

Package leaflet: Information for the patient

Rifapentine and Isoniazid Tablets

Rifapentine and Isoniazid

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 any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness seem to be the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Rifapentine and Isoniazid Tablets is and what it is used for
2. What you need to know before you take Rifapentine and Isoniazid Tablets
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1. What Rifapentine and Isoniazid Tablets is and what it is used for

Rifapentine and Isoniazid Tablets is a prescription medicine contains the active substance rifapentine and isoniazid, indicated for the treatment of active pulmonary tuberculosis caused by *Mycobacterium tuberculosis*.

2. What you need to know before you take Rifapentine and Isoniazid Tablets

Do not take Rifapentine and Isoniazid Tablets

- If you are allergic to rifapentine or isoniazid or any of the other ingredient of this medicine (listed in section 6),
- **Do not** take Rifapentine and Isoniazid Tablets if you are allergic to a group of medicines called rifamycins,
- if you have acute liver disease,
- if you have drug induced liver disease,
- if you have experienced liver damage before when taking isoniazid,
- if you have experienced severe side effects of rifapentine or isoniazid, such as drug fever, chills or inflammation of the joints before.

Warnings and precautions

Talk to your doctor or pharmacist before taking this medicine:

Rifapentine and Isoniazid Tablets should not be used:

- in people with active TB who had taken the medicines rifampin or isoniazid in the past and did not respond (resistant)
- in people who had been exposed to patients with TB that cannot be treated with isoniazid or rifampin

You should promptly report signs or symptoms consistent with liver damage. These include any of the following: unexplained lack of appetite, nausea, vomiting, dark urine, yellowing of the skin and the eyes (jaundice), rash, tingling in the hands and feet, persistent tiredness, weakness lasting longer than 3 days and/or abdominal tenderness, especially in the right upper region of your belly. Your health care provider will test your blood regularly to check for any problems with your liver. You may be at special risk for developing hepatitis (inflammation of the liver), if

- you are older than 35 years,
- if you drink alcoholic beverages daily (see “Taking Rifapentine and Isoniazid Tablets with food and drink”)
- if you have a chronic liver disease,
- if you are a user of injection drugs (e.g. heroin).

If you belong to one of these groups your health care provider will closely check your liver function.

Furthermore, you will be carefully monitored, if:

- you use any chronically administered medication concurrently (see “Taking other medicines”),
- you suffer from tingling in the hands and feet (peripheral neuropathy),
- you are pregnant
- you have HIV infection.

Peripheral neuropathy (tingling in the hands and feet) is the most common side effect of isoniazid (see “Possible side effects). If you have kidney problems, you may be at increased risk of experiencing isoniazid side effects including peripheral neuropathy.

A certain vitamin, called pyridoxine, should be administered routinely at doses of 10 mg per day during treatment with Rifapentine and Isoniazid Tablets, since it largely reduces the risk of developing peripheral neuropathy.

If you are allergic (hypersensitive) to ethionamide, pyrazinamide, niacin (nicotinic acid), or other related medications you may also be allergic to this product.

You should inform your health care provider if you have diabetes or if you have ever suffered from seizure disorders (fits), psychosis, or liver problems.

It is important that your health care provider knows about all your signs of illness even when you think they are not related to tuberculosis infection.

Children and adolescents

Rifapentine and Isoniazid Tablets is safe and effective in children older than 2 years of age who have inactive (latent TB), but it is not known if Rifapentine and Isoniazid Tablets is safe and effective for use in the treatment of active TB in children under 12 years of age.

Before you take Rifapentine and Isoniazid Tablets, tell your doctor if you:

- have active TB disease
- know that you have TB that is resistant to treatment with some medicines
- have HIV infection or taking medicines to treat HIV infection

- have liver problems
- have a condition called porphyria

Other medicines and Rifapentine and Isoniazid Tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Using Rifapentine and Isoniazid Tablets with other medicines may affect each other causing serious side effects. Rifapentine and Isoniazid Tablets may affect the way other medicines work, and other medicines may affect how Rifapentine and Isoniazid Tablets works. Especially tell your doctor if you take medicines to treat HIV infection or oral contraceptives.

Do not take Rifapentine and Isoniazid Tablets with:

- aluminium hydroxide (medicine used to treat indigestion) or
- disulfiram (medicine used for the treatment of chronic alcoholism).

Taking Rifapentine and Isoniazid Tablets with other medicines:

The active agent in Rifapentine and Isoniazid Tablets may also interact with the following medicines:

- medicines to treat epileptic seizures (e.g. phenytoin, carbamazepine, valproic acid, phenobarbital)
- medicines used to help you sleep (benzodiazepines, e.g. diazepam, flurazepam, triazolam, midazolam),
- medicines for the treatment of certain psychiatric conditions (neuroleptics, e.g. chlorpromazine, haloperidol),
- medicines for prevention of blood clots (coumarin- or indandione-derivates, e.g. warfarin, phenindione),
- medicines used in surgery (narcotics, e.g. alfentanil; anaesthetic e.g. enflurane),
- theophylline (medicine for the treatment of asthma),
- procainamide (medicine for the treatment of cardiac arrhythmias),
- corticosteroids (e.g. prednisolone, medicines for the treatment of inflammation and other diseases, such as asthma or rheumatoid arthritis),
- paracetamol (pain killer),
- medicines toxic to the liver,
- medicines toxic to the nervous system.

Ask your doctor or pharmacist for a list of these medicines if you are not sure.

Know the medicines you take. Keep a list of them to show your doctor or pharmacist when you get a new medicine.

Taking Rifapentine and Isoniazid Tablets with food and drink

Rifapentine and Isoniazid Tablets should be taken With meals

If you take Rifapentine and Isoniazid Tablets concurrently with cheese or fish, you may experience redness or itching of the skin, hot feeling, rapid or pounding heartbeat, sweating, chills or clammy feeling, headache, or light-headedness.

Do not drink alcohol while taking Rifapentine and Isoniazid Tablets. This increases your risk for liver damage.

Pregnancy and breast-feeding

Check with your doctor if you

- are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. It is not known if Rifapentine and Isoniazid Tablets will harm your unborn baby.
- are breastfeeding or plan to breastfeed. Isoniazid passes into breast milk. No harmful effects have been reported in breast-fed infants, whose mothers were receiving isoniazid.
- However, the amount of isoniazid in breast milk are so low, that you cannot rely upon breast-feeding for adequate tuberculosis prophylaxis or therapy for your child.

Driving and using machines

Rifapentine and Isoniazid Tablets may cause dizziness and other side effects to the nervous system that can impair your ability to drive and use machines.

3. How to take Rifapentine and Isoniazid Tablets

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Take Rifapentine and Isoniazid Tablets exactly as your doctor tells you to take it.

- Take Rifapentine and Isoniazid Tablets with food.
- The dose of Rifapentine and Isoniazid Tablets was decided by your health care provider based on your body weight. Also, the dosing intervals (daily or thrice weekly) most suitable for you were selected by your health care provider.
- If you cannot swallow Rifapentine and Isoniazid Tablets whole. Be sure to take all of the semisolid food with Rifapentine and Isoniazid Tablets in it right away.

Table 1: Age and weight-based dose of rifapentine and isoniazid in the treatment of latent tuberculosis infection

Regimen	Dose by age and weight band					
Three months of Rifapentine plus high dose isoniazid weekly (3HP)	Age 2 – 14 years					
	<i>Medicine, formulation</i>	10-15 kg	16-23 kg	24-30 kg	31-34 kg	>34 kg
	Isoniazid + Rifapentine FDC (300 mg/ 300 mg) tablet	1	1.5	2	2.5	2.5
	Age >14 years					
	<i>Medicine, formulation</i>	30-35 kg	36-45 kg	46-55 kg	56-70 kg	>70 kg
	Isoniazid + Rifapentine (300 mg/ 300 mg) tablet	3	3	3	3	3

If you take more Rifapentine and Isoniazid Tablets than you should

If you take more than the recommended dose of Rifapentine and Isoniazid Tablets you may be at higher risk of side effects of this medicine (see section 4, Possible side effects).

Contact your doctor or nearest emergency department immediately for advice. Keep the tablet strip with you so that you can show what you have taken.

If you forget to take Rifapentine and Isoniazid Tablets

It is important not to miss a dose of Rifapentine and Isoniazid Tablets. If you miss a dose of this medicine, take it as soon as you can, and then take your next dose at its regular time. However, if your next dose is due within 6 hours, do not take the missed dose. Wait and take the next dose at the usual time. Do not take a double dose to make up for a forgotten tablet.

If you vomit less than 1 hour after taking Rifapentine and Isoniazid Tablets, take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking this medicine.

Do not stop taking Rifapentine and Isoniazid Tablets

It is important to take all of your Rifapentine and Isoniazid Tablets and your other TB medicines. Do not skip doses.

Skipping doses may cause Rifapentine and Isoniazid Tablets to not work as well and may increase the chance that your TB will not be treatable by Rifapentine and Isoniazid Tablets or other medicines. Talk to your health care provider before you stop taking Isoniazid 300 mg tablets for any reason, particularly if you are experiencing any side effects or have another illness.

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

Do not stop taking Rifapentine and Isoniazid Tablets without talking to your doctor. Stopping Rifapentine and Isoniazid Tablets can seriously affect how well future treatment works. If Rifapentine and Isoniazid Tablets is stopped for any reason, speak to your doctor before you restart taking Rifapentine and Isoniazid Tablets tablets.

When your supply of Rifapentine and Isoniazid Tablets starts to run low, get more from your doctor or pharmacist. This is very important because the amount of virus may start to increase if the medicine is stopped for even a short time. The disease may then become harder to treat.

4. Possible side effects

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

Rifapentine and Isoniazid Tablets may cause serious side effects, including:

- **Relapse of your TB symptoms.** Active TB disease may return after improvement (relapse) in some people, especially people who do not take Rifapentine and Isoniazid Tablets exactly as their doctor tells them to. It is important that you take Rifapentine and Isoniazid Tablets exactly as your doctor tells you to. Your doctor should check you for worsening signs and symptoms of your TB while you take Rifapentine and Isoniazid Tablets.
- **change in the normal color of your skin, mouth and body fluids.** Rifapentine and Isoniazid Tablets may cause your skin, teeth, tongue, urine, feces, saliva, sputum, tears, sweat, and breast milk to turn a red-orange color. Contact lenses or dentures may become permanently stained.
- **diarrhea.** A type of diarrhea called *Clostridium difficile*-associated diarrhea (CDAD) may occur during or after taking antibiotics, including Rifapentine and Isoniazid Tablets. The severity of CDAD can range from mild diarrhea to severe diarrhea that may cause death (fatal colitis). Tell your doctor right if you have diarrhea while you take or after you stop taking Rifapentine and Isoniazid Tablets.
- worsening of a condition called porphyria.

The most common side effects of Rifapentine and Isoniazid Tablets include change in the color of body fluids to orange-red, allergic reactions and flu-like symptoms, abnormalities in liver tests, decrease in white blood cell and red blood cell count, decreased appetite, skin rash or itching, and red eyes.

Rifapentine and Isoniazid Tablets may cause serious side effects, including:

- **Liver problems.** Rifapentine and Isoniazid Tablets may cause serious liver problems. Your doctor may do a blood test to check your liver function before and while you take Rifapentine and Isoniazid Tablets. Stop taking Rifapentine Tablets and call your doctor right away if you have any of the following signs and symptoms of liver problems:

- nausea
- stomach pain
- tiredness, yellowing skin or whites of your eyes
- vomiting
- loss of appetite
- dark urine

- **Allergic reactions and flu-like symptoms.** Allergic reactions and flu-like symptoms have happened in some people taking Rifapentine and Isoniazid Tablets. 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

Signs and symptoms of a flu-like reaction may include:

- weakness
- nausea and vomiting
- chills
- itching
- shortness of breath
- fainting
- tiredness
- headache
- aches
- sweats
- chest pain
- fast heartbeat
- muscle pain
- fever
- rash
- dizziness
- cough

The most important adverse effects of Rifapentine and Isoniazid Tablets are nerve injuries (see below) and severe and sometimes fatal inflammation of the liver (hepatitis).

Very common side effects (may affect more than 1 in 10 people)

- sensations of tingling, pricking, or numbness of the skin, especially in the feet and hands (peripheral neuropathy).
- increases of liver enzymes as measured in blood samples. Usually, this enzyme increases return to normal within three months despite continued treatment. When the values rise above a certain level your health care provider may decide to stop treatment with Rifapentine and Isoniazid Tablets.

Uncommon side effects (may affect up to 1 in 100 people)

- inflammation of the liver (hepatitis)
- epileptic seizures
- inflammation of the brain
- personality changes
- memory impairment.

If you notice signs of illness suggestive of liver damage, inform your health care provider immediately (see “Take special care with Rifapentine and Isoniazid Tablets”). The frequency of the following side effects is not known.

- allergic reactions, including skin reactions, such as rash (exanthema, erythema) and/or itching (pruritus), but also severe forms with fever, blisters and involvement of the mucous membranes (e.g. erythema multiforme, Stevens-Johnson syndrome) inflammation of blood vessels (vasculitis), swollen and/or painful lymphnodes (lymphadenopathy), painful disorder affecting joints, muscles and other soft tissues (rheumatic syndrome, lupus-like syndrome) or life threatening anaphylactic reactions,
- dizziness, headache, overresponsive reflexes, tremor, vertigo (spinning sensation and loss of balance)
- confusion, disorientation, hallucination (seeing or hearing things that are not there),
- inflammation of the lungs (pneumonitis),

- build up of acid in the body (metabolic acidosis), increased blood levels of glucose, a vitamin deficiency syndrome called pellagra (with e.g. dementia, loose stools and skin inflammation) nausea, vomiting, loss of appetite, dry mouth, flatulence, constipation, abdominal pain
- difficulty in passing urine, kidney damage including kidney inflammation (interstitial nephritis) changes in the white blood cell counts (leucopenia, neutropenia, eosinophilia, agranulocytosis), possibly resulting in an increased risk of infection,
- decreased red blood cell counts (anaemia), possibly leading to fatigue, weakness and shortness of breath,
- decreased platelet count, possibly resulting in an increased risk of bruising and bleeding,
- inflammation of the joints (arthritis)
- visual changes due to inflammation of the optic nerve (optic atrophy or neuritis)

If you notice any of the side effects listed above or if any of the side effects get serious, talk to your health care provider.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Rifapentine and Isoniazid Tablets. For more information, ask your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly to the respective drug regulatory authorities. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Rifapentine and Isoniazid Tablets

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

Do not store above 30°C. Protect from excessive heat and moisture

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

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

6. Contents of the pack and other information

Packs	Description
10's Aluminium Strip	10 Tablets shall be packed per strip using plain strip aluminium foil 0.04 mm as base material and plain strip aluminium foil 0.04 mm as a lidding material
12's Aluminium Strip	12 Tablets shall be packed per strip using plain strip aluminium foil 0.04 mm as base material and plain strip aluminium foil 0.04 mm as a lidding material
14's Aluminium Strip	14 Tablets shall be packed per strip using plain strip aluminium foil 0.04 mm as base material and plain strip aluminium foil 0.04 mm as a lidding material
10's Alu-Alu Blister	10 Tablets shall be packed per Blister using cold form Alu-Alu blister foil as base material and 0.03 mm thick blister hard tampered heat seal lacquer coated printed Aluminium foil as a lidding material
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