

PATIENT INFORMATION LEAFLET

Clinical information not updated - no longer recommended for prequalified indication

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

Isoniazid/Rifampicin 150 mg/150 mg Tablets*

Isoniazid, rifampicin

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 health care provider .
- 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 are the same as yours.
- If you get any side effects, talk to your health care provider. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Isoniazid/Rifampicin 150mg/150mg Tablets is and what it is used for
2. What you need to know before you take Isoniazid/Rifampicin 150mg/150mg Tablets
3. How to take Isoniazid/Rifampicin 150mg/150mg Tablets
4. Possible side effects
5. How to store Isoniazid/Rifampicin 150mg/150mg Tablets
6. Contents of the pack and other information

1. WHAT ISONIAZID/RIFAMPICIN 150MG/150MG TABLETS IS AND WHAT IT IS USED FOR

Isoniazid/Rifampicin 150 mg/150 mg Tablets is indicated for the continuation treatment phase of tuberculosis, caused by *Mycobacterium tuberculosis* in patients weighing more than 30kg.

To help clear up your TB completely, you must keep taking this medicine for the full time of treatment, even if you begin to feel better. This is very important. It is also important that you do not miss any doses.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ISONIAZID/RIFAMPICIN 150MG/150MG TABLETS

Do not take Isoniazid/Rifampicin 150mg/150mg Tablets:

- if you are hypersensitive (allergic) to isoniazid or rifampicin, or any of the other ingredients of Isoniazid/Rifampicin 150mg/150mg Tablets (see section 6, What Isoniazid/Rifampicin 150mg/150mg Tablets contains).
- if you have acute liver disease,
- if you have drug induced liver disease,
- if you have experienced liver damage linked to isoniazid or rifampicin before,
- if you have experienced severe side effects of isoniazid or rifampicin, such as drug fever or chills,
- if you are taking artemether/lumefantrine, daclatasvir or elvitegravir.
- if you are using a medicine against HIV or HCV infection that belongs to the class of “protease inhibitors”.
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* Trade names are not prequalified by WHO. This is the national medicines regulatory authority’s (NMRA) responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

Warnings and precautions

Isoniazid/Rifampicin 150mg/150mg Tablets may cause liver disease (hepatitis). You should be attentive to symptoms that might be due to liver damage, such as unexplained loss of appetite, nausea, vomiting, dark urine, yellow discoloration of the skin (jaundice), persistent fatigue of greater than 3 days duration and abdominal pain and tenderness. If these occur, you should immediately report this to your health care provider.

You may be at special risk for developing hepatitis

- if you are older than 35 years,
- if you drink alcoholic beverages daily (see “Taking Isoniazid/Rifampicin 150mg/150mg Tablets with food and drink”)
- if you have a chronic liver disorder
- 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”),
- if you suffer from tingling in the hands and feet (peripheral neuropathy),
- if you are pregnant,
- if you are HIV- infected.

If you get flu-like symptoms such as fever, headache, muscle aches etc., you should report this to your health care provider, since Isoniazid/Rifampicin 150mg/150mg Tablets may be the cause.

Tingling in the hands and feet (peripheral neuropathy) is the most common side effect of isoniazid, one of the active agents in Isoniazid/Rifampicin 150mg/150mg Tablets (see “Possible side effects”). You should report any such symptoms to your health care provider. A certain vitamin, pyridoxine, should be administered routinely at doses of 10 mg per day during treatment with Isoniazid/Rifampicin 150mg/150mg Tablets, since it largely reduces the risk of developing neuropathy.

If you are hypersensitive to ethionamide or niacin (nicotinic acid), you should inform your health care provider, because you may also be hypersensitive to Isoniazid/Rifampicin 150mg/150mg Tablets.

If you have epilepsy or a history of psychiatric disease, you should report this to your health care provider, since it may affect your ability to tolerate Isoniazid/Rifampicin 150mg/150mg Tablets.

If you have kidney problems, diabetes or porphyria, it is important that you inform your health care provider about this, since Isoniazid/Rifampicin 150mg/150mg Tablets may then be unsuitable for you.

If you are taking cortisone or any cortisone-like drug, you should report this to your health care provider, since the cortisone dose may have to be increased while taking Isoniazid/Rifampicin 150mg/150mg Tablets.

Isoniazid/Rifampicin 150mg/150mg Tablets may cause a reddish orange discoloration of body fluids such as urine, sputum and tears. This is due to rifampicin, and does not require medical attention. Also, contact lenses may become discolored due to Isoniazid/Rifampicin 150mg/150mg Tablets.

Isoniazid/Rifampicin 150mg/150mg Tablets 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 Isoniazid/Rifampicin 150mg/150mg Tablets.

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

Other medicines and Isoniazid/Rifampicin 150mg/150mg Tablets

It is important that you tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. These may affect the action of Isoniazid/Rifampicin 150mg/150mg Tablets, or Isoniazid/Rifampicin 150mg/150mg Tablets may affect their action. Side effects of either medicine may become worse and/or the medicines may become less effective.

One should not take Isoniazid/Rifampicin 150mg/150mg Tablets with

- voriconazole (a medicine used to treat fungal infections)
- HIV or HCV protease inhibitors, drugs used to treat HIV (amprenavir, cobistat, elvitegravir, indinavir, lopinavir, nelfinavir, saquinavir) or HCV (boceprevir, telaprevir) infection.
- aluminium hydroxide (medicine used to treat diseases related to excess of gastric acid) or
- disulfiram (medicine used for the treatment of alcoholism).

The active agents in Isoniazid/Rifampicin 150mg/150mg Tablets may also interact with other medicines, including for instance:

- Drugs used to treat HIV infection (e.g. efavirenz, maraviroc, nevirapine, raltegravir, ritonavir, boceprevir, telaprevir, simeprevir)
- other antivirals (e.g. elvitegravir, dolugravir, maraviroc, daclatasvir, ledipasvir, sofosbuvir)
- Drugs used to treat fungal infections (e.g. ketoconazole, fluconazole)
- Antibiotics (e.g. clarithromycin)
- Drugs used to treat malaria (e.g. quinine)
- Immunosuppressant drugs (e.g. cyclosporine, tacrolimus, sirolimus, everolimus)
- Drugs used to treat heart conditions (e.g. verapamil, nimodipine, digoxin)
- Drugs used to treat blood lipids (e.g. simvastatin, atorvastatin)
- Some drugs used to treat diabetes (e.g. glibenclamide, glimepiride, repaglinide, metformin)
- Oral contraceptive pills
- Medicines used to treat epileptic seizures (e.g. phenytoin, carbamazepine, valproate)
- Medicines used to help you sleep (benzodiazepines, e.g. alprazolam, diazepam, flurazepam, triazolam, midazolam, zolpidem, zopiclone)
- Medicines used for the treatment of certain psychiatric conditions (neuroleptics, e.g. chlorpromazine, haloperidol, clozapine, nortriptyline)
- Medicines used for prevention of blood clots (clopidogrel, coumarin or indandione derivatives e.g. warfarin)
- Medicines used in surgery (narcotics, e.g. alfentanil, enflurane, halothane)
- theophylline (medicine used for the treatment of asthma)
- corticosteroids (e.g. prednisolone, medicines used for the treatment of inflammations and other diseases, such as asthma or rheumatoid arthritis)
- acetaminophen, paracetamol (pain killers)

Taking any of these drugs together with Isoniazid/Rifampicin 150mg/150mg Tablets may be unsuitable or require dose adjustment.

Taking Isoniazid/Rifampicin 150mg/150mg Tablets with food and drink and alcohol

Isoniazid/Rifampicin 150mg/150mg Tablets should be taken on an empty stomach (at least one hour prior to or two hours after a meal).

One should not drink alcohol while taking Isoniazid/Rifampicin 150mg/150mg Tablets. This increases the risk of liver damage.

When taken with cheese or fish (histamine- or tyramine-rich food) Isoniazid/Rifampicin 150mg/150mg Tablets may cause redness/itching of the skin, hot feeling, rapid or pounding heartbeat, sweating, chills or clammy feeling, headache, and/or lightheadedness. If you experience these side effects you should avoid eating cheese and fish while taking this medicine.

Pregnancy and breast-feeding

If you become pregnant, or are planning to become pregnant, you must contact your healthcare provider to discuss the potential benefits and risks of the tuberculosis therapy to you and your child.

Isoniazid and rifampicin are excreted into the breast milk of lactating mothers. No negative effects have been reported in breast-fed-infants whose mothers were receiving these drugs. However, drug concentrations 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

Isoniazid/Rifampicin 150mg/150mg Tablets may cause visual disturbances, dizziness and other side effects on the nervous system that can impair one's ability to drive and to use machines.

3. HOW TO TAKE ISONIAZID/RIFAMPICIN 150MG/150MG TABLETS

Isoniazid/Rifampicin 150mg/150mg Tablets should always be taken exactly as described by your health care provider. You should check with your healthcare provider if you are not sure. Isoniazid/Rifampicin 150mg/150mg Tablets is dosed according to your body weight and should be swallowed only as solid tablets.

The number of tablets, by weight band, to be taken three times weekly is shown below:

Body weight (Kg)	Number of Isoniazid/Rifampicin 150 mg/150 mg Tablets to be taken three times weekly
30 - 37.5	2
37.6 - 55	3
>55	4

The tablets should be taken on an empty stomach (at least one hour prior to or two hours after a meal).

If you have a kidney disease, your health care provider may prescribe separate formulations of the component drugs in Isoniazid/Rifampicin 150mg/150mg Tablets.

Your health care provider will decide on the duration of treatment that is suitable for you.

If you take more Isoniazid/Rifampicin 150mg/150mg Tablets than you should

If you take too many tablets, you may develop vomiting, gastrointestinal disturbances, fever, headache, dizziness, slurring of speech, hallucinations and/or visual disturbances. You may also get a reddish-orange discoloration of the skin, facial swelling and itching. You should immediately contact your health care provider or the nearest hospital emergency department for further advice.

If you forget to take Isoniazid/Rifampicin 150mg/150mg Tablets

If you miss or forget to take a dose, the missed dose should be taken as soon as possible, unless the next regular dose is scheduled within 24 hours.

Skip the missed dose if it is almost time for the next regular dose.

You should not take a double dose to make up for forgotten individual doses.

If you stop taking Isoniazid/Rifampicin 150mg/150mg Tablets

You should keep taking the medicine for as long as the health care provider has ordered, even if you are feeling better. If you stop the medicine too soon, the infection may not be completely cured. You should not stop treatment unless your healthcare provider says so.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Isoniazid/Rifampicin 150mg/150mg Tablets can cause side effects, although not everybody gets them. When treating tuberculosis, it is not always possible to differentiate between unwanted effects caused by Isoniazid/ Rifampicin 150mg/150mg Tablets, and those caused by any other medicines you may be taking at the same time. For this reason, it is important that you inform your healthcare provider of any change in your health.

The following side effects have been reported in patients treated with Isoniazid/Rifampicin 150mg/150mg Tablets:

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

The *most commonly* reported side effects (greater than 1 in every 10 patients treated) include sensations of tingling, pricking, or numbness of the skin, especially in the feet and hands (peripheral neuropathy). Your health care provider will prescribe a vitamin called pyridoxine in order to counteract this (see above, "Take special care with Isoniazid/Rifampicin 150mg/150mg Tablets"). Also, increased liver enzymes, as measured in blood samples, very commonly occur (see above, "Take special care with Isoniazid/ Rifampicin 150mg/150mg Tablets"). Usually, liver enzyme increases occur during the first 1-3 months of therapy and return to normal despite continued treatment. When the values rise above a certain level your health care provider may decide to stop treatment with Isoniazid/Rifampicin 150mg/150mg Tablets. Flushing may also occur after ingesting Isoniazid/Rifampicin 150mg/150mg Tablets

Commonly (greater than 1 in every 100 patients treated) reported side effects include a reddish discoloration of body fluids such as urine, sputum, tears, saliva and sweat. Further common side effects are diarrhoea, abdominal pain, loss of appetite, nausea and vomiting, as well as skin reactions with rash and/or itching, and disturbances of the menstrual cycle.

Uncommon side effects (greater than 1 in every 1000 patients treated but less than 1 in 100) are inflammation of the liver (hepatitis) epileptic seizures, headache, inflammation of the brain, personality changes and memory impairment. If you notice signs and symptoms suggestive of liver damage (see "Take special care with Isoniazid/Rifampicin 150mg/150mg Tablets"), you should inform your healthcare provider immediately.

Rare side effects (less than 1 in every thousand patients treated) include gastritis, bowel infection, inflammation of the kidney (nephritis), photosensitivity reactions (skin sensitivity to light) and conjunctivitis.

The following side effects have been reported in patients treated with Isoniazid/Rifampicin 150mg/150mg Tablets. However, frequency estimates for these effects are not available:

- Allergic reactions with fever, muscle aches, and cough
 - Severe skin reactions with fever, blisters and involvement of the mucous membranes or life-threatening anaphylactic reactions
 - dizziness, drowsiness
 - confusion, disorientation, hallucination,
 - inflammation of the lungs (pneumonitis)
 - inflammation of the optic nerve
 - 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)
 - metallic taste, dry mouth, flatulence, constipation.
 - difficulty in passing urine
 - 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, which may result in an increased risk of bruising and bleeding.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your health care provider as soon as possible.

5. HOW TO STORE ISONIAZID/RIFAMPICIN 150MG/150MG TABLETS

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

Store in a dry place below 25°C, protected from excessive humidity and light.

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 protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Isoniazid/Rifampicin 150mg/150mg Tablets contains

The active ingredients are 150 mg isoniazid and 150 mg rifampicin.

The other ingredients are:

Tablet core: Ascorbic acid, colloidal silicon dioxide, crospovidone, magnesium stearate, microcrystalline cellulose and pregelatinised starch.

Film-coating: Hypromellose, iron oxide red, iron oxide yellow, polyethylene glycol, simethicone emulsion, talc and titanium dioxide.

What Isoniazid/Rifampicin 150mg/150mg Tablets looks like and contents of the pack

Brown, round biconvex, film-coated tablets, with break line on one side and plain on the other side. The tablet can be divided into equal halves.

Bulk pack of 1000 tablets in a polypropylene bag, inside an HDPE container with aluminium tagger seal, also containing a silica gel bag and closed with a white LDPE cap.

PVC/PVDC-aluminium blister pack of 28 tablets (7x4), such 24 blisters are packed in a carton along with pack insert.

Supplier and Manufacturer

Supplier	Manufacturer
Lupin Limited Kalpataru Inspire 3 rd Floor, Off Western Express Highway Santacruz (East) Mumbai 400055, India Tel : +91 22 66402323 E-mail: rajeevpatil@lupinpharma.com	Lupin Limited A-28/1, M.I.D.C Industrial Area Chikalthana 431 210 Aurangabad India Phone:+91- 24-02485871

For any information about this medicinal product, please contact the supplier.

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Detailed information on this medicine is available on the World Health Organization (WHO) web site:
<http://www.who.int/prequal/>.