SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

AFARIS FC 150/75 (film-coated tablet)
AFARIS FC 300/150 (film-coated tablet)

COMPOSITION

AFARIS FC 150/75
Each film-coated tablet contains:
Rifampicin 150 mg and isoniazid 75 mg.
The other ingredients are maize starch, crospovidone, povidone, bleached shellac, sodium lauryl sulphate, sodium starch glycolate, colloidal anhydrous silica, magnesium stearate.
Coating ingredients: hypromellose, polyvinyl alcohol-part. hydrolyzed, talc, titanium dioxide (C.I. No 77891), ponceau 4R aluminium lake (C.I. No. 16255), lecithin (soya) and xanthan Gum
AFARIS FC 300/150
Each film-coated tablet contains:
Rifampicin 300 mg and isoniazid 150 mg.
The other ingredients are microcrystalline cellulose, crospovidone, povidone, bleached shellac, sodium starch glycolate, croscarmellose sodium, calcium stearate.
Coating ingredients: hypromellose, propylene glycol, diethyl phthalate, purified talc, titanium dioxide (C.I. No. 77891), colour Ponceau 4R lake (C.I. No. 16255).

PHARMACOLOGICAL CLASSIFICATION

A 20.2.3 Tuberculostatic

PHARMACOLOGICAL ACTION

Pharmacodynamics
Rifampicin and isoniazid are bactericidal antituberculosis medicines.
Rifampicin
Rifampicin inhibits the growth of *Mycobacterium tuberculosis* clinical isolates *in vitro* at concentrations of 0,06 – 0,25 mg/l. 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.

Pharmacokinetics:
Rifampicin
Absorption
Rifampicin is readily absorbed from the gastro-intestinal tract with an oral bioavailability of 68 %. C_{max} of 8 - 20 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 ± 0,8 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.

INDICATIONS

AFARIS FC is indicated in the continuation phase of treatment of pulmonary and extra-pulmonary tuberculosis in newly diagnosed patients and re-treatment of adult cases.

CONTRA-INDICATIONS

AFARIS FC is contra-indicated in patients with a history of hypersensitivity to rifamycins or isoniazid and other chemically related medicines or to any of the excipients of **AFARIS FC**.
It is contra-indicated in the presence of jaundice.
AFARIS FC is contra-indicated in patients with impaired renal or liver function, diabetes mellitus, chronic alcoholism, a history of gout, patients suffering from convulsive disorders and porphyria.
The concomitant use of **AFARIS FC** and nevirapine is contra-indicated.
AFARIS FC can cause thrombocytopenia and purpura usually with intermittent tuberculosis regimens; further administration is contra-indicated.
AFARIS FC is contra-indicated when given concurrently with the combination of saquinavir/ritonavir (see Interactions).

WARNINGS AND SPECIAL PRECAUTIONS

Rifampicin:
Patients with impaired liver function should not be given **AFARIS FC**. Should **AFARIS FC** be the only treatment option in these patients, careful monitoring of liver function, especially serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST), should be carried out prior to therapy and repeated every two to four weeks during therapy. If signs of hepatocellular damage occur, **AFARIS FC** should be withdrawn (see **CONTRA-INDICATIONS**).
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 be 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 FC** and special care should be taken in alcoholic patients or those with pre-existing liver disease should **AFARIS FC** be the only treatment option (see **CONTRA-INDICATIONS**). 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. Should thrombocytopenia or purpura occur, **AFARIS FC** should be withdrawn permanently.

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.

Isoniazid:
Use of isoniazid as contained in **AFARIS FC** is contra-indicated in patients with chronic liver disease or renal dysfunction. Should **AFARIS FC** 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 FC** in these cases may cause a more severe form of liver damage and may exacerbate convulsive disorders (see **CONTRA-INDICATIONS**).

Liver function should be checked before and during treatment with **AFARIS FC** and special care should be taken in alcoholic patients or those with pre-existing liver disease should **AFARIS FC** be the only treatment option (see **CONTRA-INDICATIONS**). Periodic eye examinations during **AFARIS FC** 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.

Effects on ability to drive and use machines
AFARIS FC 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.

INTERACTIONS

Rifampicin:
Halogenated inhalation anaesthetics, when given concomitantly with rifampicin has been reported to increase the hepatotoxicity of both agents. Ketoconazole has been reported to diminish the serum concentrations of both agents when given concomitantly.
Rifampicin has liver-enzymes inducing properties and may reduce the activity of azathioprine, chloramphenicol, cimetidine, clofibrate, corticosteroids, anticoagulants such as warfarin, ciclosporin, dapsone, diazepam, doxycycline, fluconazole, haloperidol, hexobarbitone, itraconazole, ketoconazole, methadone, oral hypoglycaemic agents, phenytoin, quinine, sulphasalazine, thyroid hormones, theophylline, and several cardiovascular medicines including beta-adrenoceptor blocking agents, digoxin, and antidysrhythmic agents such as disopyramide, lorcainide, mexiletine, propafenone, quinidine, tocainide, verapamil and other calcium-channel blocking agents, oral contraceptives, narcotics, analgesics and barbiturates, antiretroviral medicines (e.g. zidovudine, saquinavir, indinavir, efavirenz).
It may be necessary to adjust the dosage of these medicines if they are given concurrently with **AFARIS FC**. Patients using oral contraceptives should be advised to change to non-hormonal methods of birth control during therapy with **AFARIS FC**.

Alcohol
Concurrent daily consumption of alcohol may increase the risk of rifampicin-induced hepatotoxicity and increased 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.

Magnesium trisilicate, aluminium hydroxide or sodium bicarbonate reduce the bioavailability of **AFARIS FC**. The absorption of rifampicin may be reduced by concomitant administration with medicines that reduce gastric motility (anticholinergics and opioids), ketoconazole, or preparations containing bentonite (e.g. some aminosalicylic acid preparations). Daily doses of rifampicin should be given at least 1 hour before ingestion of one of these medicines.

The prothrombin time of patients receiving concurrent anticoagulant therapy may be decreased. Frequent monitoring of the prothrombin level in such patients with subsequent adjustment in anticoagulant dosage is recommended.

Diabetes may be more difficult to control.

The concentration of enalaprilat, the active metabolite of enalapril may be decreased. Dosage should be adjusted if indicated by the patient's clinical condition.

Therapeutic levels of AFARIS FC have been shown to inhibit standard microbiological assays for serum folate and Vitamin B_{12}. Thus alternative assay methods should be considered.
Transient elevation of serum bilirubin has also been observed. AFARIS FC may impair biliary excretion of contrast media used for the visualisation of the gallbladder, due to competition for biliary excretion.

Anti-retroviral agents
Rifampicin as contained in **AFARIS FC** can induce the metabolism of zidovudine, the NNRTI's delavirdine, efavirenz and nevirapine 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.
The concomitant use of **AFARIS FC** and nevirapine is contra-indicated.
Rifampicin as contained in **AFARIS FC** decreases the concentration of efavirenz and it is recommended that the dose of efavirenz be increased in patients weighing more than 50 kg.
When **AFARIS FC** is given concomitantly with the combination of saquinavir/ritonavir, the potential for hepatotoxicity is increased. Therefore, concomitant use of **AFARIS FC** with saquinavir/ritonavir is contra-indicated.

Isoniazid:
Isoniazid is an inhibitor of hepatic metabolism of medicines and 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, aminosalicylic acid, corticosteroids, ketoconazole, propranolol and large doses of pyridoxine.
Daily ingestion of alcohol may be associated with higher incidence of isoniazid hepatitis.
The metabolism of enflurane may be increased in patients receiving isoniazid, resulting in potentially nephrotoxic levels of fluoride. Isoniazid has been associated with increased concentrations or toxicity of clofazimine. Isoniazid inhibits the metabolism of primidone.
Oral absorption of isoniazid as contained in **AFARIS FC** is reduced by aluminium-containing antacids; **AFARIS FC** should be given at least 1 hour before the antacid.

Anti-retroviral agents
The clearance of isoniazid is approximately doubled when given concomitantly with zalcitabine.
AFARIS FC 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 FC** 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 FC**.

PREGNANCY AND LACTATION

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 FC 150/75
AFARIS FC 150/75 is recommended in the continuation phase of the treatment of pulmonary tuberculosis. During this phase which lasts for 4 months, **AFARIS FC 150/75** should be administered on a continuous daily basis.
The total dosage requirement is as follows:

	Daily
Rifampicin	10 mg/kg (8 to 12 mg/kg)
Isoniazid	5 mg/kg (4 to 6 mg/kg)

Daily dose is as follows:	
Number of tablets (daily)	Patient body mass (kg)
2 tablets	30 to 37*
3 tablets	38 to 54
4 tablets	55 to 70
5 tablets	71 and more*
* In practice, adult patients taking rifampicin-containing fixed-dose combination tablets will receive either 3 or 4 tablets daily. Only a small proportion of adult TB patients will fall into the categories with a body mass [illegible] 30 to 37 kg or body mass above 70 kg. [illegible] dose of rifampicin of 600 mg per day [illegible] the dose limit of 10 mg/kg [illegible]	

AFARIS FC 150/75 is not suitable for children < 12 years.

AFARIS FC 300/150
During this phase, which lasts for 4 months, **AFARIS FC 300/150** should be administered on a continuous daily basis.

The total dosage requirement is as follows:

	Daily	
Rifampicin	10 mg/kg (8 to 12 mg/kg)	maximum 600 mg per day
Isoniazid	5 mg/kg (4 to 6 mg/kg)	maximum 300 mg/day

Daily dose of AFARIS FC 300/150 is as follows:	
Number of tablets (daily)	Patient body mass (kg)
2 tablets	55 or more

AFARIS FC 300/150 is unsuitable for children under 12 years.

AFARIS FC 150/75 and **AFARIS FC 300/150** should preferably be taken on an empty stomach (30 minutes before or 2 hours after a meal) as a single dosage.
AFARIS FC 150/75 and **AFARIS FC 300/150** 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.

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.

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 efficacy 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 fever, 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.

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, acne, Stevens-Johnsons syndrome, exfoliative dermatitis.
Frequency not known: Pellagra, alopecia, urticaria.

Musculoskeletal and connective tissue disorders:
Frequency unknown: Arthralgic 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 FC** gastric lavage should be performed as soon as possible. Intensive supportive measures should be instituted and individual symptoms treated as they arise. Further treatment is symptomatic and supportive.

IDENTIFICATION

AFARIS FC 150/75:
Brown to reddish brown, round, biconvex, film coated tablet, plain on both sides.
AFARIS FC 300/150:
Brown to reddish brown, round, biconvex, film coated tablet, break line on one side and plain on other side.

PRESENTATION

AFARIS FC 150/75
HDPE Container:
Silver coloured triple laminated aluminium sachet (PET/Al/LLDPE), 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 500 and 1000 tablets.
AFARIS FC 150/75 and AFARIS FC 300/150
Blister:
Silver coloured aluminium backing foil with amber coloured (PVC/PE/PVdC) lidding foil. The blister is packed in a pre-printed carton. Pack sizes include 56 (2 blisters of 28 tablets), 84 tablets (3 blisters of 28 tablets), 672 tablets (24 blisters of 28 tablets) and 100 tablets (10 blisters of 10 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

AFARIS FC 150/75: 48/20.2.3/0748
AFARIS FC 300/150: 48/20.2.3/0749

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

Macleods Pharmaceuticals SA (Pty) Ltd.
Office Block 1,
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25 November 2016

Patient Information Leaflet

SCHEDULING STATUS

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

AFARIS FC 150/75 (film-coated tablet)
Rifampicin 150 mg and isoniazid 75 mg
AFARIS FC 300/150 (film-coated tablet)
Rifampicin 300 mg and isoniazid 150 mg

READ ALL OF THIS LEAFLET CAREFULLY BEFORE YOU START TAKING AFARIS FC

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **AFARIS FC** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

WHAT AFARIS FC CONTAINS

AFARIS FC 150/75
Each film-coated tablet contains: Rifampicin 150 mg and isoniazid 75 mg.
The other ingredients are maize starch, crospovidone, povidone, bleached shellac, sodium lauryl sulphate, sodium starch glycolate, colloidal anhydrous silica, magnesium stearate.
Coating ingredients: hypromellose, polyvinyl alcohol-part. hydrolyzed, talc, titanium dioxide (C.I. No 77891), ponceau 4R aluminate lake (C.I. No. 16255), lecithin (soya) and xanthan Gum
AFARIS FC 300/150
Each film-coated tablet contains: Rifampicin 300 mg and isoniazid 150 mg.
The other ingredients are microcrystalline cellulose, crospovidone, povidone, bleached shellac, sodium starch glycolate, croscarmellose sodium, calcium stearate.
Coating ingredients: hypromellose, propylene glycol, diethyl phthalate, purified talc, titanium dioxide (C.I. No. 77891), colour Ponceau 4R lake (C.I. No. 16255).

WHAT AFARIS FC IS USED FOR

AFARIS FC is an antimicrobial agent used in the treatment of tuberculosis (TB infection) in adults.

BEFORE YOU TAKE AFARIS FC

Do not take AFARIS FC if you suffer from any of the conditions mentioned below:
- If you are hypersensitive (allergic) to rifamycins including rifampicin, isoniazid or to any of the ingredients contained in **AFARIS FC**.
- If you have any kind of liver disease or jaundice (yellowing of the eyes and skin).
- If you have kidney disease, diabetes, suffer from alcoholism, a history of gout, suffer from convulsive disorders (epilepsy) and have porphyria.
- If you developed thrombocytopenia and purpura while taking **AFARIS FC** (bruising, nosebleeds or bleeding in the mouth and gums, rash with pinpoint red spots).
- If you develop itching with swelling or skin rash or difficulty breathing, or if the skin and eyes turn yellow while taking **AFARIS FC** do not take any more **AFARIS FC** and tell your doctor immediately.
- **AFARIS FC** and nevirapine or saquinavir/ritonavir (medicines for HIV) should not be used together.

Take special care with AFARIS FC
- **AFARIS FC** should not be given to patients whose liver is not functioning normally, however, in cases where there are no other treatment options your doctor will monitor your liver function before treatment and every two to four weeks during treatment with **AFARIS FC**.
  Tell your doctor immediately and stop taking **AFARIS FC** if you develop symptoms of hepatitis (inflammation of the liver, if left untreated, could lead to death) such as fatigue, weakness, feeling unwell, loss of appetite, nausea or vomiting. Continued use of **AFARIS FC** may cause a more severe form of liver damage and may increase convulsions ("fits").
- Your doctor will be monitoring your blood counts if you have liver disease, suffer from alcoholism or are on long-term treatment with **AFARIS FC**. Your doctor will adjust the dose of **AFARIS FC** or change your medicine based on the results of your blood tests.
  If you develop 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 FC** should not be taken and be permanently withdrawn.
- Take **AFARIS FC** as prescribed by your doctor on a continuous daily 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).
- Your doctor may prescribe periodic eye examinations as **AFARIS FC** 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 FC** to minimise adverse reactions if you are malnourished or have neuropathy (damage to the nerves resulting in poor coordination, muscle weakness, pain in the fingers or toes, or numbness).
- Urine, stools, saliva, sputum, sweat and tears may be discoloured.
- Soft contact lenses may be permanently stained.

Taking AFARIS FC with food and drink
AFARIS FC 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

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health care professional for advice before taking **AFARIS FC**.

Safety and efficacy of **AFARIS FC** during pregnancy and breastfeeding has not been established.

Driving and using machinery
AFARIS FC may cause dizziness, impaired concentration, and/or drowsiness. If you feel dizzy or drowsy while taking **AFARIS FC** do not drive and do not use any tools or machines.

Taking other medicines with AFARIS FC
AFARIS FC may change the effect of other medicines and other medicines may change the effect of **AFARIS FC**.
Do not take AFARIS FC and tell your doctor if you are taking the following medicines:
- Nevirapine, saquinavir and ritonavir (HIV medicines).

The following medicines can make **AFARIS FC** work less well:
- Preparations containing bentonite (e.g. aminosalicylic acid used for TB) and medicines used to reduce gastric motility (e.g. atropine, codeine, loperamide). Take **AFARIS FC** at least 1 hour before these medicines.
- Antacids containing magnesium trisilicate, aluminium hydroxide and other aluminium containing antacids or sodium bicarbonate for indigestion. Take **AFARIS FC** at least 1 hour before these antacids.
- Alcohol, 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).

When taking **AFARIS FC**, it is especially important to tell your doctor or healthcare professional if you are 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 (saquinavir, indinavir, lopinavir, darunavir, atazanavir, fosamprenavir).
- Other medicines include certain inhalation 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), enalapril, verapamil and other calcium channel blocking agents, 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 FC** may decrease the effectiveness of oral contraceptives. Use a reliable barrier method of contraception such as condoms while taking **AFARIS FC**.

The following when taken with **AFARIS FC** 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, darunavir, atazanavir, fosamprenavir, indinavir), stavudine and zalcitabine.
- Other medicine such as warfarin (thins blood), diazepam, triazolam (for anxiety and depression), cycloserine (TB medicine), disulfiram (treatment of alcohol dependence), enflurane (anaesthetic medicine), clofazimine (used for leprosy), theophylline (for wheezing or difficulty in breathing).
- Alcohol (daily consumption could lead to severe liver problems).

Other:
- If you are taking medicines to thin the blood, your doctor will recommend frequent blood tests to ensure you are taking the right dose of the medicines to thin the blood.
- Diabetes may be difficult to control.
- Inform your doctor that you are taking **AFARIS FC** if you are having blood test for folic acid, Vitamin B_{12} or undergoing X-ray tests of the gallbladder.

Food interactions:
- **AFARIS FC** 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 taking tyramine- and histamine-containing foods while on treatment with **AFARIS FC**.

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

HOW TO TAKE AFARIS FC

Do not share medicines prescribed for you with any other person.
Always take **AFARIS FC** 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 FC** is too strong or too weak talk to your doctor or pharmacist.

AFARIS FC is recommended in the continuation phase of the treatment of tuberculosis. During this phase **AFARIS FC** should be taken continuously on a daily basis for 4 months.
Your doctor will prescribe the required number of tablets to be taken on a daily basis based on your body weight.

Daily dose of AFARIS FC 150/75 is as follows:	
Number of tablets (daily)	Patient body mass (kg)
2 tablets	30 to 37
3 tablets	38 to 54
4 tablets	55 to 70
5 tablets	71 and more*

Daily dose of AFARIS FC 300/150 is as follows:	
Number of tablets (daily)	Patient body mass (kg)
2 tablets	55 or more

AFARIS FC 150/75 and **AFARIS FC 300/150** is unsuitable for children under 12 years.
The tablets should preferably be taken on an empty stomach (30 minutes before or 2 hours after a meal) as a single dosage.
AFARIS FC should be taken at least 1 hour before aluminium containing antacids are taken.

Do not stop taking AFARIS FC because you feel 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 take more AFARIS FC than you should
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.

In the event of overdosage consult your doctor or pharmacist. If neither is available contact the nearest hospital or poison control center.

If you forget to take AFARIS FC
If you have missed a dose of **AFARIS FC** take 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

Tell your doctor immediately 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).
- Swelling of the face, lips, tongue or throat which may cause difficulty in breathing or swallowing.
- Shortness of breath and wheezing.
- Swelling of the lungs 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.

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

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

Tell your doctor if you notice any of the following and they worry you:
- Yellow discolouration of skin or eyes.
- Heartburn, anorexia, nausea, vomiting, wind, cramps or diarrhoea, constipation, dry mouth.
- Headache, drowsiness, fatigue, inability to concentrate or confusion.
- Poor coordination, muscle weakness, pain in the fingers or toes, or numbness, unusually increased reflexes or twitching.
- Oral thrush - white, furry, sore tongue and mouth.
- Blurred vision or loss of vision with or without eye pain, eye irritation.
- Menstrual disturbances.
- Temporary hearing loss.
- Vertigo (feeling dizzy with a spinning sensation).
- Enlarged breasts.
- Skin rash, itchy rash, acne, hair loss.
- Mental illness with strange or disturbing thoughts or moods.
- Loss of memory.

Not all the side-effects reported for **AFARIS FC** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **AFARIS FC**, please consult your doctor, pharmacist or health care professional for advice.
If you notice any side-effects not mentioned in this leaflet, please inform your doctor or pharmacist.

STORAGE AND DISPOSAL INFORMATION FOR AFARIS FC

Store at or below 25 °C.
Keep the blister in the carton unit required for use. Keep aluminum sachet in the HDPE container until required for use.
Store this medicine away from light and moisture.
Any expired or outdated medicines and unused medicines can be returned to your nearest pharmacy.
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

PRESENTATION

AFARIS FC 150/75
HDPE Container:
Silver coloured triple laminated aluminium sachet (PET/Al/LLDPE), 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 500 and 1 000 tablets.
AFARIS FC 150/75 and AFARIS FC 300/150
Blister:
Silver coloured aluminium backing foil with amber coloured (PVC/PE/PVdC) lidding foil. The blister is packed in a pre-printed carton. Pack sizes include 56 (2 blisters of 28 tablets), 84 tablets (3 blisters of 28 tablets), 672 tablets (24 blisters of 28 tablets) and 100 tablets (10 blisters of 10 tablets).

IDENTIFICATION

AFARIS FC 150/75:
Brown to reddish brown, round, biconvex, film coated tablet, plain on both sides.
AFARIS FC 300/150:
Brown to reddish brown, round, biconvex, film coated tablet, break line on one side and plain on other side.

REGISTRATION NUMBER

AFARIS FC 150/75: 48/20.2.3/0748
AFARIS FC 300/150: 48/20.2.3/0749

NAME AND BUSINESS ADDRESS OF HOLDER OF THE CERTIFICATE OF REGISTRATION

Macleods Pharmaceuticals SA (Pty) Ltd.
Office Block 1,
Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock,
Ext 12, Alberton.

DATE OF PUBLICATION OF THE PATIENT INFORMATION LEAFLET

25 November 2016

AFARIS FC 150/75
AFARIS FC 300/150
PM02906704

435 mm

490 mm

SKEDULERINGSTATUS

S4

EIENDOMSNAAM EN DOSEERVORM
AFARIS FC 150/75 (filmbedekte tablet)
AFARIS FC 300/150 (filmbedekte tablet)

SAMESTELLING:
AFARIS FC 150/75
Elke filmbedekte tablet bevat:
Rifampisien 150 mg en isoniasied 75 mg.
Die ander bestanddele is mieliestysel, krospovidoon, povidoon, gebleikte skellak, natriumlourielsulfaat, natriumstyselglikolaat, anhidriese kolloïdale silika, magnesiumstearaat.
Die bedekkingsbestanddele is: hipromellose, polivinielalkohol-deel gehidroliseerde, talk, titaandioksied (C.I. No 77891), ponceau 4R aluminiumlak (C.I. No. 16255), lesitien (soja) en xantaangom.
AFARIS FC 300/150
Elke filmbedekte tablet bevat:
Rifampisien 300 mg en isoniasied 150 mg.
Die ander bestanddele is mikrokristallyne sellulose, krospovidoon, povidoon, gebleikte skellak, natriumstyselglikolaat, kroskarmellose natrium, kalsiumstearaat.
Die bedekkingsbestanddele is: hipromellose, propileenglikol, dietielftalaat, gesuiwerde talk, titaandioksied (C.I. nr. 77891), kleursel Ponceau 4R lak (C.I. Nr. 16255).

FARMAKOLOGIESE KLASSIFIKASIE
A 20.2.3 Tuberkulostatiese middels

FARMAKOLOGIESE WERKING
Farmakodinamika:
Rifampisien en isoniasied is bakteriedodende anti-tuberkulose medisyne.
Rifampisien
Rifampisien inhibeer die groei van kliniese *Mycobacterium tuberculosis* isolate *in vitro* teen konsentrasies van 0,06 - 0,25 mg/l. 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 mikolsuur wat essensiële komponente van die selwand van *Mycobacterium tuberculosis* is en tot bakteriese dood van die sel lei.

Farmakokinetika:
Rifampisien
Absorpsie:
Rifampisien word geredelik vanuit die maagdermkanaal geabsorbeer met 'n orale biobeskikbaarheid van 68 %, K_{max} van 8 - 20 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-deasetielrifampisien. 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 spinaal vloeistof 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 gedefinieer: "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 FC word aangedui in die aanhoudende fase van behandeling van pulmonêre en ekstra-pulmonêre tuberkulose in nuutgediagnoseerde pasiënte en herbehandeling van volwasse gevalle.

KONTRA-INDIKASIES:
AFARIS FC word teenaangedui in pasiënte met 'n geskiedenis van hipersensitiwiteit teen rifamisiene of isoniasied en ander chemies verwante medisyne, of teen enige van die eksipiënte van **AFARIS FC**.
Dit word teenaangedui in die teenwoordigheid van geelsug.
AFARIS FC word teenaangedui in pasiënte met ingekorte nier- of lewerfunksie, diabetes mellitus, chroniese alkoholisme, 'n geskiedenis van jig en pasiënte wat aan stuipaanvalle en porfirie ly.
Die gelyktydige gebruik van **AFARIS FC** en nevirapien word teenaangedui.
AFARIS FC kan trombositopenie en purpura veroorsaak, gewoonlik met afwisselende tuberkulose regimes; verdere toediening word teenaangedui.
Die gebruik van **AFARIS FC** word teenaangedui wanneer dit saam met die kombinasie van sakinavir/ritonavir toegedien word (sien Interaksies).

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS
Rifampisien:
AFARIS FC behoort nie aan pasiënte met ingekorte lewerfunksie toegedien te word nie. Indien **AFARIS FC** die enigste behandelingsopsie in hierdie pasiënte is, behoort sorgvuldige lewerfunksie, veral serum alanienaminotransferase (ALT) en serum aspartaataminotransferase (AST) vóór terapie, en dan elke 2 tot 4 weke gedurende terapie uitgevoer te word. Indien tekens van hepatosellulêre beskadiging voorkom, behoort **AFARIS FC** 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 FC** nagegaan te word en spesiale sorg behoort aan die dag gelê te word in pasiënte met alkoholisme of diegene met 'n reeds bestaande lewersiekte, sou **AFARIS FC** die enigste behandelingsopsie 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 gemoniteer te word, asook in pasiënte met lewerafwykings. Indien trombositopenie of purpura voorkom, behoort **AFARIS FC** permanent onttrek te word.

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

Pasiënte behoort gewaarsku te word dat verkleuring van die uriene, 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 FC**, word teenaangedui in pasiënte met chroniese lewersiekte en wanfunksie van die niere. Indien **AFARIS FC** die enigste behandelingsopsie is, behoort hierdie pasiënte noukeurig gemoniteer 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, malaise, anoreksie, naarheid of braking gemoniteer 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 FC** in hierdie gevalle kan 'n meer ernstige vorm van lewerbeskadiging veroorsaak (sien **KONTRA-INDIKASIES**).

Lewerfunksie behoort vóór en gedurende behandeling met **AFARIS FC** nagegaan te word en spesiale sorg behoort in pasiënte met alkoholisme of diegene met reeds bestaande lewersiekte aan die dag gelê te word as **AFARIS FC** die enigste behandelingsopsie is (sien **KONTRA-INDIKASIES**). Periodieke oogondersoeke gedurende behandeling met **AFARIS FC** is voorgestel.

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

Effek op die vermoë om te bestuur en masjinerie te gebruik
AFARIS FC 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.

INTERAKSIES
Rifampisien:
Daar is aangemeld dat gehalogeneerde ingeademde narkosemiddels, wanneer dit saam met rifampisien toegedien word, die hepatotoksisiteit van beide middels 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 asetopnien, chlooramfenikol, simetidien, klofibraat, kortikosteroïede, teenstolmiddels soos warfarien, siklosporien, dapsoon, diasepam, doksisiklien, flukonasool, haloperidol, heksobarbitoon, itrakonasool, ketokonasool, metadoon, orale hipoglukemiese middels, fenitoïen, kinien, sulfasalasien, tiroïedhormone, teofillien, sidovudien en verskeie kardiovaskulêre medisyne insluitende beta-adrenoseptor blokkeerders, digoksien, en antidisritmiese middels soos disopiramied, lorkainied, meksiletien, propafenoon, kinidien, tokainied en verapamiel en ander kalsiumkanaal blokkeerders, orale voorbehoedmiddels, narkotika, pynstillers en barbiturate, antiretrovirusmiddels (bv. sidovudien, sakinavir, indinavir efavirenz) verminder.
Dit mag nodig wees om die dosis van hierdie medisyne aan te pas wanneer hulle saam met **AFARIS FC** gegee word. Pasiënte wat orale voorbehoedmiddels gebruik behoort aangeraai te word om na nie-hormonale metodes van geboortebeperking gedurende terapie met **AFARIS FC** te verander.

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 gemoniteer 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.

Magnesiumtrisilikaat, aluminiumhidroksied of natriumbikarbonaat verminder die biobeskikbaarheid van **AFARIS FC**. Die absorpsie van rifampisien kan verminder word deur die gelyktydige toediening saam met medisyne wat maagmotiliteit (antichollinergiese middels en opioïede), ketokonasool of preparate wat bentoniet bevat (bv. sommige aminosalisielsuurpreparate). Die daaglikse rifampisiendosis behoort ten minste 1 uur vóór die inname van hierdie medisyne toegedien te word.

Die protrombientyd van pasiënte wat tegelykertyd antikoagulantterapie ontvang mag afneem. Gereelde monitering van die protrombienvlak in sulke pasiënte met daaropvolgende aanpassing van die antikoagulantdosis word aanbeveel.

Diabetes mag moeiliker wees om te beheer.

Die konsentrasie van enalaprilaat, die aktiewe metaboliet van enalapril mag laer wees. Die dosis behoort, wanneer dit deur die pasiënt se kliniese kondisie aangedui word, aangepas te word.

Daar is aangetoon dat terapeutiese vlakke van **AFARIS FC** die standaard mikrobiologiese bepalings vir serumfolaat en vitamien B_{12} inhibeer. Alternatiewe bepalingsmetodes behoort derhalwe oorweeg word.
Verbygaande verhogings van bilirubien is ook waargeneem. Weens kompetisie vir biliêre uitskeiding kan **AFARIS FC** die biliêre uitskeiding van kontrasmedia wat vir die visualisering van die galblaas gebruik word, belemmer.

Antiretrovirusmiddels:
Rifampisien, soos bevat in **AFARIS FC**, 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.
Die gelyktydige gebruik van **AFARIS FC** en nevirapien word teenaangedui.
Rifampisien, soos bevat in **AFARIS FC**, 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 FC**, is nodig nie.
Wanneer **AFARIS FC** gelyktydig saam met die kombinasie van sakinavir/ritonavir gegee word, neem die potensiaal vir hepatotoksisiteit toe. Daarom word die gelyktydige gebruik van **AFARIS FC** saam met sakinavir/ritonavir teenaangedui.

Isoniasied:
Isoniasied is 'n inhibeerder van die hepatiese metabolisme van medisyne en kan daarom die effekte van sommige medisyne wat tegelykertyd geneem word, vererger.
Newe-effekte kan voorkom wanneer isoniasied saam met fenitoïen, primidoon, karbamasepien, etosuksimied, bensodiasepiene soos diasepam of triasolam en warfarien toegedien word.
Toepaslike aanpassings van die dosiese van anti-stuipmiddels 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, aminosalisielsuur, kortikosteroïede, ketokonasool, propranolol en groot dosisse piridoksien.
Die daaglikse inname van alkohol kan geassosieer word met hepatitis weens isoniasied.
Die metabolisme van enflurean kan in pasiënte wat isoniasied ontvang verhoog, wat tot potensieel nefrotoksiese vlakke van fluoried kan lei. Isoniasied is geassosieer met 'n toename in die konsentrasie of toksisiteit van klosasimen. Isoniasied inhibeer die metabolisme van primidoon.
Die orale absorpsie van isoniasied soos bevat in **AFARIS FC**, word deur aluminiumbevattende teensuurmiddels verminder. **AFARIS FC** behoort ten minste 1 uur vóór die teensuurmiddel toegedien te word.

Antiretrovirusmiddels:
Die opruiming van isoniasied word byna verdubbel wanneer dit saam met salsitabien toegedien word. **AFARIS FC** behoort met sorg saam met stavudien en salsitabien gebruik te word aangesien stavudien, salsitabien en isoniasied met perifere neuropatie geassosieer is. Daar is aangemeld dat die gebruik van **AFARIS FC** 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, bloedstuwing, hipotensie) teen voedsel wat histamien bevat (bv. kabeljou, tuna, ander tropiese vis), veroorsaak. Tiramien- en histamienbevattende voedsel behoort vermy te word in pasiënte wat **AFARIS FC** ontvang.

SWANGERSKAP EN LAKTASIE
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 FC 150/75:
AFARIS FC 150/75 word aanbeveel in die aanhoudende fase van behandeling van pulmonêre tuberkulose. Gedurende hierdie fase behoort **AFARIS FC 150/75** op 'n aanhoudende daaglikse basis toegedien te word.
Die totale dosisvereiste is as volg:

	Daagliks
Rifampisien	10 mg/kg (8 tot 12)
Isoniasied	5 mg/kg (4 tot 6)

Die daaglikse dosis is as volg:	
Aantal tablette (per dag)	Liggaamsmassa van die pasiënt (kg)
2 tablette	30 tot 37
3 tablette	38 tot 54
4 tablette	55 tot 70
5 tablette	71 en meer*

*In die praktyk sal die meeste pasiënte wat 'n rifampisienbevattende vaste dosis kombinasie neem 3 tot 4 tablette per dag neem. Slegs 'n klein aantal volwasse TB pasiënte sal in die kategorie met 'n liggaamsmassa 30 tot 37 kg of meer as 70 kg val. Dit mag die maksimum rifampisiendosis van 600 mg per dag oorskry. Daar moet egter by die dosisbeperking van 12 mg/kg gehou word.

AFARIS FC 150/75 is nie geskik vir kinders < 12 jaar nie.

AFARIS FC 300/150:
Gedurende hierdie fase wat 4 maande duur, behoort **AFARIS FC 300/150** op 'n daaglikse basis toegedien te word.
Die daaglikse dosisvereiste is as volg:

	Daagliks	
Rifampisien	10 mg/kg (8 tot 12 mg/kg)	Maksimum 600 mg per dag
Isoniasied	5 mg/kg (4 tot 6 mg/kg)	Maksimum 300 mg/dag

Die daaglikse dosis van AFARIS FC 300/150 is as volg:	
Aantal tablette (per dag)	Liggaamsmassa van die pasiënt (kg)
2 Tablette	55 of meer

AFARIS FC 300/150 is nie geskik vir kinders < 12 jaar nie.

AFARIS FC 150/75 en **AFARIS FC 300/150** behoort verkieslik op 'n leë maag (30 min vóór of 2 ure na 'n maaltyd) as 'n enkel dosis geneem te word.
AFARIS FC 150/75 en **AFARIS FC 300/150** behoort ten minste 1 uur vóór aluminiumbevattende teensuurmiddels gebruik word, geneem te word.

NEWE-EFFEKTE
RIFAMPISIEN
Afwykings van die bloed- en limfstelsel:
Minder dikwels: Bloeddiskrasie, 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, oogpyn.

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

Respiratoriese, bors- en mediastinale afwykings:
Frekwensie onbekend: Pulmonêre fibrose, pneumonitis.

Gastro-intestinale afwykings:
Dikwels: Naarheid, braking, anoreksie, diarree, epigastriese ongemak.
Minder dikwels: Pseudomembraneuse kolitis.
Frekwensie onbekend: Ulseratiewe kolitis, gastro-intestinale 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 bloos uit hittegloede en jeuk, met of sonder uitslag bestaan.
Minder dikwels: Meer ernstige hipersensitiewe velreaksies, toksiese epidermale nekrolise, eksfoliërende dermatitis, erythema multiforme, insluitende Stevens-Johnson se sindroom en vaskulitis.

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 rooibruin verkleuring van die uriene, feses, speeksel, sputum, sweet en trane. Sagte kontaklense mag permanent verkleur.
Minder dikwels: Afwisselende, onderbroke of herhaaldelike behandeling met rifampisien kan die kans dat die pasiënt koors, 'n febriele reaksie met griepagtige simptome, swamoorgroeiing d.i. seer mond en longe ontwikkel, vergroot.
Frekwensie onbekend: Edeem.

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

Afwykings van die immuunstelsel:
Minder dikwels: Hipersensitiwiteitsreaksies insluitende verskeie veleruptsies, 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 tendonrefleksies, stuipaanvalle, toename in die frekwensie van stuipaanvalle 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.

Gastro-intestinale 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: Veluitslae, aknee, Stevens-Johnson se sindroom, eksfoliatiewe dermatitis.
Frekwensie onbekend: Pellagra, alopesia, urtikaria.

Muskuloskeletale en bindweefselafwykings:
Frekwensie onbekend: 'n Rumatiekagtige sindroom, hiperrefleksie.

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 rooi verkleuring van die vel en slymvliese, wat soms as "die rooimansindroom" verwys word, gesigtelike swelling, periorbitale of gesigsedeem en algemene pruritus.
Isoniasied: Simptome sal meer waarskynlik met isoniasied geassosieer word. Dit sluit hiperglukemie en metaboliese asidose, sloerende spraak, stuipaanvalle, koma, hallusinasies, respiratoriese ongemak, depressie van die sentrale senuweestelsel in; fatale episodes kan voorkom.
Algemeen: In gevalle van oordosering met **AFARIS FC** behoort maagspoeling so gou as moontlik uitgevoer te word. 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 FC 150/75:
Bruin tot rooi-bruin ronde, bikonvekse, filmbedekte tablet, glad aan beide kante.
AFARIS FC 300/150:
Bruin tot rooi-bruin ronde, bikonvekse, filmbedekte tablet met 'n breeklyn aan die een kant en glad aan die ander kant.

AANBIEDING
AFARIS FC 150/75:
HDPE houer:
Silwergekleurde drieldubbel gelamineerde aluminium sakkie (PET/Al/LLDPE) in 'n wit, plastiekhouer (HDPE) wat by die opening met aluminiumfoelie verseël is en met 'n wit HDPE deksel toegeskroef word. Pakgroottes sluit 500 en 1000 tablette in.
AFARIS FC 150/75 en AFARIS FC 300/150:
Stolpverpakking:
Silwergekleurde aluminiumfoelie met 'n ambergekleurde, driedubbele (PVC/PE/PVdC) bedekking. Die stolpstrokies word in 'n voorafgedrukte karton verpak. Pakgroottes sluit 56 (2 strokies met 28 tablette), 84 tablette (3 strokies met 28 tablette), 672 tablette (24 strokies met 28 tablette en 100 tablette (10 strokies met 10 tablette) in.

BERGINGSINSTRUKSIES
Berg by of benede 25 °C. Bewaar teen vog en lig.
Hou die aluminiumsakkie in die HDPE tot benodig vir gebruik.
Hou die stolpstrokie in die karton tot benodig vir gebruik.
HOU BUITE BEREIK VAN KINDERS

REGISTRASIENOMMER
AFARIS FC 150/75: 48/20.2.3/0748
AFARIS FC 300/150: 48/20.2.3/0749

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE
Macleods Pharmaceuticals SA (Edms.) Bpk
Kantoorblok 1,
Bassonia Estate Office Park (Oos),
Cussonialaan 1, Bassonia Rock,
Uitb. 12, Alberton.

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INLIGTINGSBLAADJIE VIR PASIËNTE

SKEDULERINGSTATUS

S4

EIENDOMSNAAM, STERKTE EN FARMASEUTIESE VORM
AFARIS FC 150/75 (filmbedekte tablet)
Rifampisien 150 mg en isoniasied 75 mg
AFARIS FC 300/150 (filmbedekte tablet)
Rifampisien 300 mg en isoniasied 150 mg

LEES DIE HELE BROSJURE SORGVULDIG VOORDAT U BEGIN OM AFARIS FC 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 FC** is vir u kind persoonlik voorgeskryf en u behoort nie u medisyne met ander mense te deel nie. Dit mag hulle skade aandoen, ookal het hulle dieselfde simptome.

WAT AFARIS FC BEVAT
AFARIS FC 150/75
Elke filmbedekte tablet bevat die aktiewe bestanddele rifampisien 150 mg en isoniasied 75 mg.
Die ander bestanddele is mieliestysel, krospovidoon, povidoon, gebleikte skellak, natriumlourielsulfaat, natriumstyselglikolaat, anhidriese kolloïdale silika, magnesiumstearaat.
Bedekkingsbestanddele: hipromellose, polivinielalkohol-deel gehidroliseerde, talk, titaandioksied (C.I. No 77891), ponceau 4R aluminiumlak (C.I. No. 16255), lesitien (soja) en xantaangom.
AFARIS FC 300/150
Elke filmbedekte tablet bevat die aktiewe bestanddele rifampisien 300 mg en isoniasied 150 mg.
Die ander bestanddele is mikrokristallyne sellulose, krospovidoon, povidoon, gebleikte skellak, natriumstyselglikolaat, kroskarmellose natrium, kalsiumstearaat.
Bedekkingsbestanddele: hipromellose, propileenglikol, dietielftalaat, gesuiwerde talk, titaandioksied (C.I. Nr. 77891), Kleur Ponceau 4R lake (C.I. Nr. 16255).

WAARVOOR AFARIS FC GEBRUIK WORD
AFARIS FC is 'n antimikrobiese middel wat in die behandeling van tuberkulose (TB-infeksie) gebruik word.

VOORDAT U AFARIS FC NEEM
MOENIE AFARIS FC neem as u aan een van die kondisies hieronder ly nie:
- As u hipersensitief (allergies) teen rifamisiene, insluitende rifampisien, isoniasied of enige van die ander bestanddele van **AFARIS FC** is.
- As u aan enige lewersiekte of geelsug (geel verkleuring van die oë en vel) ly.
- As u aan niersiekte, diabetes, alkoholisme, 'n geskiedenis van jig, kompulsiewe afwykings (epilepsie) en porfirie 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 u **AFARIS FC** neem.
- As u jeuk met swelling of uitslag van die vel of moeite met asemhaling begin ontwikkel, moet nie meer **AFARIS FC** neem nie en stel u dokter onmiddellik in kennis.
- **AFARIS FC** en nevirapien en sakinavir/ritonavir (medisyne vir MIV) behoort nie saam gebruik te word nie.

Neem spesiale sorg met AFARIS FC
- **AFARIS FC** behoort nie aan pasiënte toegedien te word wie se lewers nie normaal funksioneer nie. In gevalle waar daar geen ander behandelingsopsies bestaan nie, sal u dokter egter u lewerfunksie voor behandeling en elke twee tot vier weke gedurende behandeling met **AFARIS FC** monitor.
  Stel u dokter onmiddellik in kennis en staak die toediening van **AFARIS FC** as u 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. Die voortgesette gebruik van **AFARIS FC** kan 'n meer ernstige vorm van lewerbeskadiging veroorsaak en stuipaanvalle laat toeneem.
- U dokter sal u bloedtellings monitor as u aan 'n lewersiekte of alkoholisme ly, of indien u op langtermyn behandeling met **AFARIS FC** is. As u 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 FC** gestaak en permanent onttrek te word.
- Neem **AFARIS FC** 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 kan veroorsaak, uitslag en jeuk) of 'n griepagtige sindroom (kouekoors, duiseligheid, moeite met asemhaling, koors, hoofpyn, spierpyn, beenpyn en bewerasie) te vermy.
- U dokter mag periodieke oogondersoeke voorskryf aangesien **AFARIS FC** onduidelike sig of gesigsverlies met of sonder oogpyn en oogirritasie kan veroorsaak.
- U dokter mag vitamien B_6 (piridoksien) saam met **AFARIS FC** voorskryf om newe-effekte tot 'n minimum te beperk as u ondervoed is of aan neuropatie ly (beskadiging van die senuwees wat tot swak koördinasie, spierswakheid, pyn in die vingers of tone, of ongevoeligheid).
- Uriene, feses, speeksel, sputum, sweet en trane kan verkleur wees.
- Sagte kontaklense kan permanent verkleur word.

Die neem van AFARIS FC saam met voedsel en vloeistof
AFARIS FC behoort sonder voedsel geneem te word. Vermy tiramienbevattende voedsel (bv. kaas, rooiwyn) en histamienbevattende voedsel (bv. kabeljou, tuna en tropiese vis). Vermy alkohol.

Swangerskap en borsvoeding

> As u swanger is of u baba borsvoed, moet u asseblief u dokter, apteker of ander professionele [illegible] vir advies vra voordat u **AFARIS FC** [illegible]

Die veiligheid gedurende swangerskap en borsvoeding is nie vasgestel nie.

Bestuur en die gebruik van masjinerie
AFARIS FC kan duiseligheid, ingekorte konsentrasie en/of lomerigheid veroorsaak. As u duiselig of lomerig voel terwyl u **AFARIS FC** neem, moet u nie bestuur of met enige gereedskap of masjinerie werk nie.

Die toediening van ander medisyne saam met AFARIS FC
AFARIS FC kan die effek van ander medisyne en ander medisyne kan die effek van **AFARIS FC** beïnvloed.

Moenie AFARIS FC toedien en stel u dokter onmiddellik in kennis as u kind enige van die volgende medisyne neem:
- Nevirapien, sakinavir of ritonavir (MIV medisyne).

Die volgende medisyne kan veroorsaak dat **AFARIS FC** nie na wense werk nie:
- Preparate wat bentoniet bevat (bv. aminosalisielsuur gebruik vir TB) en medisyne wat maagmotiliteit verminder (bv. atropien, kodeïen, loperamied). Neem **AFARIS FC** ten minste een uur vóór hierdie medisyne.
- Teensuurmiddels wat magnesiumtrisilikaat, aluminiumhidroksied ander aluminiumbevattende teensuurmiddels of natriumbikarbonaat en vir indigestie, bevat. Dien **AFARIS FC** ten minste een uur voor die teensuurmiddel toe.
- Alkohol, 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).

Wanneer u **AFARIS FC** neem, is dit veral belangrik om u dokter of professionele gesondheidswerker in kennis te stel as u 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 (sakinavir, indinavir, lopinavir, duranavir, atazanavir, fosamprenavir).
- Ander medisyne sluit sekere narkosemiddels (om die spiere voor chirurgie te verslap), asetopnien, 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 geestessiekte), heksobarbitoon (sedeermiddel), metadoon (vir heroïenonttrekking), orale hipoglukemiese middels gebruik in die behandeling van diabetes, sulfasalasien gebruik in rumatoïese artritis en inflammatoriese dermsiekte), tiroïedhormone (levotiroksien), teofillien (vir hyging of moeite met asemhaling), kinien (gebruik in malaria), medisyne om u hartklop te kontroleer soos digoksien, disopiramied, lorkainied, meksiletien, propafenoon, 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 FC** kan die effektiwiteit van orale voorbehoedmiddels verminder. Gebruik 'n betroubare metode van skeidingskontrasepsie soos kondome, terwyl **AFARIS FC** geneem word.

Die volgende middels, wanneer dit saam met **AFARIS FC** geneem word, kan die voorkoms van newe-effekte verhoog:
- Medisyne wat gebruik word om epilepsie te behandel soos etosuksimied, fenitoïen, primidoon en karbamasepien. U dokter sal die dosis van die epilepsiemedikasie dienooreenkomstig aanpas).
- MIV medisyne soos MIV protease-inhibeerders (lopinavir, ritonavir, sakinavir, duranavir, atazanavir, fosamprenavir, indinavir), 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).

Ander:
- As u medisyne gebruik om die bloed te verdun, sal u dokter gereelde bloedtoetse uitvoer om te verseker dat u die korrekte dosis van die medisyne neem om die bloed te verdun.
- Dit mag moeilik wees om diabetes te beheer.
- Stel u dokter in kennis dat u **AFARIS FC** neem as u bloedtoetse vir foliensuur, vitamien B_{12} ondergaan of as u X-strale vir die galblaas laat neem.

Voedselinteraksies:
- **AFARIS FC** kan 'n wisselwerking met tiramienbevattende voedsel (kaas, rooiwyn) en met voedsel wat histamien bevat (kabeljou, 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 inname van tiramien- en histamienbevattende voedsel te vermy terwyl u op behandeling met **AFARIS FC** is.

> Stel altyd u professionele gesondheidswerker in kennis as u enige ander medisyne gebruik. Dit sluit [illegible] en tradisionele [illegible] in.

HOE OM AFARIS FC TOE TE NEEM

> Moenie medisyne wat vir u voorgeskryf is met enigiemand anders deel nie.
> Dien **AFARIS FC** 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 FC** te sterk of te swak is, moet u u dokter of apteker raadpleeg.

AFARIS FC word aanbeveel in die aanhoudende fase van behandeling van tuberkulose. Gedurende hierdie fase behoort **AFARIS FC** op 'n aanhoudende daaglikse basis vir 4 maande toegedien te word.
U dokter sal die vereiste aantal tablette wat op 'n daaglikse basis geneem word, op grond van u liggaamsmassa voorskryf.

Die daaglikse dosis van AFARIS FC 150/75 is as volg:	
Aantal tablette (per dag)	Liggaamsmassa van die pasiënt (kg)
2 tablette	30 tot 37
3 tablette	38 tot 54
4 tablette	55 tot 70
5 tablette	71 en meer*

Die daaglikse dosis van AFARIS FC 300/150 is as volg:	
Aantal tablette (per dag)	Liggaamsmassa van die pasiënt (kg)
2 Tablette	55 of meer

AFARIS FC 150/75 en **AFARIS FC 300/150** is nie geskik vir kinders < 12 jaar nie.

Die tablette behoort op 'n leë maag (30 min vóór of 2 ure na 'n maaltyd) as 'n enkel dosis geneem te word.
AFARIS FC behoort ten minste 1 uur vóór aluminiumbevattende teensuurmiddels gebruik word, geneem te word.

Moenie die gebruik van AFARIS FC staak omdat u 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 FC geneem het
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 [illegible], swelling van die [illegible] en oë en [illegible] in.

> In die geval van oordosering, raadpleeg u dokter of apteker. As hulle nie beskikbaar is nie, kontak u naaste [illegible]

As u vergeet het om AFARIS FC te neem
As u vergeet het om 'n dosis **AFARIS FC** te neem, moet u dit sodra u daarvan onthou, neem. As dit egter byna tyd vir die volgende dosis is, slaan die vergete dosis oor en gaan met die gereelde doseringskedule voort. Moet nooit die dosis verdubbel nie.

MOONTLIKE NEWE-EFFEKTE
AFARIS FC kan newe-effekte hê.
Stel u dokter onmiddellik in kennis 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).
- Swelling van die gesig, lippe, tong of keel wat moeite met asemhaling of sluk veroorsaak.
- Kortasemheid en hyging.
- Swelling van die longe wat hoes, moeite met asemhaling en hyging (simptome van pneumonitis) kan veroorsaak.
- Letselvorming en verdikking in die longe met kortasemheid (simptome van pulmonêre fibrose).
- 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 (OOT) 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 klewerige stoelgang of bloederige diarree.
- Inflammasie van die pankreas met erge boonste maagpyn, naarheid en braking.

Stel u dokter onmiddellik in kennis as u enige van die volgende newe-effekte waarneem, veral as hulle 'n paar weke nadat u met die behandeling met AFARIS FC gestaak het, voorkom:
- Erge maagkrampe.
- Waterige en erge diarree, wat ook bloederig kan wees.
- Koors in kombinasie met een of beide van bogenoemde.
U mag aan 'n ernstige kondisie 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 wanneer u een van die volgende waarneem en dit u behommer:
- Geel verkleuring van die vel of oë.
- Sooibrand, anoreksie, naarheid, braking, winderigheid, krampe of diarree, hardlywigheid, droë mond.
- Hoofpyn, lomerigheid, moegheid, onvermoë om te konsentreer of verwardheid.
- Swak koördinasie, spierswakheid, spierpyn, pyn in die vingers of tone, gevoelloosheid, ongewone toename in reflekse en trekkings.
- Mondsproei - wit wolkerige, seer tong en mond.
- Onduidelike sig, of verlies aan sig met of sonder oogpyn, oogirritasie.
- Menstruele afwykings.
- Tydelike gehoorverlies.
- Vertigo (duiseligheid met 'n draaigevoel).
- Vergroting van die borste.
- Veluitslag, jeukerige uitslag, aknee en haarverlies.
- Geestessiekte met vreemde of kommerwekkende gedagtes of buie.
- Geheueverlies.

Nie al die newe-effekte wat vir **AFARIS FC** aangemeld is, word in hierdie brosjure ingesluit nie. As u algemene gesondheid agteruitgaan of as u enige ongewone effekte ondervind terwyl u **AFARIS FC** neem, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker om advies raadpleeg.
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 FC
Berg by of benede 25 °C.
Hou die stolpstrokie in die karton tot benodig vir gebruik. Hou die aluminiumsakkie in die HDPE tot benodig vir gebruik.
Bewaar hierdie medisyne weg van lig en vogtigheid.
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
AFARIS FC 150/75:
HDPE houer:
Silwergekleurde driedubbel gelamineerde aluminium sakkie (PET/Al/LLDPE) in 'n wit, plastiekhouer (HDPE) wat by die opening met aluminiumfoelie verseël is en met 'n wit HDPE deksel toegeskroef word. Pakgroottes sluit 500 en 1000 tablette in.
AFARIS FC 150/75 en AFARIS FC 300/150:
Stolpverpakking:
Silwergekleurde aluminiumfoelie met 'n ambergekleurde, driedubbele (PVC/PE/PVdC) bedekking. Die stolpstrokies word in 'n voorafgedrukte karton verpak. Pakgroottes sluit 56 (2 strokies met 28 tablette), 84 tablette (3 strokies met 28 tablette), 672 tablette (24 strokies met 28 tablette en 100 tablette (10 strokies met 10 tablette) in.

IDENTIFIKASIE
AFARIS FC 150/75:
Bruin tot rooi-bruin ronde, bikonvekse, filmbedekte tablet, glad aan beide kante.
AFARIS FC 300/150:
Bruin tot rooi-bruin ronde, bikonvekse, filmbedekte tablet met 'n breeklyn aan die een kant en glad aan die ander kant.

REGISTRASIENOMMER
AFARIS FC 150/75: 48/20.2.3/0748
AFARIS FC 300/150: 48/20.2.3/0749

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE
Macleods Pharmaceuticals SA (Edms.) Bpk
Kantoorblok 1,
Bassonia Estate Office Park (Oos),
Cussonialaan 1, Bassonia Rock,
Uitb. 12, Alberton.

DATUM VAN PUBLIKASIE VAN HIERDIE INLIGTINGSBROSJURE
25 November 2016

435 mm
490 mm

MACLEODS

PACKAGING RESEARCH & DEVELOPMENT

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

Note : Change in composition of coating materials of 150/75 mg strength.

1. Product: AFARIS FC 150/75 / AFARIS FC 300/150	
2. Country: South Africa	3. Packaging component: Package Insert & Patient Information Leaflet
4. No. of Colours: 1 Colour	5. Pantone Shade No.: Black
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.: PM02508704
11. Artwork has been made: Actual Size	12. Pharma code No.: 27673 mini
13. Barcode/NDC no: NA	14. Supersedes Item code No: PM02508703
15. Revision no: 03	16. File Name E:\ANDA Regulatory\South Africa\Rifa300 & Iso 150\04\Afaris-PM02508704.cdr
Approved By:	17. Location: Daman

PRD	M.A. HOLDER	MEDICAL/RAD	QC	PRODN	QA
08/09/24	Vanita Rajool	08/09/24	09/09/24	09/09/24	09/09/24

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.

FRM/CQA/021/04-01

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa	PM02508701	1/11/17	27/11/2017
2) Address change	PM02508702	11-5-18	20/06/2018
3) Change in storage condition and text matter	PM02508703	27-1-21	Not Implemented
4) Change in composition of coating materials of 150/75 mg strength.	PM02508704		