

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

Isoniazid / Rifapentine Tablet, Film-coated 300mg/300mg

Read all of this leaflet carefully before you starts 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, health care provider or pharmacist.
- This medicine has been prescribed for you only. Warning: DO NOT share this medication with others. It may harm them, even if their signs of illness are 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.

What is in this leaflet:

1. What Rifapentine 300mg + Isoniazid 300 mg Tablets is and what it is used for
2. What you need to know before you take Rifapentine 300mg + Isoniazid 300 mg Tablets
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1. WHAT RIFAPENTINE 300MG + ISONIAZID 300 MG TABLETS IS AND WHAT IT IS USED FOR
Rifapentine 300mg + Isoniazid 300 mg Tablets is indicated for the treatment of latent tuberculosis caused by *Mycobacterium tuberculosis*.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE RIFAPENTINE 300MG + ISONIAZID 300 MG TABLETS

Do not take Rifapentine 300mg + Isoniazid 300 mg Tablets:

- if you are hypersensitive (allergic) (Please refer section "Warnings and Precautions" and section 4 "Possible side effects") to a group of medicines called rifamycins, Isoniazid or any of the other ingredients (Please refer section 6 for "Other Ingredients") of Rifapentine 300mg + Isoniazid 300 mg Tablets 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 Isoniazid, such as drug fever, chills or inflammation of the joints before
- flu-like and other systemic drug reactions include hypotension, urticaria, angioedema, acute bronchospasm, or conjunctivitis or weakness, fatigue, nausea; vomiting, headache, fever, aches, sweats, dizziness, shortness of breath, flushing, or chills
- In people having active TB
- 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
- In children or adolescents aged less than 14 years.

Warnings and precautions

Talk to your health care provider before taking Rifapentine 300mg + Isoniazid 300 mg Tablets.

To make sure Rifapentine 300mg + Isoniazid 300 mg Tablets are safe for you, tell your doctor if you have:

- liver disease- nausea, vomiting, upper stomach pain, itching, tired feeling, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes);
 - diarrhea. A type of diarrhea called *Clostridioides difficile*-associated diarrhea (CDAD) may occur during or after taking antibiotics, including Rifapentine. The severity of CDAD can range from mild diarrhea to severe diarrhea that may cause death (fatal colitis). Tell your doctor right away if you have diarrhea while you take or after you stop taking Rifapentine.
 - porphyria (a genetic enzyme disorder that causes symptoms affecting the skin or nervous system);
 - HIV or AIDS or are taking medicines (protease inhibitors or certain nucleoside reverse transcriptase inhibitors to treat HIV infection)
 - you have been exposed to someone with Isoniazid or rifampin resistant TB
 - You are currently taking hormonal contraceptives or planning to get pregnant since using an additional barrier method is advised
- You should inform your doctor if you have diabetes or if you have ever suffered from seizure disorders (fits), psychosis.

You may be at special risk for developing hepatitis, if

- you drink alcoholic beverages daily
- you have a chronic liver disease,
- you are a user of illicit drugs including injection drugs (e.g. heroine)*
- you have a bleeding disorder

Furthermore, you should be carefully monitored and evaluated by your healthcare provider routinely if:

- You use any medicines for chronic medical conditions. You have a medical condition that is being treated with other medications that may have drug interactions with Rifapentine 300mg + Isoniazid 300 mg Tablets
- you suffer from tingling in the hands and feet (peripheral neuropathy),
- you are pregnant
- you develop a rash or itching of your skin

A common reported side effect is peripheral neuropathy, which may present with sensations of tingling, pricking, or numbness of the skin, especially in the feet and hands. The risk for peripheral neuropathy may be higher for persons with diabetes, kidney dysfunction, alcoholism, malnutrition, and HIV on certain ARVs (e.g., zalcitabine, stavudine, didanosine).

A vitamin, called pyridoxine or Vitamin B6, can be administered routinely at doses of 10-50 mg per day as per weight during treatment with Isoniazid, since it largely reduces the risk of developing neuropathy. If you are hypersensitive (allergic) to ethionamide, pyrazinamide, niacin (nicotinic acid), or other related medications you may also be hypersensitive to this product.

It is important that your doctor or health care provider know about all your symptoms even when you think they are not related to tuberculosis infection.

Other medicines and Rifapentine 300mg + Isoniazid 300 mg Tablets

Many drugs can interact with Rifapentine and Isoniazid, including prescription and over-the-counter medicines, vitamins, and herbal products. Rifapentine may induce liver enzymes making these medications ineffective or inhibit them thereby causing the drug to be toxic due to its high concentration in the blood. Hence, it is important that any of the aforementioned medications be known to your health care provider. Tell each of your health care providers about all medicines you use now and any medicine you start or stop using including those without a prescription.

In treating your condition You should not take Isoniazid / Rifapentine Tablets 300/300mg with

- aluminum hydroxide (medicine used to treat diseases related to the gastric acid) or
- disulfiram (medicine used for the treatment of chronic alcoholism).

The active agent in Isoniazid / Rifapentine Tablets 300/300mg 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 prior to surgery (narcotics, e.g. alfentanil, 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 inflammations and other diseases, such as asthma or rheumatoid arthritis),
- paracetamol (pain killer),
- medicines toxic to the liver,
- medicines toxic to the nervous system.

- Oral Contraceptives - Use alternative form(s) of birth control

Other Rifamycin (eg. Rifampin, rifabutin) associated drug- drug interactions may be also be observed for Rifapentine – eg. Protease Inhibitors, methadone and Oral Hypoglycemics.

Rifapentine 300mg + Isoniazid 300 mg Tablets with food and drink

Follow all directions on your prescription label. It is recommended that you take this medicine with food.

- If you take the 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 Tablets. This increases your risk for liver damage.

Pregnancy and breast-feeding

Pregnancy

Safety of Rifapentine 300mg and Isoniazid 300mg has not been studied in pregnant women.

There are limited data on the pharmacokinetics and safety of rifapentine in pregnancy and therefore the use of Rifapentine in pregnancy would best await more data to ensure appropriate dosing and at least preliminary safety data for this regimen in pregnant women*. Hence use of Rifapentine 300mg + Isoniazid 300 mg Tablets require further data before it can be recommended.

- If you become pregnant, or are planning to become pregnant, you must contact your doctor or health care provider to discuss the potential benefits and risks of your tuberculosis therapy for you and your child.
- Be sure to tell your health care provider immediately, if you are or may be pregnant.

Breast feeding

It is not known whether Rifapentine passes into breast milk or if it could harm a nursing baby. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made between you and your health care provider on whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother and the benefits of breastfeeding. Rifapentine may cause a red-orange discoloration of breast milk.

Babies may be breastfed whilst on TB Preventive Treatment. However rifapentine/isoniazid (RH) should not be given to HIV exposed babies on nevirapine since rifampin decrease nevirapine levels and increase the risk of mother to child transmission of HIV. Infant breast feeding from a mother on TB Preventive Treatment should receive pyridoxine for the duration of the mothers treatment.

Isoniazid is excreted into the breast milk of lactating mothers. No negative effects have been reported in breast-fed infants, whose mothers were receiving Isoniazid.

Driving and using machines

Isoniazid 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 300MG + ISONIAZID 300 MG TABLETS

Take Rifapentine + Isoniazid once weekly for 12 weeks i.e. 12 doses

Dose by weight band -

For age > 14 years

Weight band (kg)	Dose
<30-35	3 Tablets
36-45	3 Tablets
46-55	3 Tablets
56-70	3 Tablets
>70	3 Tablets

The maximum dose of Isoniazid and Rifapentine is 900 mg.

Follow all directions on your prescription label.

Take Rifapentine 300mg + Isoniazid 300mg Tablet with food.

If you take more Rifapentine 300mg + Isoniazid 300 mg Tablets than you should

If you have taken too many tablets or if you accidentally swallow too many tablets, you may develop nausea, vomiting, lack of appetite, gastrointestinal disturbances, fever, headache, dizziness, slurred speech, hallucinations and/or visual disturbances. Marked Isoniazid overdoses lead to respiratory distress and depression of the central nervous system progressing from stupor to come, along with severe seizures. Immediately contact your doctor, health care provider or the nearest hospital emergency department for further advice.

If you stop taking Rifapentine 300mg + Isoniazid 300 mg Tablets

You should not stop treatment unless your doctor or health care provider tells you to. Talk to your health care provider before you stop taking Rifapentine 300mg + Isoniazid 300 mg Tablets for any reason, particularly if you are experiencing any side effects or have another illness such as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or jaundice. If you have any further questions on the use of this product, ask your doctor or health care provider or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Rifapentine+ Isoniazid Tablets can cause side effects, although not everybody gets them. When using for latent tuberculosis, It is not always possible to differentiate between unwanted effects caused by Rifapentine + Isoniazid Tablets or those caused by any other medicines you may be taking at the same time.

For this reason, it is important that you inform your doctor or health care provider of any change in your health.

Call your doctor at once if you have:

- diarrhea that is watery or bloody; A type of diarrhea called *Clostridioides difficile*-associated diarrhea (CDAD) may occur during or after taking antibiotics, including Rifapentine. The severity of CDAD can range from mild diarrhea to severe diarrhea that may cause death (fatal colitis). Tell your doctor right away if you have diarrhea while you take or after you stop taking Rifapentine.
- liver problems- nausea, vomiting, upper stomach pain, itching, tired feeling, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes);
- low red blood cells (anemia)-pale skin, feeling light-headed or short of breath, rapid heart rate, trouble concentrating; or
- low white blood cell counts--fever, swollen gums, painful mouth sores, pain when swallowing, skin sores, cold or flu symptoms, cough, trouble breathing.

Rifapentine can cause changes in the color of your skin or body fluids. You may notice a red-orange appearance of your skin, tears, sweat, saliva, urine, or stools. Your teeth long or the inside of your mouth may also appear red-orange. This discoloration can permanently stain contact lenses or dentures.

Common side effects may include:

- nausea, vomiting, diarrhea, loss of appetite;
- headache, joint pain;
- itching or rash;
- eye redness; or
- abnormal liver function tests.
- Signs and symptoms of allergic reaction may include: low blood pressure, hives, cough with wheezing
- Signs and symptoms of a flu-like reaction may include: chills, itching, fainting, tiredness, aches, sweats, chest pain, and fast heartbeat

Severe skin reactions: Serious skin reactions such as Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome have happened in some people taking Rifapentine but these are rare.

Stop taking Rifapentine right away and call your doctor or get emergency help if you have any of the following symptoms:

- rash
- peeling or bleeding skin
- swollen face, lips, mouth tongue or throat of your mouth or lips
- red and painful skin
- sores or blisters on the inside of your mouth or lips
- flu like syndrome i.e. (fever, chills, headache, muscle aches, fatigue,, sore throat, cough, swollen lymph nodes, nausea, diarrhea)
- In the case of Stephen Johnson Syndrome a flu like syndrome appears first followed by a painful rash that spreads and subsequent blisters

The intake of Rifapentine 300mg + Isoniazid 300 mg Tablets may increase or decrease the number of platelets in the blood.

The following side effects have been reported in patients treated with Isoniazid.

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

The most commonly reported side effects are sensations of tingling, pricking, or numbness of the skin, especially in the feet and hands (peripheral neuropathy). Also, increases of liver enzymes as measured in blood samples. Usually, these enzyme increases return to normal within three months despite continued treatment. When the values rise above a certain level your doctor may decide to stop treatment with Rifapentine 300mg + Isoniazid 300 mg Tablets *Uncommon* side effects (may affect up to 1 in 100 people) are inflammation of the liver (hepatitis), epileptic seizures, inflammation of the brain, personality changes and memory impairment. If you notice sign and symptoms suggestive of liver damage, inform your doctor or health care provider immediately.

The following side effects have been reported in patients treated with Isoniazid.

However, frequency estimates for these effects are not available:

- 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 lymph nodes (lymphadenopathy), painful disorder affecting joints, muscles and other soft tissues (rheumatic syndrome, lupus-like syndrome) or life-threatening anaphylactic reactions,
- dizziness, headache, over responsive reflexes, tremor, vertigo,
- confusion, disorientation, hallucination, - 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,
- inflammation of the joints (arthritis)
- visual changes due to inflammation of the optic nerve (optic atrophy or neuritis)

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, health care provider or pharmacist as soon as possible.

5. HOW TO STORE RIFAPENTINE 300MG + ISONIAZID 300 MG TABLETS

Store below 30°C, avoid excursion above 30°C.

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

6. CONTENTS OF THE PACK AND OTHER INFORMATION

The active ingredients are Rifapentine and Isoniazid

The other ingredients are:

Core tablet: Microcrystalline Cellulose, Pregelatinised Starch, Croscarmellose Sodium, Iron Oxide Red, Povidone K-30, Microcrystalline Cellulose, Low-Substituted Hydroxypropyl Cellulose, Calcium Stearate, Sodium Starch Glycolate type A, Sodium Ascorbate, EDTA Disodium, Sodium Lauryl Sulfate, Hydroxypropyl Cellulose.

Seal and Film Coat: Hypromellose 2910, Opadry® 03F565224 Brown.

What Rifapentine 300mg + Isoniazid 300mg mg Tablets looks like and contents of the pack

Reddish brown colored, capsule shaped, biconvex, film coated tablets debossed with "J" and "21" on either side of breakline on one side and plain on the other side packaged in following pack size:

Bilister Pack: 10 X 12's Count

Bilister Pack of 12 Tablets, such 10 blisters are packed in a carton along with pack insert.

Bilister Pack In TLP: 1 X 12's Count

Bilister Pack of 12 Tablets, such 1 blister are packed in a TLP. Place 30 nos. of TLP in shipper

Strip Pack: 7 X 6's Count

Bilister Pack of 6 Tablets, such 7 blisters are packed in a carton along with pack insert.

Strip Pack: 3 X 12's Count

Strip Pack of 12 Tablets, such 3 strips are packed in a carton along with pack insert.

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