APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

FRIPNIT PLUS 300 mg/300 mg film coated tablets

Rifapentine and Isoniazid

FRIPNIT PLUS is sugar free.

Read all of this leaflet carefully before you start taking FRIPNIT PLUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- FRIPNIT PLUS 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 is in this leaflet

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6. Contents of the pack and other information

1. What FRIPNIT PLUS is and what it is used for

FRIPNIT PLUS is used with other anti-tuberculosis (TB) medicines such as isoniazid to treat inactive (latent) tuberculosis infection and to prevent its progression to active tuberculosis disease in people aged 2 years and older who are at risk.

FRIPNIT PLUS should not be used in people with active TB.

2. What you need to know before you take FRIPNIT PLUS

Do not take FRIPNIT PLUS

- if you are hypersensitive (allergic) to rifapentine, other rifamycins (e.g. rifampicin, rifabutin), isoniazid, ethionamide, pyrazinamide (used for TB), niacin (vitamin B_3), or other chemically-related medicines or to any of the ingredients of FRIPNIT PLUS (see section 6)
- if you have a condition called porphyria (a group of disorders that can cause nerve or skin problems (blisters and itching) due to a problem with the production of blood pigment and red blood cells within the body)
- if you have acute or chronic liver disease
- alcoholism
- in patients with severe kidney failure
- if you have uncontrolled seizures
- if you are pregnant and breastfeeding
- if you are currently on antiretroviral therapy.

Warnings and precautions

Take special care with FRIPNIT PLUS

Tell your doctor or healthcare provider if you:

- have liver problems. Your doctor may do a blood test to check your liver function before and during your treatment (see Do not take FRIPNIT PLUS)
- take other medicines to treat HIV infection or take oral contraceptives as taking these medicines with FRIPNIT PLUS may make them less effective (see Other medicines and FRIPNIT PLUS)
- take a medicine called digoxin (used to make the heart beat stronger and with a more regular rhythm). Your doctor will monitor and may change your dose of digoxin as FRIPNIT PLUS may affect the way digoxin works. Even small changes need to be monitored to prevent serious side effects from occurring (also see Other medicines and FRIPNIT PLUS)
- wear contact lenses or dentures. FRIPNIT PLUS may change the normal colour of your skin, mouth and body fluids and cause your skin, teeth, tongue, urine, stools, saliva, sputum, tears, sweat, and breast milk to turn a red-orange colour. Contact lenses or dentures may become permanently stained.
- have diabetes as your diabetes may become more difficult to control while taking this medicine
- have epilepsy
- have or have ever had mental health problems (such as depression or schizophrenia)
- have any kidney problems

- are diabetic, alcoholic, malnourished, uraemic (high levels of urea in the blood), pregnant or infected with HIV, your doctor may prescribe pyridoxine (vitamin B_6) to be taken daily.

If you experience any of the following effects whilst, or after, taking FRIPNIT PLUS, tell your doctor or health care provider immediately:

- signs or symptoms of liver disease whilst on therapy (such as unexplained anorexia, nausea, vomiting, dark urine, yellowing of the skin or whites of your eyes, rash, persistent pins and needles sensation of the hands and feet, persistent fatigue, weakness of greater than 3-days duration and/or abdominal tenderness) stop taking FRIPNIT PLUS and call your doctor immediately
- if you experience symptoms of hypersensitivity (allergic reaction) after taking FRIPNIT PLUS, such as low blood pressure, hives, swelling of the face, lips, tongue or throat, difficulty breathing, red eyes or flu-like syndrome (weakness, extreme tiredness, muscle pain, nausea and vomiting, headache, fever, chills, aches, rash, itching, sweats, dizziness, shortness of breath, chest pain, cough, fainting, fast heartbeat). These may be symptoms of a serious allergic reaction and you must immediately stop taking FRIPNIT PLUS and go to the casualty department at your nearest hospital (see Possible side effects)
- the following severe skin problems syndrome have been reported with the use of FRIPNIT PLUS. If you develop any skin reaction, stop treatment immediately and contact your doctor or health care provider.

- Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) with symptoms that may include blistering, peeling or bleeding on any part of your skin with or without a rash. This includes your lips, eyes, mouth, nose, genitals, hands or feet. You may also have flu-like symptoms at the same time, such as fever, chills or aching muscles.
- drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome with symptoms that may include flu-like symptoms and a widespread rash with a high body temperature and enlarged lymph nodes. Abnormal blood test results may include increased levels of liver enzymes and an increase in a type of white blood cell (eosinophilia).

- FRIPNIT PLUS may cause a type of diarrhoea called *Clostridium difficile*-associated diarrhoea (CDAD) which may occur either during or after treatment. The severity of CDAD can range from mild diarrhoea to severe diarrhoea that may cause death (fatal colitis). Tell your doctor immediately if you experience diarrhoea either whilst, or after you have stopped taking FRIPNIT PLUS (see Possible side effects).
- if you develop any eye problems as regular eye examinations are advised while being treated with FRIPNIT PLUS.

Other medicines and FRIPNIT PLUS

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

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When taking FRIPNIT PLUS with other medicines, those taken together may affect each other, which may either result in serious side effects or cause one of the medicines to be ineffective.

Before staring therapy with FRIPNIT PLUS, tell your doctor or healthcare provider if you are taking or have recently taken any of the following:

- medicines used to treat HIV infection such as indinavir, darunavir, lopinavir, saquinavir, ritonavir, rilpivirine, zidovudine, zalcitabine
- antifungal medicines (to treat fungal infections) such as itraconazole, ketoconazole, voriconazole
- pain killers (narcotic analgesics) such as methadone, alfentanil, buprenorphine, paracetamol
- medicines used for diabetes to lower blood sugar such as repaglinide
- medicines to lower blood pressure, called calcium channel blockers such as felodipine, diltiazem, verapamil, nifedipine
- medicines to lower blood pressure called alpha or beta adrenergic antagonists such as alfuzosin, propranolol
- medicines to treat migraine, sometimes referred to as ergot alkaloid derivatives such as ergotamine
- medicines used to prevent the blood from clotting (anticoagulants) such as warfarin
- hormonal contraceptives for women. If you are using any form of contraception, such as contraceptive tablets, transdermal patches (patches used on the skin) or an implant while taking FRIPNIT PLUS, you should discuss with your doctor, or health care provider, the need to either use an additional non-hormonal means of

contraception, or to change your contraceptive pill in order to ensure your method of contraception is still effective

- medicines used to lower your immune system (used to prevent organ rejection) such as ciclosporin, tacrolimus, sirolimus
- medicines used as sedatives or to treat anxiety such as midazolam, diazepam, triazolam
- digoxin (used to make the heart beat stronger and with a more regular rhythm). Your doctor will monitor your dose of digoxin and may change it due to FRIPNIT PLUS. Even small changes need to be monitored to prevent serious side effects from occurring (see Take special care with FRIPNIT PLUS)
- medicine for the treatment of epilepsy such as carbamazepine, phenytoin or primidone
- theophylline, used for lung diseases such as asthma and bronchitis
- disulfiram for the treatment of alcoholism
- cycloserine, an antibiotic used in the treatment on tuberculosis
- para-aminosalicyclic acid or any other medicine used to treat TB
- prednisolone and anti-inflammatory medicine used to treat allergies, blood disorders, skin diseases, infections
- antacids used for indigestion should be taken at least 1 hour after taking FRIPNIT PLUS
- levodopa for the treatment of Parkinson's disease

FRIPNIT PLUS may also interact with the laboratory tests that determine folate and vitamin B_{12} in your blood. Make sure that you inform your doctor or healthcare provider that you are taking FRIPNIT PLUS before such tests are performed.

Other medicines which may affect FRIPNIT PLUS

- medicines used for inflammation (e.g. ibuprofen, diclofenac)
- medicines used to lower blood sugar in diabetes (sulfonylureas) such as glipizide
- medicines to stop your blood clotting.

FRIPNIT PLUS with food and drink

FRIPNIT PLUS may interact with foods containing histamine or tyramine (e.g. matured cheeses, cured meat, some fish like tuna, salmon and mackerel, wine and beer), causing symptoms including headache, sweating, flushing, fast, uneven or forceful heartbeat (palpitations), dizziness, feel lightheaded or faint (due to low blood pressure). These foods should be avoided if you are receiving isoniazid. Your doctor will be able to advise further.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before using FRIPNIT PLUS.

The safety of FRIPNIT PLUS during pregnancy and breastfeeding has not been established (see **Do not take FRIPNIT PLUS**). You should not be treated with FRIPNIT PLUS if you are pregnant.

You should avoid becoming pregnant while on treatment with FRIPNIT PLUS.

You should not breastfeed your baby if you are taking FRIPNIT PLUS as it is not known if FRIPNIT PLUS passes into your breast milk.

FRIPNIT PLUS may cause a red-orange discolouration of body fluids, including breast milk.

Driving and using machines:

Adverse reactions such as convulsions (fits) have been reported in patients taking FRIPNIT PLUS, you should therefore not drive, use machinery or perform any tasks that require concentration, until you are certain that LENNON ISONIAZID does not adversely affect your ability to do so.

It is not always possible to predict to what extent FRIPNIT PLUS may interfere with your daily activities.

You should ensure that you do not engage in the above activities until you are aware of the measure to which FRIPNIT PLUS affects you.

3. How to take FRIPNIT PLUS

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Do not share medicines prescribed for you with any other person. Always use FRIPNIT PLUS exactly as your doctor has instructed. You should check with your doctor or pharmacist if you are unsure.

FRIPNIT PLUS should be taken once-weekly for 12 weeks as directly observed therapy (DOT). DOT is a way of helping people during their treatment, this means your treatment will be monitored weekly by visiting your local clinic, hospital or nurse so they can make sure you take your treatment correctly.

Your doctor will calculate the number of tablets you should take weekly based on your weight. This dose will therefore be calculated for you personally.

It is important to take all of your FRIPNIT PLUS and any other TB medicine regularly and you do not skip doses. Missing doses may cause FRIPNIT PLUS to not work as well and may increase the chance that your TB will not be treatable by FRIPNIT PLUS or other medicines.

Take FRIPNIT PLUS with food.
Take FRIPNIT PLUS with food if you suffer with stomach problems. This may help prevent nausea, vomiting or stomach upsets due to the medicine.

It is preferable to take antacids at least 1 hour before or 2 hours after your dose of FRIPNIT PLUS tablets.

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If you cannot swallow tablets whole, they can be crushed and mixed with a small amount of semi-solid food. Be sure to immediately take all of the semisolid food with FRIPNIT PLUS crushed into it.

Your doctor will tell you how long your treatment with FRIPNIT PLUS will last. If you have the impression that the effect of FRIPNIT PLUS is too strong or too weak, tell your doctor or pharmacist.

If you take more FRIPNIT PLUS than you should

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

If you forget to take FRIPNIT PLUS

Since your weekly dose of FRIPNIT PLUS will be given to you via directly observed therapy (DOT), meaning you will visit, for example, your local clinic or hospital, it is unlikely that you will forget to take a dose. However, if you have missed the visit to your local clinic or hospital, visit them as soon as possible for your dose. Do not skip the whole week until the next appointment.

If you stop taking FRIPNIT PLUS

Withdrawal symptoms, which may occur, include headache, insomnia, excessive dreaming, irritability and nervousness.

4. Possible side effects

FRIPNIT PLUS can have side effects.

Not all side effects reported for FRIPNIT PLUS are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using FRIPNIT PLUS, please consult your healthcare provider for advice.

If any of the following happens, stop using FRIPNIT PLUS 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

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to FRIPNIT PLUS. 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:

- flu-like syndrome (weakness, extreme tiredness, muscle pain, nausea and vomiting, headache, fever, chills, aches, rash, itching, sweats, dizziness, shortness of breath, chest pain, cough, fainting, fast heartbeat) (see Take special care with FRIPNIT PLUS)

- hepatitis (inflammation of the liver) and other liver problems including jaundice and liver failure (symptoms may include: nausea, vomiting, stomach pain, loss of appetite, tiredness, yellowing of the skin or whites of your eyes, dark urine) (see Take special care with FRIPNIT PLUS)
- pancreatitis (inflammation of the pancreas) (symptoms may include upper abdominal pain that radiates into the back; swollen and tender abdomen; nausea and vomiting, fever and increased heart rate)
- pneumonia (infection of the lungs; symptoms may include fever and chills, cough, difficulty breathing, shortness of breath when you climb stairs)
- blistering, peeling or bleeding on any part of your skin with or without a rash (including your lips, eyes, mouth, nose, genitals, hands or feet), flu-like symptoms (fever, chills or aching muscles) which are symptoms of a serious skin reaction (Steven Johnson Syndrome/ toxic epidermal necrolysis (TEN)) which could be fatal
- a serious reaction (DRESS) with flu-like symptoms, a widespread rash with a high body temperature and enlarged lymph nodes. Abnormal blood test results may include increased levels of liver enzymes and an increase in a type of white blood cell (eosinophilia)
- skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These could be signs of a serious skin allergy called ‘erythema multiforme’
- peripheral neuritis or neuropathy, a result of damage to the nerves outside of the brain and spinal cord (peripheral nerves), often causes weakness, numbness and pain, usually in your hands and feet

- neurotoxicity- damage to brain or peripheral nervous system (this can alter the activity of the nervous system in ways that can disrupt or kill nerves).
- convulsions (fits)
- lupus-like syndrome: drug-induced lupus erythematosus (DIL) is a subset of lupus defined as a lupus-like syndrome that develops in temporal relation when you have taken some kind of medicine and resolves after you stop taking the medicine
- severe inflammation of the entire skin surface (exfoliative dermatitis)
- rheumatic diseases are characterized by inflammation that affects the connecting or supporting structures of the body (most commonly the joints, but also sometimes the tendons, ligaments, bones, and muscles) arthritis
- hepatitis and hepatitis prodromal symptoms (loss of appetite, nausea or vomiting, unusual tiredness or weakness)
- blood disorders which may make you more likely to get infections, get tired very easily, or bruise very frequently
- chills, tiredness, unusually pale skin colour, shortness of breath, fast heartbeat or dark coloured urine. These could be signs of a serious type of anaemia
- you bruise more easily than usual. Or you may have a painful rash of dark red spots under the skin which do not go away when you press on them (purpura). This could be because of a serious blood problem

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- increase in liver enzymes
- nausea, vomiting, constipation, upper abdominal pain, dry mouth, stomach irritation

Less frequent side effects:

- influenza (flu)
- headache

- skin rash/reaction, hair loss and swelling of skin
- muscle pain
- high blood sugar levels (although you may not notice any symptoms)
- acidosis (upset of the acid balance in the body) which may make you feel or be sick, be drowsy or have breath that smells of “pear drops”
- overactive reflexes (being jumpy and overreacting)
- dizziness or feeling if the room is spinning round (vertigo)
- gynaecomastia (increased size of breasts in men)
- inflammation of an optic nerve, causing blurred vision
- pellagra (a disease caused by a lack of vitamin B_3 with symptoms including inflamed skin, diarrhoea, dementia, and sores in the mouth, constipation, dry mouth)
- acne-like eruptions
- difficulty passing urine.

The following side effects have been reported but the frequency for them to occur is not known:

- irritation of the oesophagus (the tube that carries food from your throat down to your stomach).

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

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report any side effects to SAHPRA via the online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8

By reporting side effects, you can help provide more information on the safety of FRIPNIT PLUS. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

5. How to store FRIPNIT PLUS

Store all medicines out of reach of children.

Store below 25 °C. Protect from excessive heat and moisture.

Keep blisters in carton until required for use.

Do not use after the expiry date stated on the carton. Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What FRIPNIT PLUS contains

Each FRIPNIT PLUS film coated tablet contains 300 mg rifapentine and 300 mg isoniazid.

The other ingredients are:

Tablet cores

Calcium stearate, colloidal silicon dioxide, dewaxed shellac, disodium edetate, hydroxypropyl cellulose, microcrystalline cellulose, pregelatinized starch, sodium ascorbate, sodium lauryl sulphate, sodium starch glycolate.

Tablet coating (WT-MPAQ-01266P brown)

Polyvinyl alcohol, red iron oxide, soya lecithin, talcum, titanium dioxide,
xanthum gum.

What FRIPNIT PLUS looks like and contents of the pack

Brown coloured, capsule shape, biconvex, film coated tablets, score line on one side and plain on other side.

FRIPNIT PLUS is available in:

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Aluminium strips of either 10, 12 or 14 tablets per strips.

Alu-Alu blister packs of either 10, 12 or 14 tablets per blister.

Blisters and strips are packed into printed outer carton with a leaflet.

Not all pack sizes may be marketed

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