

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.**

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

Information for the patient

[TB398 trade name][†]
Rifapentine

*The warnings and instructions in this leaflet are intended for the person taking the medicine.
If you are a parent or carer responsible for giving the medicine to someone else such as a child,
you will need to apply the instructions accordingly.*

Read all 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 questions about the medicine, ask your health care provider.
- This medicine is for you only. Do not pass it on to others. It may harm them, even if their illness seems to be the same as yours.
- If you are concerned about any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [TB398 trade name] is and what it is used for
2. What you need to know before you take [TB398 trade name]
3. How to take [TB398 trade name]
4. Possible side effects
5. How to store [TB398 trade name]
6. Contents of the pack and other information

1. What [TB398 trade name] is and what it is used for

[TB398 trade name] is a medicine used to treat (TB), an infection caused by bacteria called *Mycobacterium tuberculosis*.

[TB398 trade name] is also used to prevent TB if you are at high risk of infection.

[TB398 trade name] is always given together with other medicines to treat or prevent tuberculosis. Your healthcare provider has chosen the combination that is right for your condition.

[TB398 trade name] contains the active substance rifapentine and works by stopping the bacteria responsible for the disease from multiplying in the body.

2. What you need to know before you take [TB398 trade name]

Do not take [TB398 trade name] if you:

- are allergic (hypersensitive) to rifapentine or another rifamycin antibiotic or any of the other ingredients of this medicine (listed in section 6)
- have liver problems
- have ever had liver problems or drug fever or chills after taking rifapentine
- are taking certain medicines:

[†]Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- **HIV infection medicines:** atazanavir, bicittegravir/emtricitabine/tenofovir alafenamide, darunavir, doravirine, elvitegravir/cobicistat, etravirine, fosamprenavir, lopinavir, nevirapine, rilpivirine, ritonavir, tipranavir
- **Chronic hepatitis C medicines:** daclatasvir, elbasvir/grazoprevir, glecaprevir/pibrentasvir, ledipasvir/sofosbuvir, ombitasvir/paritaprevir/ritonavir, sofosbuvir
- **Malaria medicines:** artemisinin and its derivatives (artemether, artemotil, artesunate, dihydroartemisinin)

Check with your health care provider if you are not sure.

Warnings and precautions

Liver disease

[TB398 trade name] may cause liver disease (hepatitis). When taking [TB398 trade name], your health care provider will monitor you regularly to check for any problems with your liver.

You should watch out for symptoms of liver damage, such as unexplained lack of appetite, nausea, vomiting, dark urine, yellow discolouration of the skin and the eyes (jaundice), rash, tingling in the hands and feet, persistent tiredness, weakness lasting longer than 3 days and abdominal (belly) pain and tenderness. If these occur, you should immediately tell your health care provider.

You may be at special risk for developing hepatitis if you:

- are older than 35 years
- drink alcoholic beverages daily (see '*[TB398 trade name] with food and drink*')
- have a long-term liver disorder
- are a user of injection drugs (e.g., heroin)

If you are in one of these groups, your health care provider will check your liver function more often.

Furthermore, you will be carefully monitored if you:

- are on another long-term medication (see '*Other medicines and [TB398 trade name]*')
- suffer from tingling in the hands and feet (peripheral neuropathy)
- are pregnant
- are HIV infected.

Severe skin reactions

Serious skin reactions such as Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome may happen in some people taking [TB398 trade name]. Stop taking [TB398 trade name] right away and tell your health care provider if you have any of the following symptoms: rash; red and painful skin; peeling or bleeding skin; sores or blisters on the inside of your mouth or lips; swollen face, lips, mouth tongue or throat; flu-like symptoms.

Allergic reactions and flu-like symptoms

If you get flu-like symptoms such as fever, headache and muscle aches, you should tell your health care provider, since [TB398 trade name] may be the cause. Signs and symptoms of an allergic reaction may include: low blood pressure (hypotension), hives, cough with wheezing, difficulty breathing, red eyes (conjunctivitis), lower blood platelet levels.

Diarrhoea

A type of diarrhoea called *Clostridioides difficile*-associated diarrhoea (CDAD) may occur during or after taking antibiotics, including [TB398 trade name]. The severity of CDAD can range from mild diarrhoea to severe diarrhoea that may cause death (fatal colitis). Tell your health care provider right away if you have diarrhoea while you take or after you stop taking [TB398 trade name].

Porphyria

Patients with a condition called porphyria may experience a worsening of symptoms.

Contraception

[TB398 trade name] may lower the effects of oral contraceptive pills. Therefore, a different or additional method of contraception (e.g. condoms, intra-uterine device, pessary) should be used during treatment with [TB398 trade name].

Addison's disease

[TB398 trade name] may lower the effects of corticosteroids used in Addison's disease, causing life-threatening effects (i.e., low pressure, low blood levels sugar, high blood levels of potassium).

Discolouration of body fluids

[TB398 trade name] may cause a reddish orange discolouration of body fluids such as urine, phlegm and tears. This is due to this medicine's active ingredient, rifapentine and does not require medical attention. Also, contact lenses or dentures may become permanently stained due to [TB398 trade name].

Interaction with laboratory tests

It is possible that [TB398 trade name] may interfere with some blood tests. If you need a blood test to check for folate or vitamin B12 levels tell your health care provider, you are taking [TB398 trade name] as it may affect your results.

If you are not sure if any of the above applies to you, talk to your health care provider before taking [TB398 trade name].

Other medicines and [TB398 trade name]

Tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription and herbal medicines.

Medicines you must not take with [TB398 trade name]

- **You must not take [TB398 trade name] with** certain medicines for HIV infection, chronic hepatitis C infection and malaria. This is because [TB398 trade name] may significantly decrease the amount of these medicines in your blood, preventing them from working well enough. See the full list of these medicines above under '*Do not take [TB398 trade name] if you'*.

Check with your health care provider if you are not sure.

Other medicines that can interfere with [TB398 trade name]

Where possible, you should not take [TB398 trade name] with other medicines that can cause damage to the liver, since their side effects may add up. Your health care provider will be able to advise you about any changes that may be needed to your treatment.

You should not take [TB398 trade name] with **antacids** used for indigestion.

Other medicines used for TB such as **p-aminosalicylic acid** (PAS). PAS and [TB398 trade name] should be taken at least 8 hours apart.

[TB398 trade name] may also interfere with a great number of other medicines, including, for instance:

- Medicines for **high blood pressure** such as amlodipine, atenolol, nifedipine, propranolol
- Medicines for **heart problems** or to control your heartbeat such as digoxin, antiarrhythmics (such as diltiazem, disopyramide, mexiletine, propafenone, quinidine, tocainide, verapamil)
- Medicines used to **thin the blood** such as clopidogrel, warfarin
- Medicines used to **lower cholesterol** such as atorvastatin, clofibrate, simvastatin
- **Water tablets** (diuretics) such as eplerenone

- Medicines for thought disorders known as ‘**antipsychotics**’ such as aripiprazole, chlorpromazine, clozapine, haloperidol
- Medicines to calm or **reduce anxiety** (hypnotics, anxiolytics) such as diazepam, midazolam, nitrazepam
- Medicines to help you **sleep** such as zopiclone
- Medicines used for **epilepsy** such as carbamazepine, lamotrigine, phenobarbital, phenytoin, valproic acid
- Some medicines used for **depression** such as amitriptyline, nortriptyline
- Riluzole - used for **motor neurone disease**
- Medicines used for **fungal infections** such as fluconazole, itraconazole, ketoconazole, voriconazole
- Medicines used for bacterial infections other than TB (**antibiotics**) such as chloramphenicol, ciprofloxacin, clarithromycin, cotrimoxazole, dapsone, doxycycline, levofloxacin
- Medicines used for **tuberculosis** such as bedaquiline, ethionamide, p-aminosalicylic acid
- Medicines used for **lowering your immune system** such as cyclosporine, sirolimus, tacrolimus
- Praziquantel - used for certain **worm infections**
- Atovaquone - used for **pneumonia**
- Medicines used in **malaria**: chloroquine, lumefantrine, mefloquine, quinine
- Some **hormone medicines** used for contraception such as ethinyloestradiol, levonorgestrel, norethindrone
- Some hormone medicines (anti-estrogens) used for **breast cancer** or **endometriosis** such as gestrinone, tamoxifen, toremifene
- Some medicines used for **cancer** (cytotoxics) such as imatinib, irinotecan
- Levothyroxine (thyroid hormone) used for **thyroid problems**
- Medicines used for **pain** such as codeine, fentanyl, morphine, paracetamol, pethidine
- Corticosteroids used for **inflammation** such as prednisolone
- Methadone - used for **heroin withdrawal**
- Medicines used for **diabetes** such as glibenclamide, gliclazide, glimepiride, glipizide, glyburide, repaglinide
- Theophylline - used for wheezing or **difficulty in breathing**
- Sildenafil- used to treat **male sexual erection problems**

Pregnancy and breast-feeding

Ask your health care provider for advice before taking this medicine.

Tell your health care provider if you are pregnant or planning to become pregnant. [TB398 trade name] should not be taken during pregnancy as it can affect the growth of your unborn baby and may cause complications to the mother and baby after birth.

[TB398 trade name] may make the contraceptive “pill” work less well. This means you should change to a different type of contraception. You must use a reliable barrier method of contraception such as condoms or the “coil” while taking [TB398 trade name]. If you have any questions or are unsure about this talk to your health care provider.

You should not breast-feed if you are taking [TB398 trade name]. This is because small amounts may pass into the mothers' milk. If you are breast-feeding or planning to breast-feed, talk to your health care provider before taking any medicine.

Driving and using machines

You may feel dizzy while taking [TB398 trade name]. If this happens, do not drive or use any tools or machines.

3. How to take [TB398 trade name]

Always take [TB398 trade name] exactly as your health care provider told you and finish the course. You should check with your health care provider if you are not sure.

Your health care provider will assign the dose of [TB398 trade name] appropriate for you. The following information includes only the average doses of this medicine. If your prescribed dose is different, do not change it unless your health care provider tells you to do so.

Treatment of tuberculosis

The dose of [TB398 trade name] is 4 tablets once **daily**. When used for treatment in this way, [TB398 trade name] is only suitable for people aged 12 years or older. It is taken together with other tuberculosis medicines.

Prevention of tuberculosis

Once weekly dosing

For prevention of tuberculosis, [TB398 trade name] is usually given **once a week** for a period of 3 months, i.e., 12 doses. It is given with another tuberculosis medicine called isoniazid.

The number of tablets to take each week depends on your age and weight.

For *patients aged 2 to 14 years*, the usual recommended dose is as follows:

Patient's weight	Number of tablets
10 to less than 16 kg	1
16 to less than 24 kg	1½
24 to less than 31 kg	2
31 kg and over	2½

For *patients aged over 14 years* and weighing at least 30 kg the usual recommended dose is 3 tablets of [TB398 trade name] **weekly** with isoniazid for 3 months.

Once daily dosing

Your health care provider may recommend a shorter preventive treatment, where [TB398 trade name] is given in a recommended dose of 2 tablets **daily**, together with isoniazid, for one month. This shorter preventive treatment is for adults and children aged 13 years and older only.

Always take [TB398 trade name] as your health care provider advises and ask them if you are not sure how to take your tablets.

If you take more [TB398 trade name] than you should

If you have taken too many tablets or if someone accidentally swallows some, you should contact your health care provider or the nearest hospital emergency department for further advice.

If you forget to take [TB398 trade name]

It is important that you take the medicine regularly as prescribed.

If you forget to take a **daily** dose and there are more than 6 hours till your next dose, take the missed dose as soon as possible. Then continue your treatment as before. If there are less than 6 hours till your next dose, skip the missed dose. Don't take a double dose to make up for a missed dose.

If a **weekly** dose is missed but it is remembered within the next 2 days, take the dose immediately and continue the schedule as originally planned.

If the missed dose is remembered more than 2 days later, take the missed dose immediately and change the schedule for weekly intake to the day the missed dose was taken until treatment completion.

If 4 or more weekly doses are missed, see your health care provider who may restart the full preventive treatment.

If you vomit within 1 hour of taking [TB398 trade name], the dose should be repeated.

If you stop taking [TB398 trade name]

Keep taking the medicine for as long as your health care provider has told you, even if you are feeling better. If you stop the medicine too soon, your infection may not be completely cured.

You should not stop treatment unless your health care provider tells you to.

If you have any further questions on the use of this product, ask your health care provider.

4. Possible side effects

Like all medicines, [TB398 trade name] can cause side effects, although not everybody gets them.

The table below shows side effects that may be seen in patients taking [TB398 trade name]:

	May occur in at least 1 patient in 100	May occur in less than 1 patient in 100
Blood and lymphatic system disorders	Abnormal number of platelets High number of white blood cells Low red blood cells Swollen lymph nodes	Abnormal blood clotting Bleeding outside of blood vessels (haematoma purpura) Low white blood cells
Cardiovascular and vascular disorders		Fainting Inflammation of tissue surrounding the heart (pericarditis) Low blood pressure on standing Palpitations
Eye disorders	Infection of eye membrane (conjunctivitis)	
Gastrointestinal disorders	Diarrhoea Indigestion Nausea Stomach pain Vomiting	Constipation, Dry mouth Enlarged salivary glands Inflammation of digestive system Inflammation or irritation of the passage between mouth and stomach (oesophagitis) Pancreatitis
General disorders	Fever	Chest pain Chills

		Facial swelling caused by fluid retention Feeling jittery Feeling of tiredness Feeling of weakness
Hepatobiliary disorders	High liver function tests, e.g., elevated ALT, elevated AST	Enlarged liver Increased bilirubin Jaundice (yellowing of eyes, skin)
Immune system disorders	Allergic reaction	
Investigations	Blood urea increased	
Infections and infestations		Sore throat (pharyngitis) Vaginal yeast infections and other fungal infections Viral infection
Metabolism and nutrition disorders	Decreased appetite	Alkaline phosphatase increased Elevated blood glucose Elevated blood lipids Elevated potassium in the blood Gout
Musculoskeletal and connective tissue disorders	Joint pain Back pain	Damaged muscle tissue (rhabdomyolysis) Inflamed muscles Muscle pain
Nervous system disorders	Dizziness Headache	Fits (convulsion) Impaired voice Problems with nerves that cause numbness or muscle weakness Sleepiness Tingling sensation
Pregnancy and perinatal conditions		Miscarriage
Psychiatric disorders		Anxiety Confusion Depression Disorientation Suicidal thoughts
Renal and urinary disorders		Elevated urea, creatinine in the blood
Reproductive disorders		Inflamed vagina Itchy vagina Other vagina discharge Vaginal bleeding
Respiratory, thoracic and mediastinal disorders	Cough Coughing up blood	Accumulation of fluid in the larynx (voice box) Asthma Constriction of airways (bronchospasm) Increased sensitivity of airways

		Inflammation of lung tissue (pneumonitis) Laryngitis Nose bleeding Shortness of breath Sore throat
Skin disorders	Excessive sweating Itching Rash	Hives Skin discoloration

The following serious and otherwise important adverse drug reactions are discussed in section 2 ‘Warning and Precautions’. Their frequencies are unknown.

- Severe skin reactions such as Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS)
- Discoloration of body fluids
- Diarrhoea caused by the bacterium *Clostridioides difficile*
- Porphyria: a disease affecting the skin or nervous system caused by build-up in the body of substances called porphyrins

Reporting of side effects

If you get a side effect, talk to your health care provider. This includes side effects not listed in this leaflet. You may also be able to report such effects directly to your national reporting system if one is available. By reporting side effects, you can help to improve the available information on this medicine.

5. How to store [TB398 trade name]

Do not store above 30°C. Protect from excessive heat and humidity. Avoid excursions above 30°C.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date stated on the carton after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [TB398 trade name] contains

- The active ingredient is rifapentine. Each film-coated tablet contains 300 mg rifapentine.
- The other ingredient(s) of [TB398 trade name] are:

Core tablet: microcrystalline cellulose, pregelatinised starch, low-substituted hydroxypropyl cellulose, sodium starch glycolate, sodium lauryl sulfate, hydroxypropyl cellulose, disodium edetate, sodium ascorbate, colloidal silicon dioxide and calcium stearate;

Film coating: polyvinyl alcohol-partially hydrolysed, macrogol/ polyethylene glycol, titanium dioxide, talc and iron oxide red.

There is too little sodium in this medicine to have any effect, even if you are on a low-sodium diet.

What [TB398 trade name] looks like and contents of the pack

Reddish-brown, round, film-coated tablets. They are biconvex (rounded on top and bottom) with a bevelled edge. The tablets have a break line on one side with “J” debossed (stamped into the tablet) above the break line and “37” debossed below; they are plain on the other side. The tablet can be divided into equal halves.

[TB398 trade name] is available in Alu/Alu strips. Each strip contains 10 tablets. Such 10 strips are packed in a carton. Pack size: 10 x 10 tablets.

Supplier and Manufacturer

Supplier

Macleods Pharmaceuticals Limited
304, Atlanta Arcade
Marol Church road
Andheri (East)
Mumbai – 400 059
India
Tel:+91-22-66762800
Fax:+91-22-28216599
E-mail:vijay@macleodspharma.com
sjadhav@macleodspharma.com
exports@macleodspharma.com

Manufacturer

Macleods Pharmaceuticals Limited
At Oxalis Labs
Village Theda
P.O. Lodhimajra
Tehsil Baddi, Dist. Solan
Himachal Pradesh, 174101
India
Tel:+91 01795350700, +91 01795 350701
Fax:+91-1795 661452
E-mail:nishata@macleodspharma.com

For any information about this medicine, contact the local representative of the supplier.

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Detailed information on this medicine is available on the World Health Organization (WHO) website:
<https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products>