

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets*

Read all of this leaflet carefully before you start taking this medicine.

- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

1. What Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets is and what it is used for
2. Before you take Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets
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1. WHAT ETHAMBUTOL HYDROCHLORIDE/ISONIAZID 400MG/150MG TABLETS IS AND WHAT IT IS USED FOR

Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets is indicated for the treatment of tuberculosis (diagnostic categories I and III).

It must be used as the sole antituberculosis medication and only for the continuation phase of therapy (see "Take special care with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets").

2. BEFORE YOU TAKE ETHAMBUTOL HYDROCHLORIDE/ISONIAZID 400MG/150MG TABLETS

Do not take Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets

- if you are hypersensitive (allergic) to ethambutol, isoniazid or any of the other ingredients of Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets (see section 6, What Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets contains).
- if you have an inflammation of the optic nerve (optic neuritis),
- if you have acute liver disease,
- if you have drug induced liver disease,
- if you have experienced liver damage linked to isoniazid before,
- if you have experienced severe side effects of isoniazid, such as drug fever, chills or inflammation of the joints before.

Take special care with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets

Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets must not be combined with any other antituberculosis medicine, since this may increase the risk of liver injury.

If the tuberculosis treatment regimen includes additional antituberculosis medicines, other formulations with different doses of isoniazid and ethambutol than those contained in Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets should be used.

You should promptly report signs or symptoms consistent with liver damage. These include any of the following: unexplained lack of appetite, nausea, vomiting, dark urine, yellowing of the skin and the eye white (jaundice), rash, tingling in the hands and feet, persistent tiredness, weakness lasting longer

* Trade names are not prequalified by WHO. This is under local DRA responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

than 3 days and/or abdominal tenderness, especially in the right upper region of your belly. Your doctor or health care provider will control your liver function regularly.

You may be at special risk for developing hepatitis, if

- you are older than 35 years,
- if you drink alcoholic beverages daily (see “Taking Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets with food and drink”)
- if you have a chronic liver disease,
- if you are a user of injection drugs (e.g. heroine).

If you belong to one of these groups your doctor will closely check your liver function.

You should promptly report any visual impairment, since ethambutol, one of the active agents in Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets may damage your eyes. Your doctor or health care provider will control your visual acuity prior to therapy and at regular intervals during treatment.

Patients not able to report visual changes (such as young children) and patients with visual changes prior to start of therapy with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets will be monitored more closely.

If you have abnormally high levels of uric acid in the blood or symptoms of gout your doctor will monitor you for signs of deterioration when treated with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets.

Tingling in the hands and feet (peripheral neuropathy) is the most common side effect of isoniazid, one of the active agents in Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets (see “Possible side effects”). A certain vitamin, called pyridoxine, should be administered routinely at doses of 10 mg per day during treatment with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets, since it largely reduces the risk of developing neuropathy.

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

Taking other medicines

Please tell your doctor, health care provider or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. These may affect the action of Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets, or Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets may affect their action. Side effects of either medicine may become worse and/or the medicines may become less effective.

You should not take Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets with

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

The active agents in Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets may also interact with the following medicines:

- certain medicines to treat gout (e.g. probenecid),
- medicines to treat epileptic seizures (e.g. phenytoin, carbamazepine, valproic acid)
- 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),
- medicines used prior to surgery (narcotics, e.g. alfentanil, enflurane),
- theophylline (medicine for the treatment of asthma),
- corticosteroids (e.g. prednisolone, medicines for the treatment of inflammations and other diseases, such as asthma or rheumatoid arthritis),
- acetaminophen or paracetamol (pain killers).

Taking Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets with food and drink

Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets should be taken on an empty stomach (at least one hour prior to or two hours after a meal).

Do not drink alcohol while taking Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets. This increases your risk for liver damage.

Pregnancy and breast-feeding

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.

Ethambutol and isoniazid are both excreted into the breast milk of lactating mothers. No negative effects have been reported in breast-fed-infants, whose mothers were receiving ethambutol and isoniazid.

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

Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets may cause visual disturbances, dizziness and other side effects to the nervous system that can impair your ability to drive and use machines.

3. HOW TO TAKE ETHAMBUTOL HYDROCHLORIDE/ISONIAZID 400MG/150MG TABLETS

Always take Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets exactly as your doctor or health care provider told you. You should check with your doctor, health care provider or pharmacist if you are not sure.

The dose of Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets was decided by your doctor based on your body weight.

In patients weighing 40 to <55 kg the dose is 2 tablets administered once daily.

In patients weighing 55 kg or more the dose is 3 tablets administered once daily.

Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets is not indicated for patients weighing < 40 kg as the appropriate dose reduction for the weight of the patient cannot be made.

If your dose of Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets needs to be reduced, for example if you have kidney problems, then your medicine may be changed to ethambutol and isoniazid taken as separate medicines.

Swallow Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets 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).

If you take more Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets than you should

If you have taken too many tablets or if someone accidentally swallows some, you may develop vomiting, gastrointestinal disturbances, fever, headache, dizziness, slurred speech, hallucinations and/or visual disturbances. Immediately contact your doctor, health care provider or the nearest hospital emergency department for further advice.

If you forget to take Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets

If you miss or forget to take a dose, take the missed dose as soon as possible, unless the next regular dose is scheduled within 6 hours.

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

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

If you stop taking Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets

Keep taking the medicine for as long as your doctor has ordered, even if you are feeling better. If you stop the medicine too soon, your infection may not be completely cured.

You should not stop treatment unless your doctor or health care provider tells you to.

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, Ethambutol hydrochloride/Isoniazid 400mg/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 Ethambutol hydrochloride/Isoniazid 400mg/150mg 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.

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

The most important adverse effects of ethambutol and isoniazid are visual disturbances caused by inflammation of the optic nerve, other 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) are sensations of tingling, pricking, or numbness of the skin, especially in the feet and hands (peripheral neuropathy). Also, increases of uric acid levels and liver enzymes as measured in blood samples (see "Take special care with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets") have been reported very frequently. Usually, these 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 doctor may decide to stop treatment with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets.

Commonly (greater than 1 in every 100 patients treated) reported side effects are visual changes due to inflammation of the optic nerve (optic neuritis). The frequency depends on the dose and duration of therapy. Typical initial signs include impairment of colour vision (red-green blindness) and constriction of visual field (central or peripheral scotoma). These changes are often reversible after

discontinuation of treatment with ethambutol. If you notice any visual disturbance, please inform your doctor or health care provider immediately.

Uncommon side effects (greater than 1 in every 1000 patients treated) are inflammation of the liver (hepatitis) epileptic seizures, inflammation of the brain, personality changes and memory impairment. If you notice sign and symptoms suggestive for liver damage, inform your doctor or health care provider immediately (see “Take special care with Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets”).

The following side effects have been reported in patients treated with ethambutol and 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) or life-threatening anaphylactic reactions,
- dizziness, headache, drowsiness,
- confusion, disorientation, hallucination,
- inflammation of the lungs (pneumonitis),
- gout, 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, 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,
Decreased platelet count, possibly resulting 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 doctor, health care provider or pharmacist as soon as possible.

5. HOW TO STORE ETHAMBUTOL HYDROCHLORIDE/ISONIAZID 400MG/150MG TABLETS

Keep out of the reach and sight of children.

Do not store above 30°C.

Store in the original container.

Do not use Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets contains

The active ingredients are ethambutol hydrochloride and isoniazid.

The other ingredients are:

Core tablet: Dicalcium phosphate, gelatin, magnesium stearate, sodium starch glycollate and sorbitol.

Film-coat: Hypromellose, polyethylene glycol, talc, titanium dioxide and Quinoline Yellow aluminium lake.

What Ethambutol hydrochloride/Isoniazid 400mg/150mg tablets looks like and contents of the pack

Yellow coloured, round, biconvex, film-coated tablet, plain on both the sides.
The tablet should not be divided.

The primary packs are blister cards composed of PVC-PVDC film sealed with aluminium foil. Each pack contains 100 (10x10), 392 (14x28) or 672 (24x28) tablets.

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For any information about this medicinal product, please contact the local representative of the supplier: Mr. Tejas Patwari, email : tejas.patwari@cadilapharma.co.in

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