

PACKAGE LEAFLET: INFORMATION FOR THE USER

Rifater® 50, 120, 300mg Tablets

(isoniazid, rifampicin, pyrazinamide)

Important things you need to know about Rifater Tablets

- It is very important that you take Rifater Tablets exactly as your doctor has told you.
- You must keep taking it until your doctor tells you to stop
- If you are taking any other medicines, including medicines you have bought from the pharmacy or shop, you must make sure your doctor knows
- Rifater Tablets make all your body fluids an orange or red colour. Do not worry - this is normal and not harmful
- Take Rifater Tablets on an empty stomach. This means at least 30 minutes before food or 2 hours after food
- While you are taking Rifater Tablets, you should not eat matured cheeses, cured meat, some fish (like tuna, salmon and mackerel) or drink wine and beer (see 'Taking Rifater Tablets with food, drink and alcohol')
- If you get a temperature, are sick, begin to feel more unwell, lose your appetite or have yellowing of the skin, gums or eyes, you must talk to your doctor straight away

Read the rest of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it to others. It may harm them, even if their signs of illness are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. See section 4.

The name of your medicine is Rifater 50, 120, 300mg Tablets, but will be referred to as Rifater Tablets throughout the remainder of the leaflet.

What is in this leaflet

- What Rifater Tablets are and what they are used for
- What you need to know before you take Rifater Tablets
- How to take Rifater Tablets
- Possible side effects
- How to store Rifater Tablets
- Contents of the pack and other information

1. What Rifater Tablets are and what they are used for

Rifater Tablets contain three different medicines called isoniazid, rifampicin and pyrazinamide. They all belong to a group of medicines called anti-tuberculous drugs. They work by killing the bacteria that cause tuberculosis.

Rifater Tablets are used to treat tuberculosis (also known as TB).

2. What you need to know before you take Rifater Tablets



Do not take Rifater Tablets if:

- You are allergic (hypersensitive) to
 - isoniazid
 - rifampicin
 - pyrazinamide
 - any of the other ingredients of the Rifater Tablets (see section 6) Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- You have yellowing of the skin and eyes (jaundice)
- You are taking saquinavir or ritonavir for an HIV infection (see 'Other medicines and Rifater Tablets' below)
- You are taking medicine called lurasidone (medicine for schizophrenia and bipolar disorders), as rifampicin may reduce the blood levels of lurasidone

Do not take if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking Rifater Tablets.



Warnings and precautions

Talk to your doctor or pharmacist before taking Rifater Tablets if:

- You have a history of kidney disease
- You experience poor coordination, poor balance, change in speech, involuntary eye movements (see section 4)
- You have liver problems
- You have any kidney problems and if you are having more than 600mg rifampicin per day
- You have diabetes. Your diabetes may become more difficult to control while taking this medicine
- You have or have ever had gout (pain or swelling in the joints)
- You are coughing up blood
- You have epilepsy
- You have or have ever had mental health problems (such as depression or schizophrenia)
- You feel numb or weak in your arms and legs (peripheral neuropathy)
- You have an HIV infection
- You are under weight or malnourished
- You drink alcohol every day or you are an alcoholic
- You inject yourself with drugs
- You are a black or Hispanic woman
- You have a rare blood problem called 'porphyria'
- You have a problem with bleeding or a tendency to bruise easily
- You have a history of lung inflammation (interstitial lung disease/pneumonitis)
- Your symptoms of tuberculosis return or get worse (see section 4)
- You develop a rash or experience any symptoms of thrombotic microangiopathy during your treatment (see section 4)
- You doctor has told you that your body takes a long time to get rid of some drugs (you have a slow acetylator status)
- You wear contact lenses. Taking Rifater Tablets may permanently stain soft contact lenses
- The person taking this medicine is a child
- You are aged 65 years or older

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Rifater Tablets.

Lung inflammation

Inform your doctor immediately while taking this medicine if

you develop new or sudden worsening of shortness of breath, possibly with a dry cough or fever not responding to antibiotic treatment. These could be symptoms of lung inflammation (interstitial lung disease/pneumonitis) and can lead to serious breathing problems due to collection of fluid in the lungs and interfere with normal breathing which can lead to life threatening conditions.

Liver problems

You should not take rifampicin, a component of Rifater Tablets, if you have previously taken any rifampicin containing medicinal product and had liver problems. If you are unsure talk to your doctor. Inflammation of the liver has been reported in patients taking rifampicin with symptoms developing within a few days to a few months following the start of treatment. **Stop using rifampicin and contact a doctor** if you have symptoms of liver problems (see section 4).

Serious skin reactions

Serious skin reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP) have been reported with the use of Rifater Tablets.

- SJS/TEN can appear initially as reddish target spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications or be fatal.

- DRESS appears initially as flu-like symptoms and a rash on the face then an extended rash with a high body temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes.
- AGEP appears at the initiation of treatment as a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The most common location: mainly localized on the skin folds, trunk, and upper extremities.

The highest risk for occurrence of serious skin reactions is within 2 days to 2 months after treatment initiation depending on the condition. **If you develop a serious rash or another of these skin symptoms, stop taking Rifater Tablets and contact your doctor or seek medical attention immediately.**

Blood Tests

Your doctor will need to check your blood before you take this medicine. This will help your doctor know if any changes happen to your blood after taking this medicine. If you are aged 35 years or older, you will also need to have monthly blood tests to check how your liver is working.



Other medicines and Rifater Tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Rifater Tablets can affect the way some other medicines work. Also, some medicines can affect the way Rifater Tablets work.

Tell your doctor or pharmacist if you are pregnant and planning or required to undergo pregnancy termination using mifepristone.

In particular, do not take this medicine, and tell your doctor, if you are taking:

- ✗ Saquinavir or ritonavir used for HIV infection
- ✗ Lurasidone used for schizophrenia and bipolar disorders

The following medicines can make Rifater Tablets work less well:

- Antacids used for indigestion. Take Rifater Tablets at least 1 hour before taking antacids
- Other medicines used for TB such as P-aminosalicylic acid (PAS) and cycloserine. PAS and Rifater Tablets should be taken at least 8 hours apart

Tell your doctor if you are taking any of the following medicines:

Heart and blood medicines

- Medicines for high blood pressure
- Medicines for heart problems or to control your heartbeat
- Medicines used to thin the blood such as warfarin and clopidogrel
- Medicines used to lower cholesterol
- Water tablets (diuretics) such as eplerenone

Mental health, epilepsy and motor neurone medicines

- Medicines for thought disorders known as 'antipsychotics' such as haloperidol
- Medicines to calm or reduce anxiety (hypnotics, anxiolytics)
- Medicines to help you sleep (barbiturates)
- Medicines used for epilepsy such as phenytoin and carbamazepine
- Some medicines used for depression such as amitriptyline and nortriptyline
- Riluzole - used for motor neurone disease

Medicines for infections and the immune system

- Some medicines used for an HIV infection such as stavudine and zalcitabine
- Some medicines used for viral infections such as indinavir, efavirenz, amprenavir, nelfinavir, atazanavir, lopinavir, nevirapine, daclatasvir, simeprevir, sofosbuvir and telaprevir
- Medication for the treatment of fungal infections such as caspofungin, fluconazole, itraconazole, ketoconazole
- Medicines used for bacterial infections (antibiotics)
- Dapsone (an antibiotic) with rifampicin may cause haematological toxicity including a decrease in bone marrow and blood cells, and methaemoglobinaemia (decrease in oxygen in your blood caused by changes in red blood cells)
- Medicines used for lowering your immune system such as ciclosporin, sirolimus and tacrolimus
- Praziquantel - used for tapeworm infections
- Atovaquone - used for pneumonia

Hormone and cancer medicines

- Some hormone medicines (oestrogen, systemic hormones, progestogens) used for contraception or some types of cancer such as ethinyloestradiol, levonorgestrel or dydrogesterone
- Some hormone medicines (anti-oestrogens) used for breast cancer or endometriosis such as tamoxifen, toremifene and gestrinone
- Some medicines used for cancer (cytotoxics) such as imatinib
- Levothyroxine (thyroid hormone) used for thyroid problems
- Irinotecan - used for cancer

Pain, inflammation and gout medicines

- Non-steroidal anti-inflammatory drugs (NSAIDs) such as etoricoxib, aspirin and indomethacin
- Medicines used for pain such as codeine, morphine, fentanyl or pethidine
- Paracetamol and rifampicin can increase the risk of liver damage
- Corticosteroids used for inflammation such as hydrocortisone, betamethasone and prednisolone
- Methadone - used for heroin withdrawal
- Sulfipyrazone - used for gout

Other medicines

- Medicines used for diabetes
- Medicines used to relax muscles before surgery (anaesthetics) such as halothane
- Medicines used for erection problems such as tadalafil
- Some medicines used for feeling sick or being sick such as ondansetron and aprepitant
- Probenecid (used with a medicine called cidofovir to stop kidney damage)
- Other antibiotic medicines such as cefazolin
- Quinine - used for malaria
- Theophylline - used for wheezing or difficulty in breathing

Rifater Tablets with food, drink and alcohol

Isoniazid 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 and breast-feeding

Talk to your doctor before taking this medicine if you are pregnant, plan to get pregnant or think you are pregnant. Rifater Tablets may make the contraceptive "pill" work less well. This means you should change to a different type of contraception. Instead, you must use a reliable barrier method of contraception such as condoms or the "coil" while taking Rifater Tablets. If you have any questions or are unsure about this talk to your doctor or pharmacist.

You should not breast-feed if you are taking Rifater Tablets. This is because small amounts may pass into the mothers' milk. If you are breast-feeding or planning to breast-feed, talk to your doctor or pharmacist before taking any medicine.



Driving and using machines

You may feel dizzy or faint, have problems with vision or have other side effects that could affect your ability to drive while taking this medicine. If this happens, do not drive or use any tools or machines.

Rifater Tablets contain:

- **Sucrose:** If you have been told by your doctor that you cannot tolerate some sugars, talk to your doctor before taking Rifater Tablets
- **Sodium:** This medicine contains less than 1 mmol sodium (23 mg) per daily dose, that is to say essentially 'sodium-free'.

3. How to take Rifater Tablets

Always take Rifater Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Keep taking this medicine

- You must take the tablets every day for the whole time the doctor has told you to take them
- **Do not** stop and start taking the tablets. This may increase the risk of side effects and your TB will not be treated properly

How to take the tablets

- Take this medicine by mouth
 - Swallow the tablets whole, with a drink of water
 - Take at least 30 minutes before a meal or 2 hours after a meal
 - Take all your tablets together each day, as a single dose
 - **Do not** give this medicine to children
 - If you feel the effect of your medicine is too weak or too strong, do not change the dose yourself, but ask your doctor
- Your doctor may ask you to take Vitamin B6 during treatment with Rifater Tablets, especially if you are malnourished, elderly or a diabetic.

How much to take

The usual dose is:

Adults and the Elderly

- Between 3 and 6 tablets each day. The amount depends on your body weight
- If you are elderly, your doctor may monitor your treatment more closely.

Use in children and adolescents

This medicine is not recommended for use in children and adolescents.

If you take more Rifater Tablets than you should

If you take more Rifater Tablets than you should, tell a doctor or go to a hospital casualty department straight away. Take the medicine pack with you. This is so the doctor knows what you have taken.

You may feel sick (nausea), be sick (vomiting), have stomach pain, itching or a headache. You may also feel tired, sleepy, dizzy, light-headed, have blurred or strange visions (hallucinations) and faint or feel faint. Other signs of taking too much includes swelling of the face, eyes or eyelids, slurring of speech, difficulty breathing, fast heartbeat, uneven heartbeats, fits and heart attack.

If you forget to take Rifater Tablets

If you forget a dose, take it as soon as you remember it. However, if it is nearly time for the next dose, skip the missed dose. **Do not** take a double dose to make up for the forgotten tablets.

If you stop taking Rifater Tablets

Keep taking Rifater Tablets until your doctor tells you to stop. Do not stop taking Rifater Tablets just because you feel better. If you stop, your infection may get worse.

Tests

Taking Rifater Tablets may affect the results of some blood tests. In particular, tests for folate, vitamin B12 and liver function. If you are going to have a blood test, it is important to tell your doctor that you are taking Rifater Tablets.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking and go to a hospital straight away if you notice any of the following serious side effects:

- You have an **allergic reaction**. The signs may include: a rash, swallowing or breathing problems, wheezing, swelling of your lips, face, throat or tongue.
- Nausea (feeling sick) or vomiting (being sick), fever, feeling tired, loss of appetite (anorexia), dark-coloured urine, light-coloured faeces, yellowing of the skin or whites of the eyes, itching, rash or upper stomach pain. These symptoms may be signs of liver injury (hepatitis, may affect up to 1 in 100 people).
- Serious skin rashes including Steven-Johnson syndrome, toxic epidermal necrolysis. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. **See also section 2.**
- Widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome). **See also section 2.**
- A red, scaly widespread rash with bumps under the skin and blisters accompanied by fever at the initiation of treatment (acute generalized exanthematous pustulosis). **See also section 2.**
- 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
- Hair loss
- You have severe bleeding (haemorrhage)
- Paradoxical drug reaction - Symptoms of tuberculosis can return, or new symptoms can occur after initial improvement during treatment. Paradoxical reactions have been reported as early as 2 weeks and as late as 18 months after beginning anti-tuberculosis treatment. Paradoxical reactions are typically associated with fever, swollen lymph nodes (lymphadenitis), breathlessness, and cough. Patients with paradoxical drug reaction can also experience headaches, loss of appetite, and weight loss
- You have chills, tiredness, unusually pale skin colour, shortness of breath, fast heartbeat or dark coloured urine. This could be signs of a serious type of anaemia
- You have blood in your urine or an increase or decrease in amount of urine you produce. You may also get swelling, especially of the legs, ankles or feet. This may be caused by serious kidney problems
- You have a sudden severe headache. This could be a sign of bleeding in the brain
- New or sudden worsening of shortness of breath and wheezing, possibly with a cough or fever. These could be symptoms of inflammation of the lungs (interstitial lung disease/pneumonitis).
- You get confused, sleepy, cold clammy skin, shallow or difficult breathing, a racing heartbeat or your skin is paler than normal. These could be signs of shock

- You get more infections more easily than normal. Signs include fever, sore throat or mouth ulcers. This could be because you have a low number of white blood cells
- You have bleeding from your nose, ear, gums, throat, skin or stomach. Signs may include a feeling of tenderness and swelling in your stomach, purple spots on your skin and black or tar-like stools
- Symptoms related to cerebellar syndrome: poor coordination, poor balance, change in speech, involuntary eye movements.

If you experience any of the following serious side effects contact your doctor as soon as possible:

- Inflammation of the pancreas, which causes severe pain in the abdomen and back (pancreatitis, frequency not known).
- Mental problems with unusual thoughts and strange visions (hallucinations)
- Your stomach ulcer gets worse
- Severe watery diarrhoea that will not stop and you are feeling weak and have a fever. This may be something called 'Pseudomembranous colitis'
- Your fits get worse, or you start to have fits
- Flu-like symptoms including chills, fever, headache, dizziness and bone pains
- Inflammation of the liver – yellowing of the skin and white part of eyes, increase in the blood level of liver enzymes.
- Blood clots in small blood vessels (thrombotic microangiopathy) – Symptoms may include increased bruising, bleeding, fever, extreme weakness, headache, dizziness or light-headedness. Your doctor may find changes in your blood and the function of your kidneys.

Tell your doctor as soon as possible if you have any of the following side effects:

- Water retention (oedema) which may cause swollen face, stomach, arms or legs
- Muscle weakness or pain or loss of muscle reflexes
- Dizziness, feel lightheaded and faint especially when you stand or sit up quickly (due to low blood pressure)
- Swollen fingers, toes or ankles
- Being unable to concentrate, feeling nervous, irritable or depressed
- Balance problems with dizziness (vertigo)
- Feeling very tired and weak or difficulty sleeping (insomnia)
- Unusual skin sensations such as feeling numb, tingling, pricking, burning or creeping on the skin (paraesthesia)
- Short-term memory loss, anxiety, being less alert or responsive
- Blurred or distorted eyesight
- Wasting of muscles or other body tissues
- Weight loss, night sweats and fever. These could be signs of a blood condition called eosinophilia
- Feeling sick (nausea) or being sick (vomiting)

Tell your doctor or pharmacist if any of the following side effects get serious or lasts longer than a few days:

- Acne
- Loss of appetite (anorexia)
- Headache
- Skin flushing or itching
- Painful, red, swollen joints
- Pain or discomfort when passing urine
- Irregular periods
- Constipation, diarrhoea, stomach discomfort or dry mouth
- Breast enlargement in men
- Increased thirst, going to the toilet more often and feeling tired. Your blood sugar may be high
- Inflammation of the blood vessels.

Other side effects you should discuss with your doctor if you are concerned about them

You notice a discoloration (yellow, brown, orange or red colour) in your teeth, urine, sweat, phlegm (sputum), saliva or tears. This is quite common, and you need not worry. However, the colour may permanently stain soft contact lenses. The colour in tears may last for some time after you have stopped having Rifater Tablets.

Blood tests

A blood test may show changes in the way the liver is working

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Rifater Tablets

Keep out of the sight and reach of children.

Do not use Rifater Tablets after the expiry date which is stated on the carton and label after 'EXP'. The expiry date refers to the last day of that month.

Do not store above 25°C. Store in the original package.

If your medicine shows any signs of deterioration or discolouration, consult your doctor or pharmacist for advice. If damaged, please tell your doctor or pharmacist.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines no longer required. These measures will help protect the environment.

6. Contents of the pack and other information

What Rifater Tablets contain:

- The active substances are isoniazid, rifampicin and pyrazinamide. Each tablet contains 50mg of isoniazid, 120mg of rifampicin and 300mg of pyrazinamide.
- The other ingredients are low-substituted carmellose sodium, sodium lauryl sulphate, calcium stearate, sucrose, gum Arabic, talc, magnesium carbonate, kaolin, titanium dioxide (E171), povidone, colloidal silica anhydrous, aluminium oxide hydrate, iron oxide (E172), carnauba wax, white wax, colophony, solid paraffin.

What Rifater Tablets look like and contents of the pack

The tablets are light pink, smooth, shiny, round and sugar coated. Each pack contains 100 tablets.

PL 20774/2435 Rifater 50, 120, 300mg Tablets

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Manufactured by: Sanofi S.p.A., Via Valcanello, 4-03012 Anagni (FR), Italy. Procured from within the EU. Product Licence Holder: Quadrant Pharmaceuticals Limited, Lynstock House, Lynstock Way, Lostock, Bolton, BL6 4SA. Repackaged by: Maxearn Limited, Unit 29, Oakhill Trading Estate, Devonshire Road, Worsley, Manchester, M28 3PT.

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