

## **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.*

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\* [https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification\\_Feb2017\\_newtempl.pdf](https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf)

## Information for the patient

[TB06 trade name]<sup>†</sup>  
Rifampicin/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 questions about the medicine, 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 seem 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 [TB068 trade name] is and what it is used for
2. What you need to know before you take [TB068 trade name]
3. How to take [TB068 trade name]
4. Possible side effects
5. How to store [TB068 trade name]
6. Contents of the pack and other information

#### 1. What [TB068 trade name] is and what it is used for

[TB068 trade name] is a combination of two medicines, rifampicin and isoniazid, that act against the bacteria that cause tuberculosis (TB).

[TB068 trade name] is indicated in adults and adolescents 10 years and older and weighing at least 25 kg for the treatment of tuberculosis, or preventive treatment of tuberculosis in those at particular risk.

#### 2. What you need to know before you take [TB068 trade name]

##### Do not take [TB068 trade name] if you:

- are hypersensitive (allergic) to isoniazid or rifampicin, or any of the other ingredients of [TB068 trade name] (see section 6, What [TB068 trade name] contains).
- have acute liver disease,
- have drug-induced liver disease,
- have experienced liver damage linked to isoniazid or rifampicin before,
- have experienced severe side effects of isoniazid or rifampicin, such as drug fever or chills,
- if you are using voriconazole (a medicine used to treat fungal infections)
- if you are using a medicine against HIV infection that belongs to the class of protease inhibitors or a medicine against Hepatitis C that belongs to the class of direct acting antivirals.

### Warnings and precautions

[TB068 trade name] 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.

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<sup>†</sup> Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

You may be at special risk for developing hepatitis

- if you are older than 35 years,
- if you drink alcoholic beverages daily (see “[TB068 trade name] 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 “Other medicines and [TB068 trade name]”),
- 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 [TB068 trade name] 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 [TB068 trade name] (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 [TB068 trade name], 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 [TB068 trade name].

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 [TB068 trade name].

If you have kidney problems, diabetes or porphyria, it is important that you inform your health care provider about this, since [TB068 trade name] 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 [TB068 trade name].

[TB068 trade name] 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 discoloured due to [TB068 trade name].

[TB068 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 [TB068 trade name].

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.

#### **Other medicines and [TB068 trade name]**

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 [TB068 trade name], or [TB068 trade name] may affect their action. Side effects of either medicine may become worse and/or the medicines may become less effective.

You should not take [TB068 trade name] with:

- voriconazole (a medicine used to treat fungal infections).
- HIV protease inhibitors (drugs used to treat HIV infection).
- direct acting antivirals for the treatment of chronic Hepatitis C.
- aluminium hydroxide (medicine used to treat diseases related to the gastric acid)

The active agents in [TB068 trade name] may also interact with a great number of other medicines, including for instance:

- drugs to treat HIV infection (e.g. efavirenz, nevirapine)
- drugs to treat fungal infections (e.g. ketoconazole, fluconazole)
- antibiotics (e.g. clarithromycin)
- drugs to treat malaria (e.g. quinine)
- immunosuppressant drugs (e.g. cyclosporine, tacrolimus)
- drugs to treat heart conditions (e.g. verapamil, digoxin)
- drugs to treat blood lipids (e.g. simvastatin)
- some drugs to treat diabetes (e.g. glibenclamide)
- oral contraceptive pills
- medicines to treat epileptic seizures (e.g. phenytoin, carbamazepine, valproate)
- 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 derivatives, e.g. warfarin)
- medicines used at surgery (narcotics, e.g. alfentanil, enflurane)
- corticosteroids (e.g. prednisolone, medicines for the treatment of inflammations and other diseases, such as asthma or rheumatoid arthritis)
- medicines to treat pain (e.g. morphine, paracetamol)
- codeine (medicine to treat cough)
- disulfiram (medicine used for the treatment of chronic alcoholism).

Taking any of these drugs together with [TB068 trade name] may be unsuitable or require dose adjustment.

### **[TB068 trade name] with food and drink**

[TB068 trade name] should be taken on an empty stomach (at least one hour prior to or two hours after a meal).

You should not drink alcohol while taking [TB068 trade name]. This increases the risk of liver damage. When taken with cheese or fish (histamine- or tyramine-rich food) [TB068 trade name] 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 health care provider to discuss the potential benefits and risks of the tuberculosis therapy for 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**

[TB068 trade name] may cause visual disturbances, dizziness and other side effects on the nervous system that can impair your ability to drive and to use machines.

### 3. How to take [TB068 trade name]

**Always take your medicine exactly as your health care provider has told you.** You should check with your health care provider if you are not sure.

The dose of [TB068 trade name] is decided based on your body weight, as shown in the table below:

Body weight	Dose
25–39 kg	2 tablets once daily
40–54 kg	3 tablets once daily
55–69 kg	4 tablets once daily
70 kg and over	5 tablets, or as determined by your health care provider, once daily

Your health care provider will tell you how long you need to continue taking the medicine.

[TB068 trade name] is not recommended for adolescents and children younger than 10 years or weighing less than 25 kg.

#### How to take [TB068 trade name]

[TB068 trade name] should be swallowed with water or another drink.

The tablets should be taken on an empty stomach (at least one hour prior to or two hours after a meal). You should take the medicine once daily. Try to take [TB068 trade name] at the same time each day.

#### If you take more [TB068 trade name] than you should

If you accidentally take too many tablets, immediately contact your health care provider or the nearest hospital emergency department. Take the tablet container with you so that you can easily describe what you have taken. If you have taken too much [TB068 trade name], you may vomit or get other problems with your stomach or gut, fever, headache, dizziness, slurring of speech, hallucinations and/or visual disturbances. You may also get a reddish-orange discolouration of the skin, facial swelling and itching.

#### If you forget to take [TB068 trade name]

It is important not to miss a dose. If you miss or forget to take a dose, the missed dose should be taken as soon as possible, unless it is less than 6 hours till your next dose, in which case skip the missed dose and just take the next regular dose.

Do not take a double dose to make up for a forgotten tablet.

If you vomit less than 1 hour after taking this medicine, take another dose. You do not need to take another dose if you were sick more than 1 hour after taking [TB068 trade name].

#### If you stop taking [TB068 trade name]

Do not stop taking this medicine without checking with your health care provider. Stopping your tablets too early may no longer protect you from the infection or cause it to come back.

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

### 4. Possible side effects

Like all medicines, [TB068 trade name] can cause side effects, although not everybody gets them. When treating tuberculosis, it is not always possible to differentiate between unwanted effects caused by [TB068 trade name], 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 health care provider of any change in your health.

The following side effects have been reported in patients treated with [TB068 trade name]:

The most important adverse effects of isoniazid and rifampicin 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). Your health care provider will prescribe a supplementary medicine with a vitamin called pyridoxine, in order to counteract this (see above, “Take special care with [TB068 trade name]”).
- increased liver enzymes as measured in blood samples (see above, “Take special care with [TB068 trade name]”). 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 [TB068 trade name].
- Flushing

### **Common side effects**

*(may affect up to 1 in 10 people):*

- reddish discoloration of body fluids such as urine, sputum, tears, saliva and sweat.
- diarrhoea
- stomach pain
- loss of appetite,
- feeling sick (nausea)
- vomiting
- skin reactions with rash and/or itching
- disturbances of the menstrual cycle.

### **Uncommon side effects**

*(may affect up to 1 in 100 people)*

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

If you notice signs of illness suggestive for liver damage (see “Take special care with [TB068 trade name]”), you should inform your health care provider immediately.

### **Rare side effects**

*(may affect up to 1 in 1000 people)*

- inflammation of the stomach lining (gastritis)
- infection of the intestines (bowel infection)
- inflammation of the kidney (nephritis)
- skin sensitivity to light (photosensitivity reactions)
- inflammation or swelling of the conjunctiva or pinkeye (conjunctivitis)

### **Side effects of which it is not known how often they may occur**

- 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 (optic neuritis)
- 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.

### **Reporting of side effects**

If you get any side effects, talk to your health care provider. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

### **5. How to store [TB068 trade name]**

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

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

**PVC/ PVDC Aluminum and PVC/PE/PVDC Aluminum Blister packs:** Store below 25°C, protected from excessive humidity. Protect from light.

**Alu/Alu Blister pack:** Store below 30°C, protected from excessive humidity.. Protect from light.

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 [TB068 trade name] contains**

The active ingredients are rifampicin and isoniazid.

The other ingredients of [TB068 trade name] are:

#### *Core tablet:*

Microcrystalline cellulose, Crospovidone, Pregelatinized starch, Ascorbic acid, Colloidal silicon dioxide and Magnesium stearate

#### *Film coat:*

Hypromellose, Polyethylene glycol, Talc, Titanium dioxide, Colour iron oxide red and Simethicone

#### **What [TB068 trade name] looks like and contents of the pack**

[TB068 trade name] are brick-red, capsule shaped tablets, biconvex, film coated tablets with break-line on one side and plain on the other side.

The break-line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

#### *Blister packs*

The primary packs are blister cards of 6 tablets (comprised of orange PVC/PVDC foil sealed with aluminium foil lid). Such 15 blister cards are packed in a carton with one pack insert.

Pack size: 15 x 6 Tablets.

The primary packs are blister cards of 28 tablets (comprised of green PVC/PVDC foil sealed with aluminium foil lid). Such 24 interlocked blister cards are packed in a carton with one partition after 12 cards and one insert in each partition.

Pack size: 24 x 28 Tablets.

Cold form Alu/Alu blister pack (Laminated aluminium foil, one side bright and shining, the other side relatively dull for cold forming blister pack).

The primary packs are blister cards of 28 tablets Such 24 blisters kept in a carton with one pack insert.  
Pack size: 24 x 28Tablets

The primary packs are blister cards of 28 tablets (comprised of PVC/PE/PVDC foil sealed with aluminium foil lid). Such 24 blister cards are packed in a carton.  
Pack size: 24 x 28 Tablets

*Bottle pack*

Tablets are packed in a sealed polypropylene bag, which is packed inside a white HDPE container together with one, a 1 gram silica gel bag with foam on top of the bag and the container is sealed with aluminium tagger. An insert is placed above the container is shrink wrapped. Pack size: 1000 Tablets.

**Supplier and Manufacturer**

***Supplier***

Lupin Ltd  
Kalpataru Inspire  
3rd Floor, Off Western Express Highway  
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***Manufacturer***

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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/pqweb/medicines>