

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

[TB285 trade name][†]
Isoniazid

*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 [TB285 trade name] is and what it is used for
2. What you need to know before you take [TB285 trade name]
3. How to take [TB285 trade name]
4. Possible side effects
5. How to store [TB285 trade name]
6. Contents of the pack and other information

1. What [TB285 trade name] is and what it is used for

[TB285 trade name] is a medicine used to treat tuberculosis (TB), an infection caused by bacteria called *Mycobacterium tuberculosis*. It is always given together with other medicines to treat tuberculosis. Your health care provider has chosen the combination that is right for your condition.

[TB285 trade name] is also used on its own or with other medicines to prevent TB if there is a high chance you could catch tuberculosis.

[TB285 trade name] contains the active substance isoniazid, which is an antibiotic that kills the bacteria responsible for TB by preventing them from making their protective cell wall.

2. What you need to know before you take [TB285 trade name]

Do not take [TB285 trade name]:

- if you are allergic (hypersensitive) to isoniazid or any of the other ingredients of [TB285 trade name] listed at the end of this leaflet
- if you have any sort of acute liver disease
- if you have ever had liver problems after taking isoniazid or any other medicine
- if you had previously experienced other severe side effects with isoniazid, such as fever, chills or inflammation of the joints.

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

Warnings and precautions

Talk to your health care provider before taking [TB285 trade name]. Tell your health care provider before starting the medicine if you have:

- liver problems such as long-term liver disease
- kidney problems
- diabetes
- epilepsy
- mental problems (psychosis)
- existing damage to your nerves (peripheral neuropathy) that causes a sensation of tingling in the hands or feet
- HIV infection
- malnutrition

Also tell your health care provider if you are allergic to the medicines ethionamide, pyrazinamide, or niacin (nicotinic acid) – this may make it more likely that you will also be allergic to [TB285 trade name].

It is also important that you tell your health care provider if you are pregnant, or if you drink alcohol regularly or use injection drugs like heroin.

If any of these apply, your health care provider will discuss your treatment with you, and explain whether you will need additional checks in case you get side effects.

When taking [TB285 trade name] your health care provider will test your blood regularly to check for any problems with your liver. Tell your health care provider straight away if you get signs or symptoms that could suggest liver damage. The symptoms to look out for 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 soreness or tenderness in your belly, especially on the right just under your ribs.

You may be at higher risk of liver problems if:

- you are older than 35 years
- you drink alcohol daily (see “Taking [TB285 trade name] with food and drink”)
- you have a long-term liver disease
- you use recreational drugs by injection (e.g. heroin).

If any of these apply to you, your health care provider will test for liver problems more often. If serious liver problems develop your health care provider may recommend you to change your treatment and stop taking [TB285 trade name].

Peripheral neuropathy (tingling in the hands and feet) is the most common side effect of isoniazid (see “Possible side effects”). If you have kidney or liver problems, you may be at increased risk of experiencing isoniazid side effects including peripheral neuropathy. You may also be more likely to get peripheral neuropathy if you are malnourished, have diabetes, are dependent on alcohol, have HIV infection, are an infant or teenager, or are pregnant or breastfeeding. Your health care provider will check on you regularly if any of these apply.

Your health care provider may recommend that you take vitamin B6 (pyridoxine) while you are being treated with [TB285 trade name], since it reduces the risk of developing peripheral neuropathy.

It is important that your health care provider knows about any illness you get, even when you think it is not related to tuberculosis infection or your medicine.

Resistance

This medicine must always be taken with other TB medicines and in the way your health care provider recommends. Using the medicine alone or not following the recommended doses allows the disease to become resistant to the medicine, so your treatment may no longer work to cure your TB.

Other medicines and [TB285 trade name]

Tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Make sure you mention herbal medicines you might have been taking. These may affect the action of [TB285 trade name], or [TB285 trade name] may affect their action. Side effects of either medicine may become worse and/or the medicines may become less effective.

Where possible, [TB285 trade name] should not be used together with other medicines that can cause damage to the liver or the nerves, since their side effects may add up and increase the risks. Your health care provider will be able to advise you about any changes that may be needed to your treatment.

[TB285 trade name] should not be given with antacids (medicines for indigestion) especially those that contain aluminium hydroxide, as they lower the dose of isoniazid that your body absorbs.

It is not known whether isoniazid interacts with medicines to treat hepatitis C infection (direct-acting antivirals, such as daclatasvir, elbasvir, glecaprevir, grazoprevir, ledipasvir, ombitasvir, paritaprevir, pibrentasvir, simeprevir, sofosbuvir, velpatasvir or voxilaprevir). However, since hepatitis C causes chronic liver disease, you will need to be very carefully monitored during treatment with isoniazid if you are also being treated with these medicines.

Taking [TB285 trade name] with other medicines

The active substance in [TB285 trade name] may also interact with the following medicines:

- medicines to treat epileptic seizures (e.g. phenytoin, carbamazepine, primidone)
- benzodiazepine medicines used to treat anxiety or help you sleep (e.g. diazepam, flurazepam, triazolam, midazolam, chlorzoxazone)
- stavudine, zalcitabine (used for the treatment of HIV)
- medicines used in surgery (strong painkillers, e.g. alfentanil; anaesthetics e.g. enflurane)
- levodopa (medicine for the treatment of Parkinson's disease)
- 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)
- disulfiram (medicine to treat dependence on alcohol).

Taking [TB285 trade name] with food and drink

[TB285 trade name] should be taken on an empty stomach (at least one hour before or two hours after a meal). This helps your body absorb isoniazid more easily.

Isoniazid may react with foods containing histamine or tyramine (e.g. matured cheeses, cured meat, some oily fish like tuna, salmon and mackerel, wine and beer), causing symptoms including headache, sweating, flushing, fast, uneven or forceful heartbeat (palpitations), dizziness, feeling lightheaded or faint (due to low blood pressure). These foods should be avoided if you are receiving isoniazid.

Do not drink alcohol while taking [TB285 trade name]. This increases your risk of liver damage.

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 advantages and disadvantages of your tuberculosis therapy for you and your child. Be sure to tell your health care provider immediately if you are or think you may be pregnant.

Isoniazid passes into breast milk in small amounts, but these are not enough to protect your child from TB or treat any TB infection they may get. No harmful effects have been reported in breast-fed infants whose mothers were receiving isoniazid. However, your health care provider may recommend that you and your baby take vitamin B6 (pyridoxine) to reduce any risks.

Driving and using machines

[TB285 trade name] may cause dizziness and other side effects to the nervous system that can impair your ability to drive and use machines. If you have any of these side effects, do not drive or use any tools or machines.

3. How to take [TB285 trade name]

Your health care provider will decide on the right doses and combination of medicines to treat your TB, based on your age, weight and condition, including whether your TB is resistant to standard treatments.

For the treatment of TB, [TB285 trade name]) must be used with other medicines.

Always take [TB285 trade name] exactly as your health care provider has told you. Check with your health care provider if you are not sure.

Do not change the dose unless your health care provider tells you to. Your treatment may need to go on for many months, but it is important to take the full course of treatment recommended by your health care provider, even if you feel better.

Swallow [TB285 trade name] whole with water or another drink.

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

For information on how to take the other medicines you need for your TB treatment, discuss with your health care provider and read the leaflets that come with those medicines as well.

Treatment of tuberculosis

If [TB285 trade name] is added to other TB medicines to manage TB resistant to standard medicines, the dose of isoniazid selected depends on your weight. Your health care provider will work out the right dose for you. The typical recommended dose is 2 tablets daily if you weigh 46 kg or more.

In children weighing 16 to 24 kg a dose of 1 tablet of [TB285 trade name] may be given. For other children (weighing less than 16 kg or more than 24 but less than 46 kg), another product should be used instead of [TB285 trade name].

For **TB that responds to standard medicines**, products containing a combination of all the necessary medicines in one tablet are usually given. If your health care provider needs to use [TB285 trade name] with other medicines given separately, he or she will work out the right dose for you based on your age and weight. Always take the medicine as recommended by your health care provider.

Prevention of tuberculosis

When isoniazid is used to prevent tuberculosis, it can be used alone, as well as with other TB medicines. The dose of [TB285 trade name] depends on whether other medicines are used as well, and on the weight of the person taking the medicine. Your health care provider will prescribe the appropriate medicines and advise you on the right doses to take.

If [TB285 trade name] is used on its own, then the usual dose in people weighing 25 to 65 kg is 1 tablet of [TB285 trade name] daily, but other products containing different amounts of isoniazid may be needed to achieve the right dose if you weigh more or less than this.

Taking pyridoxine with [TB285 trade name]

Your health care provider will often recommend that you also take a supplement containing pyridoxine (vitamin B6). Pyridoxine can help reduce the chance of getting peripheral neuropathy, a side effect affecting the nerves that causes tingling, pricking or numbness, especially of your hands and feet. Taking pyridoxine is especially advisable if you are pregnant or breastfeeding, have HIV infection, malnutrition, alcohol dependence, kidney problems or diabetes. It is also recommended in children and adolescents or if you are taking high doses of isoniazid.

Typical recommended doses of pyridoxine are:

12.5 mg once daily in children aged under 5 years
25 mg once daily in those 5 years and older

Your health care provider may recommend higher doses of pyridoxine if you are at greater risk or symptoms of peripheral neuropathy begin to develop.

If you take more [TB285 trade name] than you should

If you accidentally take too much of [TB285 trade name], contact your health care provider or nearest emergency department for advice. Take the tablet container with you so that you can easily describe what you have taken.

If you forget to take [TB285 trade name]

It is important not to miss a dose of [TB285 trade name]. If you realise you have missed a dose of this medicine:

- if it is *6 or more hours until your next dose is due*, take the missed dose as soon as you can, and then take your next dose at its regular time.
- *if your next dose is due within 6 hours*, do not take the missed dose. Wait and just 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 [TB285 trade name], take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking this medicine.

If you stop taking [TB285 trade name]

Don't stop taking [TB285 trade name] without your health care provider's advice. Talk to your health care provider before you stop taking [TB285 trade name] for any reason, particularly if you are experiencing any side effects or have another illness.

If you have stopped your treatment with [TB285 trade name] for any reason, speak to your health care provider before you start taking [TB285 trade name] again.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. When treating tuberculosis, it is not always possible to distinguish between unwanted effects caused by [TB285 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 tell your health care provider of any change in your health.

If you get any of the following side effects, contact your health care giver as soon as possible:

- yellowing of the skin or whites of the eyes, or urine getting darker and stools paler, tiredness, weakness, malaise, loss of appetite, nausea or vomiting caused by liver problems (hepatitis)
- severe pain in the abdomen and back which can be signs of inflammation of the pancreas
- severe extensive skin damage and blistering, often with flu-like symptoms (toxic epidermal necrolysis or TEN)
- a drug reaction that causes rash, fever, inflammation of internal organs, blood abnormalities and general illness (DRESS syndrome).

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

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, these enzyme increases return to normal within 3 months despite continued treatment. When the values rise above a certain level your health care provider may decide to stop treatment with [TB285 trade name].

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

- inflammation of the liver (hepatitis), which can cause yellowing of the skin or whites of the eyes, or urine getting darker and stools paler, fatigue, weakness
- epileptic fits (seizures)
- inflammation of the brain
- mental disturbances including psychotic reactions such as hallucinations and delusions
- memory problems.
- eye problems such as visual disturbances and eye pain

Rare side effects (*may affect up to 1 in 1 000 people*)

- A drug reaction that causes rash, fever, inflammation of internal organs, haematologic abnormalities and systemic illness (DRESS syndrome)
- Severe extensive skin damage (blistering on the skin and in body openings such as the mouth and nose): toxic epidermal necrolysis (life-threatening reaction with flu-like effects and blistering in the skin, mouth, eyes and genitals)

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 lymph nodes (lymphadenopathy)
 - painful disorder affecting joints, muscles, tendons (rheumatic syndrome)
 - connective tissue disorders such as lupus syndrome which can affect the skin and kidneys (symptoms may include a butterfly-shaped rash over the cheeks and nose, tiredness, a high temperature, feeling or being sick, joint pain and weight loss)
 - fever
- vertigo (spinning sensation and loss of balance)
- elevated mood, personality changes
- inflammation of the lungs (pneumonitis), scarring of the lungs (interstitial lung disease)
- build-up of acid in the body (metabolic acidosis); increased blood levels of glucose; a vitamin B3 deficiency syndrome called pellagra (with symptoms such as dementia, loose stools and skin inflammation); vitamin B6 deficiency (irritability, difficulty sleeping, weak muscles, cracks at the corner of the mouth and weight loss)
- nausea, vomiting, loss of appetite, dry mouth, constipation, abdominal pain
- 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 tiredness, weakness and shortness of breath
- decreased platelet count, possibly resulting in an increased risk of bruising and bleeding
- inflammation of the joints (arthritis)
- muscle weakness, overactive reflexes
- increased size of breasts in men (gynaecomastia)
- loss of hearing and ringing in your ears may occur if you have severe problems with your kidneys
- inflammation of the pancreas, which causes severe pain in the abdomen and back
- a positive test result for antibodies against your body's tissues
- withdrawal symptoms, which may occur after you stop taking [TB285 trade name], include headache, insomnia, excessive dreaming, irritability and nervousness.

Side effects with this medicine are more common in people aged over 35 and in people who break down isoniazid more slowly. The risk of having side effects increases with high doses of [TB285 trade name].

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.

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.

For reporting of adverse events and PV related queries please write to Email: ProductSafety@viatris.com.

5. How to store [TB285 trade name]

Do not store above 30°C. Store in the original container. Protect from light.

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

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

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 [TB285 trade name] contains

- The active ingredient(s) is 300 mg isoniazid.
- The other ingredients are: mannitol, microcrystalline cellulose, croscarmellose sodium, povidone, pregelatinized starch, colloidal anhydrous silica and stearic acid. What
- [TB285 trade name] looks like and contents of the pack

White to off-white, round, biconvex, beveled edge tablet debossed with M on one side and IS1 on the other side.

No score line.

HDPE bottle (with desiccant)

HDPE bottle pack with desiccant comprising of round wide mouth white HDPE bottle with white opaque polypropylene screw cap with aluminium induction sealing liner wad.

Desiccant: Plastic canister with perforation for breathing, containing silica gel (or) a sachet containing activated silica gel. Adsorbent cotton: Well bleached cotton fibre, soft, hair like white filaments.

Pack sizes: 30 tablets and 1000 tablets

HDPE bottle (without desiccant)

HDPE bottle pack comprising of round wide mouth white HDPE bottle with white opaque polypropylene screw cap with aluminium induction sealing liner wad. Adsorbent cotton: Well bleached cotton fibre, soft, hair like white filaments.

Pack sizes: 30 tablets and 1000 tablets

Supplier and Manufacturer

Supplier and Manufacturer

Supplier

Mylan Laboratories Limited
Plot No. 564/A/22
Road No. 92, Jubilee Hills
Hyderabad – 500096, Telangana
India
Email: ProductSafety@viatris.com

Manufacturer

Mylan Laboratories Limited
Plot No. H-12 & H-13
MIDC, Waluj Industrial Area
Aurangabad – 431136
Maharashtra State
India

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

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