**.
  Tell your doctor immediately and stop giving **AFARIS PAED 75/50** if your child develops symptoms of hepatitis (inflammation of the liver, if left untreated, could lead to serious consequences) such as fatigue, weakness, feeling unwell, loss of appetite, nausea or vomiting.
- Your doctor will be monitoring your child's blood counts if your child has liver disease or is on long-term treatment with **AFARIS PAED 75/50**. If your child develops low platelet counts (blood cells responsible for clotting) with symptoms of easy or excessive bruising, bleeding into the skin that appears as a rash of pinpoint-sized reddish-purple spots usually on the lower legs, prolonged bleeding from cuts, spontaneous bleeding from the gums or nose and blood in urine or stools, then **AFARIS PAED 75/50** should not be given and be permanently withdrawn (see Do not give).
- If other serious complications due to the medicine occur such as kidney failure, or blood diseases, **AFARIS PAED 75/50 should be stopped and never restarted.**
- Urine, faeces, saliva, sputum, sweat and tears may be coloured red-orange by **AFARIS PAED 75/50**.
- Your doctor may prescribe additional blood tests to monitor your child's adrenal hormone, thyroid hormone and vitamin D levels.
- Soft contact lenses may be permanently stained.
- Your doctor may prescribe periodic eye examinations as **AFARIS PAED 75/50** may cause blurred vision or loss of vision with or without eye pain and may also cause irritation of the eyes.
- Your doctor may prescribe Vitamin B_6 (pyridoxine) with **AFARIS PAED 75/50** to minimise adverse reactions if your child is malnourished or has neuropathy (damage to the nerves resulting in poor coordination, muscle weakness, pain in the fingers or toes, or numbness).
- Give **AFARIS PAED 75/50** to your child as prescribed by your doctor on a continuous basis without interruption to avoid developing side effects such as a serious allergic reaction (swelling of the hands, feet, ankles, lips, mouth or throat, which may cause difficulty in breathing, rash and itching) or a "flu-like" syndrome (chills, dizziness, difficulty breathing, fever, headache, muscle pain, bone pain and shivering).

Taking AFARIS PAED 75/50 with food and drink
AFARIS PAED 75/50 should be taken without food. Avoid tyramine-containing foods (e.g. cheese, red wine) and histamine-containing foods (e.g. skipjack, tuna, tropical fish). Avoid alcohol.

Pregnancy and breastfeeding
Safety during pregnancy and breastfeeding has not been established.
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **AFARIS PAED 75/50**.

Driving and using machinery
AFARIS PAED 75/50 may cause dizziness, impaired concentration, and/or drowsiness. If you experience these symptoms, avoid potentially hazardous tasks such as driving or operating machinery.

Important information about some of the ingredients of AFARIS PAED 75/50
Phenylketonurics: Phenylketonuric patients should be advised that **AFARIS PAED 75/50** contain phenylalanine (a component of aspartame).

Giving other medicines with AFARIS PAED 75/50
Always tell your healthcare professional if your child is taking any other medicine. (This includes complementary or traditional medicines).

AFARIS PAED 75/50 may change the effect of other medicines and other medicines may change the effect of **AFARIS PAED 75/50**.
Do not give AFARIS PAED 75/50 and tell your doctor if your child is taking the following medicines:
- Nevirapine, saquinavir and ritonavir (HIV medicines).

The following medicines can make **AFARIS PAED 75/50** work less well:
- Alcohol, alfentanil (for pain during surgery), aminosalicylic acid (TB medicine), corticosteroids such as hydrocortisone, betamethasone and prednisolone (for treating inflammatory conditions), ketoconazole (for fungal infections), propranolol (for high blood pressure) and high doses of pyridoxine (vitamin B_6).
- Antacids containing magnesium trisilicate, aluminium hydroxide or sodium bicarbonate and other aluminium containing antacids for indigestion. Give **AFARIS PAED 75/50** at least 1 hour before the antacid.

When you are giving **AFARIS PAED 75/50**, it is especially important to tell your doctor or healthcare professional if your child is taking any of the following medicines as your doctor may have to adjust the dose of the medicine:
- Medicines used to treat epilepsy such as ethosuximide, phenytoin and carbamazepine.
- Medicines such as itraconazole, fluconazole and ketoconazole used for treating fungal infections.
- HIV medicine such as zidovudine, delavirdine, efavirenz, HIV-protease inhibitors (lopinavir, duranavir, atazanavir, fosamprenavir, indinavir).
- Other medicines include certain anaesthetic medicines (to relax muscles prior to surgery), azathioprine, ciclosporin (immune suppressants), chloramphenicol, cycloserine, dapsone, doxycycline (medicines used for infections), cimetidine (used to treat ulcers), clofibrate (lowers cholesterol), corticosteroids such as hydrocortisone, betamethasone and prednisolone (for treating inflammatory conditions), warfarin (thins blood), diazepam, (for anxiety and depression), haloperidol (for mental illness), hexobarbitone (sedative), methadone (for heroin withdrawal), oral hypoglycaemic medicines used in diabetes treatment), sulphasalazine (used for rheumatoid arthritis and inflammatory bowel disease), Thyroid hormones (levothyroxine), theophylline (for wheezing or difficulty in breathing), quinine (used in malaria), medicines to control your heartbeat such as digoxin, disopyramide, lorcainide, mexiletine, propafenone, quinidine, tocainide, medicines to treat heart problems such as beta blockers (propranolol), verapamil and other calcium channel blocking medicines, medicines used for severe pain such as codeine, morphine, fentanyl or pethidine, medicines used for pain and fever such aspirin and medicines to help you sleep known as barbiturates (e.g. phenobarbitone).
- **AFARIS PAED 75/50** may decrease the effectiveness of oral contraceptives. Use a reliable barrier method of contraception such as condoms while taking **AFARIS PAED 75/50**.

The following when taken with **AFARIS PAED 75/50** may increase the incidence of side effects:
- Medicines used to treat epilepsy such as ethosuximide, phenytoin, primidone and carbamazepine (your doctor will adjust the dose of the epilepsy medication accordingly).
- HIV medicine such as HIV-protease inhibitors (lopinavir, ritonavir, saquinavir, duranavir, atazanavir, fosamprenavir), stavudine and zalcitabine.
- Other medicine such as warfarin (thins blood), diazepam, triazolam (for anxiety and depression), cycloserine (TB medicine), disulfiram (treatment of alcohol dependence), theophylline (for wheezing or difficulty in breathing).
- Alcohol (daily consumption could lead to severe liver problems).

Food interactions:
- **AFARIS PAED 75/50** may interact with tyramine-containing foods (cheese, red wine) and to foods containing histamine (e.g. skipjack, tuna, other tropical fish) resulting in headache, sweating, palpitations (heart beating too hard or too fast), flushing and low blood pressure. Avoid giving tyramine- and histamine-containing foods to your child while on treatment with **AFARIS PAED 75/50**.

HOW TO GIVE AFARIS PAED 75/50
Do not share medicines prescribed for you with any other person.
Always give **AFARIS PAED 75/50** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of **AFARIS PAED 75/50** is too strong or too weak talk to your doctor or pharmacist.

AFARIS PAED 75/50 is recommended in the continuation phase of the treatment of pulmonary tuberculosis. **During this phase AFARIS PAED 75/50 should be given on a continuous daily basis.**

Your doctor will prescribe the required number of tablets to be given on a daily basis based on your child's body weight.
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 (30 minutes before or 2 hours after a meal) as a single dosage. **AFARIS PAED 75/50** should be given at least 1 hour before aluminium containing antacids are taken.

Do not stop giving AFARIS PAED 75/50 because your child feels better.
If the full treatment prescribed by your doctor is not completed, some of the bacteria causing the TB infection may not be killed. These bacteria may continue to grow and multiply so the TB infection may not clear completely or it may return.

If you give more AFARIS PAED 75/50 than you should
In the event of overdosage consult your doctor or pharmacist. If neither is available contact the nearest hospital or poison control center.
Symptoms include nausea, vomiting, stomach pain, dizziness, high blood sugar levels, high levels of acid in the blood, hallucinations, difficulty in breathing and central nervous system depression with seizures and coma. Other signs of overdosage includes bright-red discolouration of the skin and mucous membranes, decreased mental alertness, swelling of the face and "puffy eyes" and generalised itching.
If any of the above symptoms occur, get medical help immediately by calling your nearest doctor or healthcare professional.

If you forget to give your child AFARIS PAED 75/50
If your child has missed a dose of **AFARIS PAED 75/50** give it as soon as you remember. However, if it is almost time for the next dose, skip the missed dose and go back to your regular scheduling. Never double the dose.

POSSIBLE SIDE EFFECTS
AFARIS PAED 75/50 can have side effects.
Not all the side effects reported for **AFARIS PAED 75/50** are included in this leaflet. Should your child's general health worsen or if your child experiences any untoward effects while taking **AFARIS PAED 75/50**, please consult your doctor, pharmacist or healthcare professional for advice.
If any of the following happens, stop taking AFARIS PAED 75/50 and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting
- yellowing of the skin and eyes, also called jaundice

These are all very serious side effects. If you have them, you may have had a serious reaction to **AFARIS PAED 75/50**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- Red and/or itchy skin, blisters or pimples.
- Skin condition with severe blisters and bleeding in the lips, eyes, mouth, nose and genitals (symptoms of Stevens Johnson Syndrome).
- Widespread scaling of the skin with itching, skin redness and hair loss (symptoms of exfoliative dermatitis).
- Shortness of breath and wheezing.
- Lung disease causing coughing, difficulty breathing and wheezing (symptoms of pneumonitis).
- Scarring and thickening in the lungs with shortness of breath (symptoms of pulmonary fibrosis).
- Blood in the urine or any other urination disturbances.
- Fever, chills, headache or dizziness.
- Bone pain.
- Bruising, nosebleeds or bleeding in the mouth and gums, rash with pinpoint red spots.
- Fatigue, weakness, malaise (feeling unwell), anorexia (loss of appetite), nausea or vomiting.
- Abdominal pain, blood in the stool, ongoing bouts of diarrhoea that do not respond to over-the-counter (OTC) medicines or an unexplained fever lasting more than a day or two (symptoms of ulcerative colitis).
- Bleeding from the stomach wall with vomiting blood or material that looks like coffee grounds, bleeding from the back passage, black sticky bowel motions (stools) or bloody diarrhoea.
- Inflammation of the pancreas with severe upper stomach pain, nausea and vomiting.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor immediately if your child has any of the following side effects, particularly if they occur several weeks after stopping treatment with AFARIS PAED 75/50:
- Severe stomach cramps.
- Watery and severe diarrhoea, which may also be bloody.
- Fever, in combination with one or both of the above.

You child may have a serious condition affecting the bowel, which may need urgent medical attention.
Do not give any diarrhoea medicine without first checking with your doctor.

Tell your doctor if you notice any of the following:
Frequently occurring side effects:
- Heartburn, anorexia, nausea, vomiting, wind, cramps or diarrhoea, constipation, dry mouth.
- Skin reactions with flushing and itching, with or without a rash.
- Aching muscles, muscle tenderness or weakness, not caused by exercise.
- Reddish-orange to reddish-brown discolouration of the urine, faeces, saliva, sputum, sweat and tears.
- Soft contact lenses may be permanently stained.
- Numbness or weakness of the arms and legs.
- Increase in liver enzymes.

Less frequent side effects:
- Increase in some white blood cells (eosinophilia).
- Lack of white blood cells resulting in frequent infections such as fever, severe chills, sore throat or mouth ulcers (leucopenia).
- Tiredness, headaches, being short of breath when exercising, dizziness, looking pale and yellowing of the skin and/or eyes (haemolytic anaemia).
- High blood glucose levels.
- High levels of acid in the blood.
- Mental illness with strange or disturbing thoughts or moods.
- Loss of memory.
- Headache, dizziness, drowsiness, fatigue, inability to concentrate or confusion.
- Poor coordination, pain in the fingers or toes, or numbness, unusually increased reflexes or twitching.
- Fits or increase in fits if you are an epileptic patient.
- Blurred vision or loss of vision with or without eye pain, eye irritation.
- Menstrual disturbances.
- Oral contraceptives may become less effective.
- Temporary hearing loss.
- Vertigo (feeling dizzy with a spinning sensation).
- Skin rash, itchy rash, acne, hair loss.
- Enlarged breasts.
- Oral thrush - white, furry, sore tongue and mouth.
- Swelling of hands, ankles or feet.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

STORAGE AND DISPOSAL INFORMATION FOR AFARIS PAED 75/50
Store at or below 25 °C.
Keep the aluminium sachet in the HDPE container until required for use.
Keep the blister in the carton until required for use.
Store this medicine away from light and moisture. Do not store in the bathroom cabinet.
Any expired or outdated medicines and unused medicines can be returned to your nearest pharmacy.
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

PRESENTATION OF AFARIS PAED 75/50
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 and 100 tablets.

IDENTIFICATION OF AFARIS PAED 75/50
Brick red mottled, 9.5 mm circular, uncoated biconvex tablets having deep score on one side and plain surface on other side.

REGISTRATION NUMBER
51/20.2.3/0852

NAME AND BUSINESS ADDRESS OF HOLDER OF THE CERTIFICATE OF REGISTRATION
MACLEODS PHARMACEUTICALS SA (PTY) LTD
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DATE OF PUBLICATION OF THE PATIENT INFORMATION LEAFLET
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SKEDULERINGSTATUS

S4

EIENDOMSNAAM EN DOSEERVORM
AFARIS PAED 75/50 (Orale oplosbare tablet).

SAMESTELLING
AFARIS PAED 75/50
Elke oplosbare tablet bevat rifampisien 60 mg en isoniasied 50 mg.
Die ander bestanddele is mikrokristallyne sellulose, krospovidoon, povidoon, gebleikte skellak, kroskarmellose natrium, framboosgeursel, magnesiumstearaat.
Bevat aspartaam. Suikervry

FARMAKOLOGIESE KLASSIFIKASIE
A 20.2.3 Tuberkulostatiese middels.

FARMAKOLOGIESE WERKING
Antimikrobiese medisyne.
Farmakodinamiese eienskappe
Rifampisien en isoniasied is bakteriedodende anti-tuberkulose medisyne wat beide teen tuberkulose werk. Isoniasied is bakteriedodend teen vinnig verdelende mikroörganismes en bakteriostaties teen rustende basille.

Rifampisien:
Rifampisien inhibeer die groei van *Mycobacterium tuberculosis* isolate. Rifampisien bind aan die β-subeenheid van DNA-afhanklike RNA-polimerase (*rpoB*) om 'n stabiele medisyne-ensiemkompleks te vorm. Rifampisienbinding onderdruk die kettingformasie in RNA sintese.

Isoniasied:
Isoniasied is bakteriedodend en die meganisme van werking is om deur passiewe diffusie in die basille in te dring. Daarna inhibeer isoniasied die biosintese van mikoliensure wat essensiële komponente van die selwand van *Mycobacterium tuberculosis* is en tot bakteriese dood van die sel lei.

Farmakokinetiese eienskappe:
Rifampisien
Absorpsie
Rifampisien word geredelik vanuit die maagdermkanaal geabsorbeer met 'n orale biobeskikbaarheid van 68 % vir 'n 150 mg dosis, K_{max} van 2,1 µg/mL en t_{max} van 1,5 - 2,0 ure. Die absorpsie van rifampisien word met ongeveer 30 % verminder wanneer dit saam met voedsel geneem word.
Verspreiding:
Rifampisien word wyd deur die liggaam versprei en besit goeie penetrasie in baie weefsels. Die vlakke in die SSS bereik egter slegs ongeveer 5 % van dié in die plasma. Rifampisien is ongeveer 85 % proteïengebonde.
Metabolisme:
Rifampisien word deur mikrosomale β-esterases en cholienesterases gemetaboliseer wat die asetielgroep by posisie 25 verwyder. Dit lei tot 25-O-desasetielrifampisien. Rifampisien word ook deur hidrolise na 3-formielrifampisien gemetaboliseer. 'n Belangrike baan vir rifampisienopruiming is CYP3A4. Weens outo-induksie verminder rifampisien met herhaalde toediening sy eie area onder die konsentrasie-tydkurwe (AOK).
Opruiming:
Die halfleeftyd van rifampisien wissel van 2 - 5 ure. Rifampisien en sy metaboliete word deur die gal uitgeskei en deur die feses opgeruim, met urienopruiming wat vir een derde en minder van die metaboliete verantwoordelik is.

Isoniasied:
Absorpsie:
Isoniasied word geredelik vanuit die maagdermkanaal geabsorbeer met 'n orale biobeskikbaarheid van 100 % vir 'n 300 mg dosis; K_{max} van 3,4 - 7,4 µg/mL vir vinnige asetileerders en K_{max} van 5,2 - 9 µg/mL vir stadige asetileerders, t_{max} van 1,1 ± 0,5 ure vir vinnige asetileerders en 1,1 ± 0,6 ure vir stadige asetileerders. Die absorpsie van isoniasied word deur voedsel en teensuurmiddels verminder.
Verspreiding
Die verhouding van isoniasied in die epiteel voeringsvloeistof tot dié in die plasma is 1 - 2 en vir SSV 0,9. Ongeveer 10 % van isoniasied is proteïengebonde.
Metabolisme.
Isoniasied word deur hepatiese arielamien *N*-asetieltransferase tipe 2 (NAT2) gemetaboliseer. Isoniasied word na *N*-asetielisoniasied in reaksies wat asetiel ko-A gebruik, ge-N-asetileer. Asetielisoniasied word deur die niere uitgeskei; asetielisoniasied kan ook na asetielhidrasien en daarna deur CYP2E1 na hepatotoksiese metaboliete omgeskakel word. Alternatiewelik kan asetielhidrasien verder deur NAT2 na diasetielhidrasien, wat nie toksies is nie, geasetileer word. Isoniasiedopruiming in pasiënte word as een of twee fenotipiese groepe geklassifiseer: "stadige" asetileerders en "vinnige" asetileerders. Vinnige asetileerders sal asetielhidrasien vinnig verwyder, terwyl stadige asetileerders of die induksie van CYP2E1 tot meer toksiese metaboliete sal lei.
Opruiming:
Die halfleeftyd van isoniasied wissel van 1,1 ± 0,1 ure vir vinnige asetileerders en 3,1 ± 1,1 vir stadige asetileerders. Van 75 tot 95 % van 'n dosis isoniasied word binne 24 uur in die uriene uitgeskei, hoofsaaklik as asetielisoniasied en isonikotiensuur.

INDIKASIES:
AFARIS PAED 75/50 word aangedui vir longtuberkulose in kinders.

KONTRA-INDIKASIES:
AFARIS PAED 75/50 word teenaangedui in pasiënte met 'n geskiedenis van hipersensitiwiteit teen rifampisiene of isoniasied en ander chemies verwante medisyne, of teen enige van die eksipiënte van **AFARIS PAED 75/50.**
Dit word teenaangedui in die teenwoordigheid van geelsug of in pasiënte met ingekorte lewerfunksie.
AFARIS PAED 75/50 word teenaangedui in pasiënte met matig tot erg ingekorte nier- of lewerfunksie, diabetes mellitus, chroniese alkoholisme, 'n geskiedenis van jig en pasiënte wat aan stuipafwykings en porfirie ly.
Die gelyktydige gebruik van **AFARIS PAED 75/50** en nevirapien word teenaangedui.
Die gebruik van **AFARIS PAED 75/50** word teenaangedui wanneer dit saam met die kombinasie van sakinavir/ritonavir toegedien word (sien **INTERAKSIES**).
Swangerskap en laktasie (sien **MENSLIKE REPRODUKSIE**).

WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS:
Rifampisien:
AFARIS PAED 75/50 behoort nie aan pasiënte met ingekorte lewerfunksie toegedien te word nie. Indien **AFARIS PAED 75/50** die enigste behandelingsopsie in hierdie pasiënte is, behoort sorgvuldige lewerfunksie, veral serumglutamien/oksaalsuurtransaminase AST en serum glutamien/piroduiwesuur transaminase ALT vóór terapie, en dan elke 2 tot 4 weke gedurende terapie uitgevoer te word. Indien tekens van hepatosellulêre beskadiging voorkom, behoort **AFARIS PAED 75/50** onttrek te word (sien **KONTRA-INDIKASIES**).
'n Verslag wat 'n matige toename in bilirubien- en/of transaminasevlak aandui is op sigself nie 'n indikasie vir die onderbreking van behandeling nie. Die besluit behoort eerder na herhaling van die toetse gemaak te word, met inagneming van die neiging in die vlakke en hulle dan saam met die pasiënt se kliniese kondisie te oorweeg.

Lewerfunksie behoort vóór en gedurende behandeling met **AFARIS PAED 75/50** nagegaan te word en spesiale sorg behoort aan die dag gelê te word in alkoholiste of diegene met 'n reeds bestaande lewersiekte wees (sien **KONTRA-INDIKASIES**). Dosisaanpassing word vereis wanneer daar 'n bewys van inkorting van lewerfunksie is en die behandeling moet moontlik verander word as daar meer ernstige lewertoksisiteit voorkom. Bloedtellings behoort gedurende verlengde periodes van behandeling gemonitor te word, asook in pasiënte met lewerafwykings (sien **KONTRA-INDIKASIES**).
As ander ernstige komplikasies ontstaan bv. nierversaking of hemolitiese anemie, behoort **AFARIS 75/50** onttrek en nooit weer heringestel te word nie.

Weens die moontlikheid van immunologiese reaksies, insluitende anafilakse, wat met onderbroke terapie (minder as 2 tot 3 keer per week) voorkom, behoort pasiënte noukeurig gemonitor te word. Pasiënte behoort teen onderbreking van doseringsregimens gewaarsku te word, aangesien hierdie reaksies kan voorkom.

Pasiënte behoort gewaarsku te word dat verkleuring van die urien, feses, speeksel, sputum, sweet en trane kan voorkom. Pasiënte behoort verder gewaarsku te word dat sagte kontaklense permanent kan verkleur.

Isoniasied:
Die gebruik van isoniasied, soos bevat in **AFARIS PAED 75/50**, word teenaangedui in pasiënte met chroniese lewersiekte en wanfunksie van die niere. Indien **AFARIS PAED 75/50** die enigste behandelingsopsie is, behoort hierdie pasiënte noukeurig gemonitor te word. Erge en soms fatale hepatitis wat met isoniasiedterapie geassosieer word, kan voorkom, soms selfs eers na maande van behandeling. Die risiko vir die ontwikkeling van hepatitis is ouderdomsverwant. Pasiënte behoort vir prodromale simptome van hepatitis, soos moegheid, swakheid, 'n algemene gevoel van ongesteldheid, anoreksie, naarheid of braking gemonitor te word. Indien hierdie simptome ontwikkel of tekens wat op lewerbeskadiging dui waargeneem word, behoort behandeling onmiddellik gestaak te word. Die voortgesette gebruik van **AFARIS PAED 75/50** in hierdie gevalle kan 'n meer ernstige vorm van lewerbeskadiging veroorsaak (sien **KONTRA-INDIKASIES**).

Lewerfunksie behoort vóór en gedurende behandeling met **AFARIS PAED 75/50** nagegaan te word en spesiale sorg behoort in alkoholiste of diegene met reeds bestaande lewersiekte aan die dag gelê te word as **AFARIS PAED 75/50** die enigste behandelingsopsie is (sien **KONTRA-INDIKASIES**).

Periodieke oogondersoeke gedurende behandeling met **AFARIS PAED 75/50** is voorgestel.

Vitamien B_6 (teen 'n dosis van 15 tot 50 mg per dag behoort saam met isoniasied toegedien te word om newe-effekte in ondervoede pasiënte en diegene wat tot neuropatie predisponeer, tot 'n minimum te beperk.

Die gebruik van isoniasied behoort noukeurig gemonitor te word in pasiënte met stadige asetileerderstatus (sien Farmakokinetiese eienskappe), 'n geskiedenis van psigose, 'n geskiedenis van perifere neuropatie en MIV-infeksie.

Effek op die vermoë om te bestuur en masjinerie te gebruik:
AFARIS PAED 75/50 kan duiseligheid, ingekorte konsentrasie en/of lomerigheid veroorsaak. Pasiënte behoort daarom aangeraai te word dat, as hulle hierdie simptome ondervind, hulle potensieel gevaarlike take soos motor bestuur of met masjinerie werk, behoort te vermy.

Fenielketonurie: Pasiënte met fenielketonurie behoort ingelig te word dat **AFARIS PAED 75/50** fenielalanien ('n komponent van aspartaam) bevat.

INTERAKSIES
Rifampisien:
Die gelyktydige gebruik van **AFARIS PAED 75/50** en nevirapien word teenaangedui.
Wanneer **AFARIS PAED 75/50** saam met die kombinasie van sakinavir/ritonavir toegedien word, neem die potensiaal vir lewertoksisiteit toe. Daarom word die gelyktydige gebruik van **AFARIS PAED 75/50** saam met sakinavir/ritonavir nie aanbeveel nie.

Daar is aangemeld dat gehalogeneerde ingeademde narkosemiddels, wanneer dit saam met rifampisien toegedien word, die hepatotoksisiteit van beide rifampisien en isoniasied verhoog.
Daar is aangemeld dat ketokonasool die serumkonsentrasie van beide middels verlaag wanneer hulle saam toegedien word.
Rifampisien besit lewerensiem induserende eienskappe en kan die aktiwiteit van asatioprien, chlooramfenikol, simetidien, klofibraat, kortikosteroïede, kumarien teenstolmiddels, siklosporien, dapsoon, diasepam, doksisiklien, flukonasool, haloperidol, heksobarbitoon, itrakonasool, ketokonasool, metadoon, orale hipoglukemiese middels, fenitoïen, kinien, sulfasalasien, tirotedhomone, teofillien, sidovudien en verskeie kardiovaskulêre medisyne insluitende beta-adrenoseptor blokkeerders, digoksien, en antidiritmiese middels soos dispiramied, lorkainied, meksiletien, propafenoon, kinidien, tokainied en verapamiel en ander kalsiumkanaalblokkeerders, orale voorbehoedmiddels, narkotika, pynstillers en barbiturate verminder. Dit mag nodig wees om die dosis van hierdie medisyne aan te pas wanneer hulle saam met **AFARIS PAED 75/50** gegee word. Pasiënte wat orale voorbehoedmiddels gebruik behoort aangeraai te word om na nie-hormonale metodes van geboortebeperking gedurende terapie met **AFARIS PAED 75/50** te verander.
Magnesiumtrisilikaat, aluminiumhidroksied of natriumbikarbonaat verminder die biobeskikbaarheid van **AFARIS PAED 75/50**.

Alkohol
Die gelyktydige daaglikse inname van alkohol kan die risiko van rifampisiengeïnduseerde hepatotoksisiteit en metabolisme van rifampisien verhoog. Dosisaanpassings van rifampisien mag nodig wees en pasiënte behoort noukeurig vir tekens van hepatotoksisiteit gemonitor te word.

Kortikosteroïede
Die gelyktydige gebruik saam met rifampisien kan die metabolisme van kortikosteroïede deur induksie van mikrosomale ensieme in die lewer verhoog. Dit lei tot 'n afname in die plasmakonsentrasie van kortikosteroïede. Dosisaanpassing van die kortikosteroïed kan moontlik vereis word.

Antiretrovirusmiddels
Rifampisien, soos bevat in **AFARIS PAED 75/50**, kan die metabolisme van sidovudien, die NNTTIs delavirdien, efavirens en nevirapien en die MIV-protease-inhibeerders induseer, wat tot subterapeutiese plasmakonsentrasies kan lei. Verder inhibeer MIV-protease-inhibeerders die metabolisme van rifampisien wat tot verhoogde plasmakonsentrasies van rifampisien en 'n toename in die voorkoms van newe-effekte lei.
Rifampisien, soos bevat in **AFARIS PAED 75/50**, verminder die konsentrasie van efavirens en daar word aanbeveel dat die dosis van efavirens verhoog word in pasiënte wat meer as 60 kg weeg; geen dosisaanpassing van rifampisien, soos bevat in **AFARIS PAED 75/50**, is nodig nie.

Isoniasied:
Isoniasied is daarvoor bekend dat dit sekere sitochroom P450 ensieme te inhibeer en dat rifampisien hierdie ensieme induseer. Oor die algemeen is die impak van die kompeterende effekte van rifampisien en isoniasied op die metabolisme van medisyne wat biotransformasie deur die geaffekteerde bane ondergaan, onbekend. Daarom behoort sorg aan die dag gelê te word wanneer saam met middels wat deur sitochroom P450 gemetaboliseer word, voorgeskryf word. Om die optimum terapeutiese bloedvlakke te behou, mag die dosisse van hierdie medisyne wat deur hierdie medisyne gemetaboliseer word, aangepas moet word wanneer **AFARIS PAED 75/50** begin of gestaak word.
Aangesien isoniasied 'n inhibeerder van die hepatiese metabolisme van medisyne is, kan dit die effekte van sommige medisyne wat tegelykertyd geneem word, vererger.
Newe-effekte het voorgekom wanneer isoniasied saam met fenitoïen, primidoon, karbamasepien, etosuksemied, bensodiasepiene soos diasepam of triasolam en warfarien toegedien is. Toepaslike aanpassings van die dosisse van antistuipmiddels behoort gemaak te word.
Die plasmakonsentrasies van teofillien kan verhoog word.
'n Toename in newe-effekte van die sentrale senuweestelsel het voorgekom wanneer isoniasied saam met sikloserien en disulfiram toegedien is.
Isoniasied kan geaffekteer word deur middels soos alkohol, alfentaniel, aminosalisielsuur, kortikosteroïede, ketokonasool, propranolol en groot dosisse piridoksien.
Die orale absorpsie van isoniasied soos bevat in **AFARIS PAED 75/50**, word deur aluminiumbevattende teensuurmiddels verminder. **AFARIS PAED 75/50** behoort ten minste 1 uur voor die teensuurmiddel toegedien te word.
Die gelyktydige gebruik van **AFARIS PAED 75/50** met die chroniese gebruik van parasetamol mag die potensiaal vir isoniasied geïnduseerde hepatotoksisiteit verhoog.

Antiretrovirusmiddels
Die opruiming van isoniasied word byna verdubbel wanneer dit saam met salsitabien toegedien word. **AFARIS PAED 75/50** behoort met sorg saam met salsitabien en stavudien gebruik te word aangesien stavudien, salsitabien en isoniasied met die ontwikkeling van perifere neuropatie geassosieer is. Daar is aangemeld dat die gebruik van **AFARIS PAED 75/50** saam met stavudien die voorkoms van perifere neuropatie verhoog.

Voedselinteraksies
Weens die gedeeltelike monoamienoksidase inhiberende aktiwiteit van isoniasied, kan 'n interaksie met tiramienbevattende voedsel (kaas, rooiwyn) voorkom. Diamienoksidase kan ook geïnhibeer word wat 'n oormatige reaksie (bv. hoofpyn, sweet, hartkloppings, hittegloede, hipotensie) teen voedsel wat histamien bevat (bv. katonkel, tuna, ander tropiese vis), veroorsaak. Tiramien- en histamienbevattende voedsel behoort vermy te word in pasiënte wat **AFARIS PAED 75/50** ontvang.

MENSLIKE REPRODUKSIE
Die veiligheid gedurende swangerskap en laktasie is nie vasgestel nie.
Rifampisien en isoniasied beweeg deur die plasenta en beide word in borsmelk uitgeskei.

DOSIS EN GEBRUIKSAANWYSINGS
AFARIS 75/50 word aanbeveel in die aanhoudende fase van behandeling van longtuberkulose. Gedurende hierdie fase behoort **AFARIS 75/50** op 'n aanhoudende daaglikse basis toegedien te word.
Die totale dosisvereiste is as volg:

	Daagliks	Maksimum daaglikse dosis
Rifampisien	15 mg/kg (10 tot 20)	600 mg
Isoniasied	10 mg/kg (7 tot 15)	300 mg

Die daaglikse dosis word deur die aanbevole daaglikse vereiste hierbo bereken om die dosis meer akkuraat volgens liggaamsmassa te reguleer.

Tabel 1: Berekening van die dosis	
Aantal tablette	**Vir babas/kinders met 'n liggaams-massa (kg):**
1 tablet	4 - 7
2 tablette	8 - 11
3 tablette	12 - 15
4 tablette	16 - 24
Volwasse dosis aanbeveel	25 +

Die tablette kan in so min as 5 ml water opgelos of gekou word, en behoort verkieslik as 'n enkel dosis op 'n leë maag geneem te word.

AFARIS PAED 75/50 behoort ten minste een uur voor aluminiumbevattende teensuurmiddels geneem te word.

NEWE-EFFEKTE
RIFAMPISIEN
Afwykings van die bloed- en limfsisteem:
Minder dikwels: Bloeddiskrasieë, ongewone bloeding of kneusing, trombositopenie, purpura, hemolise, eosinofilie, leukopenie, hemolitiese anemie.

Afwykings van die immuunstelsel:
Frekwensie onbekend: Anafilakse en skok.

Afwykings van die senuweestelsel:
Minder dikwels: Verwardheid, lomerigheid, hoofpyn, ataksie, duiseligheid, perifere neuropatie en algemene gevoelloosheid.

Oogafwykings:
Minder dikwels: Onduidelike sig, oogirritasie.

Afwykings van die oor en labirint:
Minder dikwels: Verbygaande gehoorverlies.

Respiratoriese, bors- en mediastinale afwykings:
Frekwensie onbekend: Longfibrose, pneumonitis, kortademheid en hyging.

Gastrointestinale afwykings:
Dikwels: Naarheid, braking, anoreksie, diarree, epigastriese ongemak.
Minder dikwels: Pseudomembraneuse kolitis.
Frekwensie onbekend: Ulseratiewe kolitis, gastrointestinale bloeding.

Hepatobiliêre afwykings:
Minder dikwels: Hepatitis (wat fataal kan wees), hepatitis prodromale simptome wat verlies aan eetlus, naarheid of braking, ongewone moegheid of swakheid kan insluit. Verhoging in serumtransaminasevlakke.

Afwykings van die vel en subkutane weefsels:
Dikwels: Velreaksies wat tipies uit hittegloede en jeuk, met of sonder uitslag bestaan.
Minder dikwels: Meer ernstige hipersensitiewe velreaksies, toksiese epidermale nekrolise, afskilferende dermatitis, erythema multiforme, insluitende Stevens-Johnson se sindroom en vaskulitis, middelinteraksie met eosinofilie en sistemiese simptome (DRESS).

Muskuloskeletale en bindweefselafwykings:
Dikwels: Spierswakheid en miopatie.

Nier- en urienafwykings:
Minder dikwels: Interstisiële nefritis, nierversaking.

Reproduksiestelsel- en borsafwykings:
Minder dikwels: Afwykings van die menstruele siklus, afname in die effektiwiteit van orale voorbehoedmiddels.

Algemene afwykings en kondisies by die plek van toediening:
Dikwels: Rooi-oranje tot rooi-bruin verkleuring van die uriene, feses, speeksel, sputum, sweet en trane. Sagte kontaklense mag permanent verkleur.
Minder dikwels: Afwisselende, onderbroke of hernaaldelike behandeling met rifampisien kan die kans dat die pasiënt koors, 'n febriele reaksie met griepagtige simptome, swamgroeiing d.i. seer mond en longe ontwikkel, vergroot.
Frekwensie onbekend: Edeem.

ISONIASIED:
Afwykings van die bloed- en limfsisteem:
Minder dikwels: Verskeie hematologiese afwykings insluitende eosinofilie, agranulositose, trombositopenie en verskeie anemieë.

Afwykings van die immuunstelsel:
Minder dikwels: Hipersensitiwiteitsreaksies insluitende verskeie velerupsies, koors, limfadenopatie en vaskulitis, lupusagtige reaksies.

Metabolisme en voedingsafwykings:
Minder dikwels: Hiperglukemie, metaboliese asidose.

Psigiatriese afwykings:
Minder dikwels: Psigotiese reaksies (gekenmerk deur delusies, hallusinasies en verwardheid), ingekorte geheue.

Afwykings van die senuweestelsel:
Dikwels: Perifere neuropatie.
Minder dikwels: Polineuritis geassosieer met parestesie, spierswakheid, verlies aan tendonreflekse, stuipaanvalle, toename in die frekwensie van stuipaanvalle in pasiënte met epilepsie.

Oogafwykings:
Minder dikwels: Optiese neuritis (onduidelike sig of verlies aan sig, met of sonder oogpyn).

Afwykings van die oor en labirint:
Minder dikwels: Vertigo.

Gastrointestinale afwykings:
Dikwels: diarree, naarheid en braking, maagpyn, hardlywigheid, droë mond, pankreatitis.

Hepatobiliêre afwykings:
Dikwels: Hepatitis (soms fataal), hepatitis prodromale simptome (verlies aan eetlus, naarheid of braking, ongewone moegheid of swakheid). Verbygaande toenames in lewerensieme.

Afwykings van die vel en subkutane weefsel:
Minder dikwels: Velreaksies, pellegra, aknee, Stevens-Johnson se sindroom, eksfoliatiewe dermatitis.
Frekwensie onbekend: Alopesie, urtikarie.

Nier- en urienafwykings:
Minder dikwels: Urienretensie.

Afwykings van die reproduksiestelsel en bors:
Minder dikwels: Ginekomastie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Rifampisien: Akute oordosering met rifampisien het 'n kenmerkende helder rooi verkleuring van die vel en slymvliese, wasama soms as "die rooimansindroom" verwys word, geestelike afstomping, peri-orbitale of gesigsedeem en algemene pruritus veroorsaak.
Isoniasied: Simptome sal meer waarskynlik met isoniasied geassosieer word. Dit sluit hiperglukemie en metaboliese asidose, sleepspraak, stuipaanvalle, koma, hallusinasies, respiratoriese ongemak, depressie van die sentrale senuweestelsel in; fatale episodes kan voorkom.
Algemeen: In gevalle van oordosering met **AFARIS PAED 75/50** mag die toediening van 'n geaktiveerde houtskoolpap help om die oorblywende medisyne uit die maagdermkanaal te verwyder. 'n Antiëmetikum mag nodig wees om erge naarheid en braking te voorkom. Intensiewe ondersteunende maatreëls behoort ingestel te word en individuele simptome behoort behandel te word wanneer hulle voorkom. Verdere behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:
AFARIS 75/50:
Baksteenrooi, gespikkelde, kapsulevormige, onbedekte tablette met 'n diep breeklyn aan die een kant en glad aan die ander kant.

AANBIEDING:
AFARIS 75/50

HDPE houer:
Tablette word in 'n deurskynende, selfseëlende LDPE polisakkie verpak en verder in 'n silwer gekleurde driedubbel gelamineerde aluminiumsakkie (LDP/PET/AL) in 'n wit plastiekhouer (HDPE) wat by die bek met 'n aluminiumoortjie gebêre word en dan met 'n HDPE skroefdeksel gesluit word. Pakgroottes sluit 100 tablette in.
Alu-alu Stolpverpakking:
Tablette word in silwergekleurde aluminiumfoelie (sag getemper), gelamineer met lae-digtheid poliëtileen film as bedekking en vormingsmateriaal verpak. Die stolpstrokie word in 'n vooraf gedrukte karton verpak. Pakgroottes sluit 28, 56, 84 en 112 tablette in.

BERGINGSINSTRUKSIES:
Berg by of onder 25 °C. Beskerm teen vogtigheid en lig.
Hou die aluminiumsakkie in die HDPE houer tot benodig vir gebruik.
Hou die strokie in die karton tot benodig vir gebruik.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
51/20.2.3/0852

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:
MACLEODS PHARMACEUTICALS SA (EDMS.) BPK.
Grondvloer, Blok 1
Bassonia Estate Kantoorpark (Oos)
Cussoniarylaan 1
Bassonia Rock Uitbr. 12
Alberton
Gauteng

DATUM VAN PUBLIKASIE VAN DIE VOUBILJET
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SKEDULERINGSTATUS:

S4

EIENDOMSNAAM, STERKTE EN FARMASEUTIESE VORM:
AFARIS PAED 75/50 (orale oplosbare tablet)
Rifampisien 75 mg en isoniasied 50 mg.

LEES DIE HELE BROSJURE SORGVULDIG VOORDAT U BEGIN OM AFARIS PAED 75/50 TOE TE DIEN.
- Hou hierdie blaadjie. U mag dit moontlik weer wil lees.
- Indien u enige verdere vrae het, moet u asseblief u dokter of apteker raadpleeg.
- **AFARIS PAED 75/50** is vir u kind persoonlik voorgeskryf en u behoort nie u kind se medisyne met ander mense te deel nie. Dit mag hulle skade aandoen, ookal is hul simptome dieselfde as u kind s'n.

WAT AFARIS PAED 75/50 BEVAT
AFARIS PAED 75/50 bevat die aktiewe bestanddele rifampisien 75 mg en isoniasied 50 mg.
Die ander bestanddele is mikrokristallyne sellulose, krospovidoon, povidoon, gebleikte skellak, kroskarmellose natrium, aspartaam, framboosgeursel, magnesiumstearaat.
Bevat aspartaam. Suikervry.

WAARVOOR AFARIS PAED 75/50 GEBRUIK WORD
AFARIS PAED 75/50 is 'n antimikrobiese middel wat in die behandeling van longtuberkulose (TB-infeksie van die longe) in kinders gebruik word.

VOORDAT U AFARIS PAED 75/50 TOEDIEN
Moenie AFARIS PAED 75/50 toedien as u kind aan een van die kondisies hieronder ly nie:
- As u kind hipersensitief (allergies) teen rifamisiene, insluitende rifampisien, isoniasied of ander chemies verwante medisyne soos etioamied, pirasinamied, niasien of enige van die ander bestanddele van **AFARIS PAED 75/50 is.**
- As u kind aan enige lewersiekte of geelsug (geel verkleuring van die oë en vel) ly.
- **AFARIS PAED 75/50** behoort nie saam met nevirapien, sakinavir en ritonavir (gebruik in die behandeling van MIV) gebruik te word nie.
- As u kind aan enige niersiekte ly.
- As u kind aan porfirie ly.
- As u kind 'n geskiedenis van jig het.
- As u kind 'n diabeet is.
- As u kind aan epilepsie ly.
- As u kind trombositopenie en purpura (kneusing, bloeding van die neus, of bloeding in die mond of tandvleis, uitslag met rooi speldepunt kolletjies) ontwikkel het terwyl hy/sy **AFARIS PAED 75/50** geneem het.
- As u kind swanger is of haar kind borsvoed.

As u kind jeuk met swelling of uitslag van die vel of moeite met asemhaling begin ontwikkel, of as die vel en oë geel verkleur terwyl hy/sy **AFARIS PAED 75/50** neem, moenie meer **AFARIS PAED 75/50** toedien nie en stel u dokter onmiddellik in kennis.

Neem spesiale sorg met AFARIS PAED 75/50:
- Voordat u **AFARIS PAED 75/50 toedien**, moet u u dokter in kennis stel as u kind aan epilepsie ly.
- **AFARIS PAED 75/50** behoort nie aan kinders toegedien te word wie se lewers nie normaal funksioneer nie. In gevalle waar daar geen ander behandelingsopsies bestaan nie, sal u dokter egter u kind se lewerfunksie voor behandeling en elke twee tot vier weke gedurende behandeling met **AFARIS PAED 75/50** monitor.
- Stel u dokter onmiddellik in kennis en staak die toediening van **AFARIS PAED 75/50** as u kind simptome van hepatitis (inflammasie van die lewer wat, indien nie behandel word nie, tot die dood kan lei) soos moegheid, swakheid, 'n algemene gevoel van ongesteldheid, verlies aan eetlus, naarheid of braking ontwikkel.
- U dokter sal u kind se bloedtellings monitor as u kind aan 'n lewersiekte ly, of indien hy/sy op langtermyn behandeling met **AFARIS PAED 75/50** is. As u kind lae plaatjietellings (bloedselle wat vir bloedklonting verantwoordelik is) ontwikkel met simptome van maklike of oormatige kneusing, bloeding in die vel wat as 'n uitslag met speldepunt rooi-pers kolletjies voorkom, gewoonlik op die onderbene, verlengde bloeding van snywonde, spontane bloeding van die tandvleis of neus en bloed in die uriene of stoelgang, behoort die toediening van **AFARIS PAED 75/50** gestaak en permanent onttrek te word (sien Moenie **AFARIS PAED 75/50** toedien nie).
- As ander ernstige komplikasies weens hierdie medisyne voorkom soos nierversaking of bloedsiektes, **behoort AFARIS PAED 75/50 gestaak en nooit weer heringestel te word nie.**
- Uriene, feses, speeksel, sputum, sweet en trane kan rooi-oranje deur **AFARIS PAED 75/50** verkleur.
- Jou dokter mag addisionele bloedtoetse voorskryf om jou kind se adrenalehormoon, skildklierhormoon en vitamien D-vlakke te monitor.
- Sagte kontaklense kan permanent verkleur word.
- U dokter mag periodieke oogondersoeke voorskryf aangesien **AFARIS PAED 75/50** onduidelike sig of gesigsverlies met of sonder oogpyn en oogirritasie kan veroorsaak.
- U dokter mag vitamien B_6 (piridoksien) saam met **AFARIS PAED 75/50** voorskryf om newe-effekte tot 'n minimum te beperk as u kind ondervoed is of aan neuropatie ly (beskadiging van die senuwees wat tot swak koördinasie, spierswakheid, pyn in die vingers of tone, of ongevoeligheid).
- Dien **AFARIS PAED 75/50** aan u kind toe soos deur u dokter voorgeskryf op 'n aanhoudende basis sonder onderbreking, om die ontwikkeling van newe-effekte soos 'n ernstige allergiese reaksie (swelling van die hande, voete, enkels, lippe, mond of tong wat moeite met asemhaling, uitslag en jeuk) of 'n griepagtige sindroom (kouekoors, duiseligheid, moeite met asemhaling, koors, hoofpyn, spierpyn, beenpyn en bewerasie) te vermy.

Die neem van AFARIS PAED 75/50 saam met voedsel en vloeistof:
AFARIS PAED 75/50 behoort sonder voedsel geneem te word. Vermy tiramienbevattende voedsel (bv. kaas, rooiwyn) en histamienbevattende voedsel (bv. katonkel, tuna en tropiese vis). Vermy alkohol.

Swangerskap en borsvoeding:
Die veiligheid gedurende swangerskap en borsvoeding is nie vasgestel nie.
As u swanger is of u baba borsvoed, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker vir advies nader voordat u **AFARIS PAED 75/50** neem.

Bestuur en die gebruik van masjinerie:
AFARIS PAED 75/50 kan duiseligheid, ingekorte konsentrasie en/of lomerigheid veroorsaak. As u hierdie simptome ondervind, moet u gevaarlike take soos om te bestuur of met enige masjinerie te werk, vermy.

Belangrike inligting oor sommige van die bestanddele van AFARIS PAED 75/50:
Fenielketonurie: Pasiënte met fenielketonurie behoort in kennis gestel te word dat **AFARIS PAED 75/50** fenielalanien ('n komponent van aspartaam) bevat.

Die toediening van ander medisyne saam met AFARIS PAED 75/50:
Stel altyd u professionele gesondheidswerker in kennis as u enige ander medisyne neem. Dit sluit komplementêre en tradisionele medisyne in.

AFARIS PAED 75/50 kan die effek van ander medisyne en ander medisyne kan die effek van **AFARIS PAED 75/50** beïnvloed.
Moenie AFARIS PAED 75/50 toedien en stel u dokter onmiddellik in kennis as u kind die volgende medisyne neem:
- Nevirapien, sakinavir of ritonavir (MIV medisyne).

Die volgende medisyne kan veroorsaak dat **AFARIS PAED 75/50** nie na wense werk nie:
- Alkohol, alfentaniel (vir pyn gedurende chirurgie), aminosalisielsuur (TB medisyne), kortikosteroïede soos hidrokortisoon, betametasoon en prednisoloon (vir die behandeling van inflammatoriese kondisies, ketokonasool (vir swaminfeksies), propranolol (vir hoë bloeddruk) en hoë dosisse piridoksien (vitamien B_6).
- Teensuurmiddels wat magnesiumtrisilikaat, aluminiumhidroksied of natriumbikarbonaat en ander aluminiumbevattende teensuurmiddels vir indigestie, bevat. Dien **AFARIS PAED 75/50** ten minste een uur voor die teensuurmiddel toe.

Wanneer u **AFARIS PAED 75/50** toedien, is dit veral belangrik om u dokter of professionele gesondheidswerker in kennis te stel as u kind enige van die volgende medisyne gebruik, aangesien dit moontlik vir u dokter nodig sal wees om die dosis van die medisyne aan te pas.
- Medisyne wat gebruik word om epilepsie te behandel soos etosuksimied, fenitoïen en karbamasepien.
- Medisyne soos itrakonasool, flukonasool en ketokonasool wat gebruik word om swaminfeksies te behandel.
- MIV-medisyne soos sidovudien, delavirdien, efavirens, MIV-protease-inhibeerders (lopinavir, duranavir, atasanavir, fosamprenavir, indinavir).
- Ander medisyne sluit sekere narkosemiddels (om die spiere voor chirurgie te verslap), asatioprien, siklosporien (immuunonderdrukkers), chlooramfenikol, sikloserien, dapsoon, doksisiklien (medisyne gebruik vir infeksies), simetidien (gebruik vir ulkusse), klofibraat (verlaag cholesterol), kortikosteroïede soos hidrokortisoon, betametasoon en prednisoloon (vir die behandeling van inflammatoriese kondisies), warfarien (bloedverdunner), diasepam (vir angs en depressie), haloperidol (vir geestesiekte), heksobarbitoon (sedeermiddel), metadoon (vir heroïenonttrekking), orale hipoglukemiese middels gebruik in die behandeling van diabetes, sulfasalasien gebruik in rumatiese artritis en inflammatoriese dermsiekte), tirotedhomone (levotiroksien), teofillien (vir hyging of moeite met asemhaling), kinien (gebruik in malaria), medisyne om u hartklop te kontroleer soos digoksien, disopramied, lorkaïnied, meksiletien, propfenoon, kinidien, tokainied, medisyne om hartprobleme te behandel soos betablokkeerders (propranolol), verapamiel en ander kalsiumkanaalblokkeerders, medisyne gebruik vir erge pyn soos kodeïen, morfien, fentaniel of petidien, medisyne gebruik vir pyn en koors soos aspirien en medisyne om u te help slaap soos barbiturate (bv. fenobarbitoon).
- **AFARIS PAED 75/50** kan die effektiwiteit van orale voorbehoedmiddels verminder. Gebruik 'n betroubare metode van skeidingskontrasepsie soos kondome, terwyl **AFARIS PAED 75/50** geneem word.

Die volgende middels, wanneer dit saam met **AFARIS PAED 75/50** geneem word, kan die voorkoms van newe-effekte verhoog:
- Medisyne wat gebruik word om epilepsie te behandel soos etosuksemied, fenitoïen, primidoon en karbamasepien. U dokter sal die dosis van die epilepsiemedikasie dienooreenkomstig aanpas).
- MIV medisyne soos MIV protease-inhibeerders (lopinavir, ritonavir, sakinavir, duranavir, atasanavir, fosamprenavir), stavudien en salsitabien.
- Ander medisyne soos warfarien (verdun die bloed), diasepam, triasolam (vir angs en depressie), sikloserien (TB medisyne), disulfiram (behandeling van alkoholafhanklikheid), teofillien (vir hyging en moeite met asemhaling).
- Alkohol (daaglikse inname kan tot erge lewerprobleme lei).

Voedselinteraksies:
- **AFARIS PAED 75/50** kan 'n wisselwerking met tiramienbevattende voedsel (kaas, rooiwyn) en met voedsel wat histamien bevat (katonkel, tuna en ander tropiese vis) toon wat tot hoofpyn, sweet, hartkloppings (hart klop te hard of te vinnig), hittegloede en lae bloeddruk lei. Probeer om die toediening van tiramien- en histamienbevattende voedsel aan u kind te vermy terwyl hy/sy op behandeling met **AFARIS PAED 75/50 is.**

HOE OM AFARIS PAED 75/50 TOE TE DIEN
Moenie medisyne wat vir u voorgeskryf is met enigiemand anders deel nie.
Dien **AFARIS PAED 75/50** altyd toe presies soos deur u dokter voorgeskryf. Bevestig met u dokter of apteker as u onseker is. As u van mening is dat die effek van **AFARIS PAED 75/50** te sterk of te swak is, moet u u dokter of apteker raadpleeg.

AFARIS PAED 75/50 word aanbeveel in die aanhoudende fase van longtuberkulose. **Gedurende hierdie fase behoort AFARIS PAED 75/50 op 'n aanhoudende daaglikse basis toegedien te word.**
U dokter sal die aantal tablette wat u daagliks benodig op grond van u kind se liggaamsmassa voorskryf.
Die tablette kan in so min as 5 ml water opgelos, of gekou word en behoort verkieslik op 'n leë maag (30 minute vóór of twee ure na 'n maaltyd) as 'n enkel dosis geneem te word. **AFARIS PAED 75/50** behoort ten minste een uur vóór die inname van aluminiumbevattende teensuurmiddels geneem te word.

Moenie die gebruik van AFARIS PAED 75/50 staak omdat u kind beter voel nie.
As die volle behandeling soos deur u dokter voorgeskryf, nie voltooi word nie, mag sommige van die bakterieë wat vir die TB-infeksie verantwoordelik is, nie gedood word nie. Hierdie bakterieë kan aanhou om te groei en vermenigvuldig sodat die infeksie nie heeltemal opklaar nie, of dit kan terugkeer.

As u te veel AFARIS PAED 75/50 toegedien het:
In die geval van oordosering moet u u dokter of apteker raadpleeg. As hulle nie beskikbaar is nie, kontak u naaste hospitaal of gifbeheersentrum.
Simptome sluit naarheid, braking maagpyn, duiseligheid, hoë bloedsuikervlakke, hoë suurvlakke in die bloed, hallusinasies, moeite met asemhaling en onderdrukking van die sentrale senuweestelsel met stuipaanvalle en koma in. Ander tekens van oordosering sluit helder rooi verkleuring van die vel en slymvliese, afname in geestelike skerpheid, swelling van die gesig en oë en algemene jeuk in.
As enige van hierdie simptome voorkom, moet u onmiddellik mediese hulp kry deur u dokter of professionele gesondheidswerker te raadpleeg.

As u vergeet het om AFARIS PAED 75/50 aan u kind toe te dien:
As u kind vergeet het om 'n dosis **AFARIS PAED 75/50** te neem, moet u dit sodra u daarvan onthou, toedien. As dit egter byna tyd vir die volgende dosis is, slaan die oorgeslaande dosis oor en gaan met die gereelde doseringskedule voort. Moet nooit die dosis verdubbel nie.

MOONTLIKE NEWE-EFFEKTE
AFARIS PAED 75/50 kan newe-effekte hê;
Nie al die newe-effekte wat vir **AFARIS PAED 75/50** aangemeld is, word in hierdie brosjure ingesluit nie. As u kind se algemene gesondheid agteruitgaan of as u kind enige ongewone effekte ondervind terwyl hy/sy **AFARIS PAED 75/50** neem, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker om advies raadpleeg.

Indien enige van die volgende gebeur, moet u ophou om AFARIS PAED 75/57 te neem en onmiddellik u dokter in kennis stel, of gaan na die ongevalle afdeling van u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, mond of keel wat moeite met sluk of asemhaling kan veroorsaak
- uitslag of jeuk
- floute
- geel verkleuring van die vel en oë (geelsug)

Hierdie is almal ernstige newe-effekte. As u hulle ondervind, het u moontlik 'n ernstige reaksie teen **AFARIS PAED 75/50** gehad. u het moontlik dringende mediese hulp of hospitalisering nodig.

Stel u dokter onmiddellik in kennis of gaan na u naaste hospitaal as u enige van die volgende waarneem:
- Rooi en/of jeukerige vel, blasies of puisies.
- Velkondisie met erge blaasvorming en bloeding van die lippe, oë, mond, neus en genitalieë (simptome van Stevens-Johnson se sindroom).
- Wydverspreide afskilfering van die vel met jeuk, rooiheid van die vel en haarverlies (simptome van eksfoliatiewe dermatitis).
- Kortademheid en hyging.
- Longsiekte wat hoes, moeite met asemhaling en hyging (simptome van pneumonitis) kan veroorsaak.
- Letselvorming en verdikking in die longe met kortademheid (simptome van longfibrose).
- Bloed in die uriene of enige ander urienafwykings.
- Koors, kouekoors, hoofpyn of duiseligheid.
- Beenpyn.
- Kneusing, neusbloeding of bloeding van die mond en tandvleis, uitslag met speldepunt rooi kolletjies.
- Moegheid, swakheid, malaise (algemene gevoel van ongesteldheid), anoreksie (verlies aan eetlus), naarheid of braking.
- Buikpyn, bloed in die stoelgang, aanhoudende episodes van diarree wat nie op oor-die-toonbank (ODT) medisyne reageer nie of 'n onverklaarde koors wat langer as 'n dag of twee voortduur (simptome van ulseratiewe kolitis).
- Bloeding vanuit die maagwand met braking van bloed of materiaal wat soos koffiemoer lyk, bloeding vanuit die rektum, swart kleierige stoelgang of bloederige diarree.
- Inflammasie van die pankreas met erge boonste maagpyn, naarheid en braking.

Hierdie is almal ernstige newe-effekte. U het moontlik mediese aandag nodig.

Stel u dokter onmiddellik in kennis as u kind enige van die volgende newe-effekte toon, veral as hulle etlike weke nadat daar met die behandeling met AFARIS PAED 75/50 gestaak is, voorkom:
- Erge maagkrampe.
- Waterige en erge diarree, wat ook bloederig kan wees.
- Koors in kombinasie met een of beide van bogenoemde.

U kind mag aan 'n ernstige kondisies van die dermkanaal ly wat dringende mediese aandag vereis.
Moenie enige medisyne vir diarree neem voordat u nie u dokter geraadpleeg het nie.

Stel u dokter in kennis as u een van die volgende waarneem:
Dikwels voorkomende newe-effekte:
- Sooibrand, anoreksie, naarheid, braking, winderigheid, krampe of diarree, hardlywigheid, droë mond.
- Velreaksies met hittegloede en jeuk, met of sonder uitslag.
- Spierpyn, -teerheid of -swakheid wat nie deur oefening veroorsaak word nie.
- Rooi-oranje tot rooi-bruin verkleuring van die urien, feses, speeksel, sputum, sweet en trane.
- Sagte kontaklense mag permanent verkleur.
- Gevoelloosheid en swakheid van die arms en bene.
- Toename in lewerensieme.

Minder dikwels voorkomende newe-effekte:
- Toename in sommige witbloedselle (eosinofilie).
- Tekort aan witbloedselle wat tot gereelde infeksies soos koors, erge koue koors, seer keel en mondulkusse (leukopenie).
- Moegheid, hoofpyn kortademheid met oefening, duiseligheid, bleekheid en geel verkleuring vel en/of oë (hemolitiese anemie).
- Hoë bloedglukosevlakke.
- Hoë suurvlakke in die bloed.
- Geestessiekte met vreemde of kommerwekkende gedagtes of buie.
- Geheueverlies.
- Hoofpyn, duiseligheid, lomerigheid, onvermoë om te konsentreer of verwardheid.
- Swak koördinasie, spierswakheid, spierpyn, pyn in die vingers of tone, gevoelloosheid, ongewone toename in reflekse en trekkings.
- Stuiptrekkings of toename in stuiptrekkings as jy 'n epileptiese pasiënt.
- Onduidelike sig, of verlies aan sig met of sonder oogpyn, oogirritasie.
- Menstruele afwykings
- Orale voorbehoedmiddels mag minder effektief raak.
- Tydelike gehoorverlies.
- Vertigo (duiseligheid met 'n wraakgevoel).
- Veluitslag, jeukerige uitslag, aknee en haarverlies.
- Vergroting van die borste.
- Mondsproei - wit wollerige seer tong en mond.
- Swelling van die hande, enkels of voete.

As u enige newe-effekte ondervind wat nie in hierdie brosjure genoem word nie, moet u asseblief u dokter of apteker raadpleeg.

OPBERGING EN WEGDOEN VAN AFARIS PAED ODT:
Berg by of onder 25 °C.
Hou die aluminiumsakkie in die HDPE houer tot benodig vir gebruik.
Hou die strokie in die karton tot benodig vir gebruik.
Bewaar hierdie medisyne weg van lig en vogtigheid. Moenie in die badkamerkabinet berg nie.
Enige medisyne wat verval het en enige ongebruikte medisyne kan na u naaste apteker teruggeneem word.
BERG ALLE MEDISYNE BUITE DIE BEREIK VAN KINDERS.

AANBIEDING

HDPE Houer:
Tablette word in 'n deurskynende, selfseëlende LDPE polisakkie verpak en verder in 'n silwer gekleurde driedubbel gelamineerde aluminiumsakkie (LDP/PET/AL) in 'n wit plastiekhouer (HDPE) wat by die bak met 'n aluminiumoortjie gebêre word en dan met 'n HDPE skroefdeksel gesluit word. Pakgroottes sluit 100 tablette in.
Alu-Alu stolpverpakking:
Tablette word in silwergekleurde aluminiumfoelie (sag getemper), gelamineer met lae-digtheid poliëtileen film as bedekking en vormingsmateriaal verpak. Die stolpstrokie word in 'n vooraf gedrukte karton verpak. Pakgroottes sluit 28, 56, 84 en 100 tablette in.

IDENTIFIKASIE:
AFARIS PAED 75/50:
Baksteen rooi, gespikkelde, 9,5 mm ronde, onbedekte tablette met 'n diep breeklyn aan die een kant en glad aan die ander kant.

REGISTRASIENOMMER:
51/20.2.3/0852

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:
MACLEODS PHARMACEUTICALS SA (EDMS.) BPK.
Grondvloer, Blok 1
Bassonia Estate Kantoorpark (Oos)
Cussoniarylaan 1
Bassonia Rock Uitbr. 12
Alberton
Gauteng

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26 Oktober 2018

PACKAGING RESEARCH & DEVELOPMENT

MACLEODS

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

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2. Country: South Africa	3. Packaging component: Package Insert & Patient Information Leaflet
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6. Specification: 40 gsm bible paper	
7. Machine Layout No.: NA	8. Dimensions: 435 x 490 mm
9. Design / Style: NA	10. Item code No.: PM03052701
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29/10/19	Rashmi Gosai	30/10/19	31/10/19	31/10/19	6/11/19

Note: 1. To follow overleaf checklist for approval of Artwork / Print proof.

Instructions to Vendor :

1. Before processing, please ensure First pull out / Commercial supply should match with approved Artwork with respect to Design, Size, Fonts & Text.
2. Print proof to represent full printing area with Station Numbers.

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa	PM03052701		