

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.

* https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[TB360 trade name][†]
Isoniazid/rifampicin

*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 [TB360 trade name] is and what it is used for
2. What you need to know before you take [TB360 trade name]
3. How to take [TB360 trade name]
4. Possible side effects
5. How to store [TB360 trade name]
6. Contents of the pack and other information

1. What [TB360 trade name] is and what it is used for

[TB360 trade name] is a combination of two antimycobacterial agents, rifampicin and isoniazid.

[TB360 trade name] is used in children weighing less than 25 kg, for the prevention and treatment of tuberculosis caused by the bacterium *Mycobacterium tuberculosis*.

This product is intended for use in children. Safety information on use in adults is also provided.

2. What you need to know before you take [TB360 trade name]

Do not take [TB360 trade name] if you:

- are hypersensitive (allergic) to isoniazid or rifampicin, or any of the other ingredients of [TB360 trade name] (see section 6, What [TB360 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.

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

Warnings and precautions

[TB360 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 discolouration 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 “[TB360 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 [TB360 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 [TB360 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 [TB360 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 [TB360 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 [TB360 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 [TB360 trade name].

If you have kidney problems, diabetes or porphyria, it is important that you inform your health care provider about this, since [TB360 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 [TB360 trade name].

[TB360 trade name] may cause a reddish orange discolouration 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 [TB360 trade name].

[TB360 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 [TB360 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 [TB360 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 [TB360 trade name] , or [TB360 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 [TB360 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 [TB360 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 [TB360 trade name] may be unsuitable or require dose adjustment.

[TB360 trade name] with food and drink

[TB360 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 [TB360 trade name]. This increases the risk of liver damage.

When taken with cheese or fish (histamine- or tyramine-rich food) [TB360 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

[TB360 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.

[TB360 trade name] also contains 2mg of aspartame per tablet. Aspartame is a source of phenylalanine. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

3. How to take [TB360 trade name]

[TB360 trade name] should always be taken exactly as described by the health care provider. You should check with your health care provider if you are not sure.

The dose of [TB360 trade name] depends on the patient's weight. The medicine should be given once daily. Try to give [TB360 trade name] at the same time each day.

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

Children weighing less than 25 kg

The following table shows the doses for prevention or treatment of tuberculosis according to children's weight:

Patient's weight	Dose
4-7 kg	1 tablet
8-11 kg	2 tablets
12-15 kg	3 tablets
16-24 kg	4 tablets
> 25 kg	--*

*For these patients, formulations containing more isoniazid/rifampicin should be used.

[TB360 trade name] is not recommended for children with a body weight of less than 4 kg.

Kidney disease

If the child has kidney-disease, then the health care giver may prescribe separate formulations of the component drugs in [TB360 trade name].

Liver disease

If the child has liver disease, the health care provider will apply special precautionary measures (see section 2).

How to take [TB360 trade name]

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

Disperse the tablets in drinking water before giving the dose. Each tablet should be dispersed in a minimum of 10 mL of water, the maximum volume of water recommended for dispersion of a dose is 50 mL

Instructions for giving {DotWHOPAR_ProductName}

- Look up the child's weight in the above dosing table
- Then look under number of tablets of [TB360 trade name] which shows how many tablets of [TB360 trade name] will be required
 1. The required amount of drinking water should be taken in a small and clean cup and the required number of tablets should be added. At least 10 mL drinking water should be used to disperse the tablets.
 2. The cup should be gently swirled until tablets disperse, and the entire mixture should be given/taken immediately.
 3. The cup should be rinsed with an additional 10 mL water, which should be drunk by the patient to ensure the entire dose is taken.

If the child takes more [TB360 trade name] than they should

If the child accidentally takes too many tablets, immediately contact the 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 the child has taken too much [TB360 trade name], he or she may develop vomiting, gastrointestinal disturbances, fever, headache, dizziness, slurring of speech, hallucinations and/or visual disturbances. The child may also get a reddish-orange discolouration of the skin, facial swelling and itching.

If you forget to give [TB360 trade name]

It is important not to miss a dose. If a dose is missed, the missed dose should be given as soon as possible, unless the next regular dose is scheduled within 6 hours. Skip the missed dose if it is almost time for the next regular dose.

Do not give a double dose to make up for a forgotten dose.

If the child vomits less than 1 hour after taking this medicine, give them another dose. You do not need to give another dose if they were sick more than 1 hour after taking [TB360 trade name].

If you stop giving [TB360 trade name]

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

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

4. Possible side effects

Like all medicines, [TB360 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 [TB360 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 [TB360 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 [TB360 trade name] ").
- increased liver enzymes as measured in blood samples (see above, "Take special care with [TB360 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 [TB360 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 [TB360 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 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 [TB360 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 blister and carton after EXP. The expiry date refers to the last day of that month.

Store below 30°C. Store in a dry place protected from moisture. Avoid excursions above 30°C

Do not use this medicine if you notice visible signs of deterioration and that it is different from the description below.

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 [TB360 trade name] contains

- The active ingredients are Isoniazid and Rifampicin
 - The other ingredients of [TB360 trade name] are microcrystalline cellulose, crospovidone, colloidal silicon dioxide, pregelatinized starch, ascorbic acid, magnesium stearate, colour ponceau 4R (Cochineal red A), saccharin sodium, raspberry flavour, strawberry flavour and aspartame
- There is too little sodium in this medicine to have any effect, even if you are on a low-sodium diet.

What [TB360 trade name] looks like and contents of the pack

[TB360 trade name] is a brick red coloured, flat faced beveled edged, mottled, circular uncoated tablet, plain on both sides and with a characteristic flavour.

[TB360 trade name] is packed in:

Strip pack

Plain aluminium/aluminium strip. Each strip contains 6 or 28 tablets. Such strips are packed in a carton.

Pack sizes: 1x10, 14 x 6's tablets and 3 x 28's tablets.

Blister pack

Plain aluminium/cold forming aluminium-aluminium blister card. Each blister card contains 28 tablets. Such 3 blisters are packed in a carton.

Pack sizes: 1x5, 3 x 28's tablets.

Supplier and Manufacture

Supplier

Lupin Limited
Kalpataru Inspire
3rd Floor, Off Western Express Highway,
Santacruz (East), Mumbai 400055,
India
Tel: 91-22-66402323
Email: global@lupin.com

Manufacturer

Lupin Limited
A-28/1, MIDC Area, Chikalthana
Aurangabad 431210
India
Tel: +91 240 6612444
fax: + 91 240 2484121
e-mail: jitendrarane@lupin.com

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

This leaflet was last revised in September 2023

Detailed information on this medicine is available on the World Health Organization (WHO) website:
<https://extranet.who.int/pqweb/medicines>