Packaging leaflet: information for the user

Isoniazid Atb 100 mg tablets
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 any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may do harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

In this leaflet:

1. What Isoniazid Atb is and what it is used for

Isoniazid Atb contains isoniazid as active substance that belongs to the group of antimycobacterial drugs, drugs for tuberculosis treatment, hydrazides.
Isoniazid is an antibiotic used in:
- treatment of active pulmonary or extra-pulmonary tuberculosis in combination with other tuberculostatics;
- treatment of symptomatic tuberculosis on primo-infection;
- by way of exception in the treatment of atypical infections with mycobacterial susceptible (sensitivity determined by minimum inhibitory concentration). This treatment is based on a combination of active antibiotics;
- tuberculosis prophylaxis..

2. What you need to know before you take Isoniazid Atb

Do not take Isoniazid Atb
- If you are allergic to isoniazid or any of the other ingredients of the medicine (see Section 6);
- If you have severe hepatic failure.

Warnings and precautions
Talk to your doctor or pharmacist before taking Isoniazid Atb
- If you have liver problems your doctor may reduce the doses.

Before starting the treatment with isoniazid your doctor will recommend an initial testing of hepatic function (transaminase, alkaline phosphatase, and total bilirubin). Hepatic function monitoring will be

carried out weekly in the first month of treatment, and monthly during the next months of treatment. A moderate increase of values (< 3 times normal value) does not require discontinuation of the treatment. In case of increased hepatic transaminases values (5 times higher than normal values), the treatment should be discontinued until the normalizing of the result of liver enzymes, then resume treatment for tuberculosis. Your doctor will individualize the treatment relating to your clinical condition.

Severe and sometimes fatal hepatitis may occur even after many months of treatment. The risk of hepatitis is increased in patients over 35 years of age and: chronic alcohol consumption, pre-existing liver disease, IV drug users and black or Hispanic women. Tell your doctor to monitor the common prodromal symptoms of hepatitis such as fatigue, weakness, malaise, anorexia, nausea or vomiting. If these symptoms appear or if suggestive signs of hepatic damage are detected, isoniazid should be discontinued.

- If you have a severe kidney disease;
- If you have diabetes (characterized by high blood glucose) – because your diabetes may be difficult to control;
- If you have epilepsy or other severe psychiatric diseases;
- If you notice any numbness, unusual tingling or weakness in your hands and feet (peripheral neuropathy) or you are treated with stavudine. Your doctor could ask a neurological investigation and recommend vitamin B6 that reduces the risk of neuropathy;
- Malnourished patients;
- Daily use or in excess of alcohol;
- If your doctor told that you have a disease which slows drug metabolism in your body ("slow acetylator");
- If you are allergic to ethionamide, pyrazinamide, niacin (nicotinic acid) or other related medications you may also be hypersensitive to isoniazid.

Other medicines and Isoniazid Atb

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

- Combination of isoniazid with pyrazinamide can cause an increase of hepatotoxicity. The treatment with isoniazid should be discontinued in case of occurrence of hepatitis. The same effect can occur in case of enzymatic inductors (e.g. rifampicin, barbiturates), acetaminophen or paracetamol.
- It is not recommended the concomitant administration of isoniazid with: carbamazepine and valproate (increase in serum level of carbamazepine accompanied by overdosage signs as inhibition of hepatic metabolism of carbamazepine) or disulfiram (behavioural and coordination disorders); benzodiazepine; stavudine.
- Avoid concomitant use of isoniazid and other neurotoxic medications.
- Isoniazid enhances the effect of phenytoin and inhibits primidone metabolism.
- Salts and aluminium hydroxide reduce gastrointestinal absorption of isoniazid. Take these medicines more than 2 hours before or after isoniazid, if possible.
- Halogenated volatile anaesthetics enhance the hepatotoxic effect of isoniazid due to a large quantity of toxic metabolites of isoniazid. In case of a scheduled surgery isoniazid treatment is discontinued with caution a week before and is continued only after 15 days;
- Glucocorticoids decrease isoniazid serum level. The mechanism invoked is increase of the isoniazid hepatic metabolism and decrease of the glucocorticoids metabolism.
- Isoniazid decreases ketoconazole serum levels. The time interval between the administrations of the two antibiotics must be at least 12 hours. Serum level of ketoconazole should be monitored and dosage increases should be made if necessary.
- Concomitant administration of isoniazid with stavudine increases the risk of peripheral neuropathy by accumulating of the side effects.

- In some patients, concomitant administration of isoniazid with ethionamide may cause maniac outbursts, acute delirium or depression. Also, concomitant administration of ethionamide and isoniazid increased isoniazid serum level for both fast and slow acetylators. In case of extreme necessity pyridoxine will be administered and side effects of isoniazid will be monitored (peripheral neuritis, hepatoxicity, encephalopathy).
- Monitor your INR in case of concurrent administration of isoniazid and anticoagulants (warfarin).

Isoniazid may cause a false positive response to copper sulfate glucose tests; enzymatic glucose tests will be measured for patients taking isoniazid.

Isoniazid Atb with food, drink and alcohol
Ethanol consumption increases the risk of hepatic disorders during the treatment with isoniazid.
Tyramine-containing foods (cheese, red wine etc.) and histamine-containing foods (e.g. tuna, tropical fishes) should be avoided.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
There are no controlled clinical studies regarding the use of isoniazid during pregnancy. If the treatment for tuberculosis is efficient, it should not be changed due to the pregnancy only if the potential benefit justifies the potential risk to the foetus. If necessary, isoniazid administration will be closely monitored during pregnancy and breast-feeding.
Pyridoxine (vitamin B_6) will be administered in pregnant woman in order to avoid neurological side effects in neonate.
Isoniazid passes into breast milk. No negative effects have been reported in breast-fed-infants, whose mothers were receiving isoniazid. Isoniazid will be administered after evaluation of risk to benefit ratio evaluation during breast-feeding.

Driving and using machines
Isoniazid has a moderate influence on the on ability to drive or use machines.
Isoniazid may cause neurological reactions; therefore caution is recommended when use this medicine if these reactions can be associated with a risk.

Isoniazid Atb contains lactose. If your doctor warned you about your intolerance to certain categories of glucides, please ask him before taking any medicine.

3. How to take Isoniazid Atb

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is:
Adults: 5-10 mg isoniazid/kg daily for continuous treatment and 10-15 mg/kg daily mg for intermittent therapy regimens.
The maximum daily dosage of isoniazid is 300 mg in treatment regimen 7/7 and 900 mg in treatment regimen 3/7.
Children: 5-10 mg isoniazid/kg daily and not exceed 300 mg/day.
Children weighing more than 25 kg should be treated according to the recommended adult treatment.

Due to pharmaceutical form isoniazid should not be administered in children under 6 years old than after crushing and dissolution of the tablet in a glass of water; to increase compliance, in water can be added sweetener.

Elderly: low doses are not necessary.
Reduce the dose to 100-200 mg/day in case of chronic liver failure.

Do not exceed 300 mg/day in case of severe renal insufficiency. It will take into account the creatinine clearance:

Creatinine clearance mL / min	Doses	Frequency
10-50	300 mg	every 24 hours
<10	200 mg	every 24 hours

In severe renal failure, dialysis patients, isoniazid will be given at the end of haemodialysis session.
Isoniazid should be administered orally, in a single dose in the morning, 30 minutes before meal.
Generally, new cases of pulmonary or extra-pulmonary tuberculosis involve an initial phase that lasts two months and includes daily administration of isoniazid with rifampicin, ethambutol and pyrazinamide. Initial phase is followed by the continuation phase of 4 months when isoniazid is administered concurrently with rifampicin, 3 days per week.

Isoniazid is used in chemoprophylaxis, administered in monotherapy daily (7/7), 10 mg/kg/day or 200 mg/m^2 body surface area in children, 5 mg/kg daily in adults (maximum 300 mg daily) at least 6 months.

Treatment with Isoniazid Atb should be followed throughout the period recommended by your doctor. Tuberculosis regimen is standardized according to National TB Prevention, Surveillance and Control-2015.

If you take more Isoniazid Atb than you should
Nausea, vomiting, dizziness, blurred vision, hallucinations may occur after ½ -3 hours if you take more isoniazid than you should. It can be installed coma with involuntary contraction of muscles (convulsions) and deficiency of oxygen at the blood and tissue level (anoxia), which can be fatal.
In case of overdose it can occur metabolic acidosis, ketonuria and hyperglycaemia.
Maximum lethal dose is 200 mg/kg.
If such symptoms occur, tell your doctor or go to a hospital emergency department straight away.
Haemodialysis may be efficient.

If you forget to take Isoniazid Atb
If you forgot a dose, take it as soon as you remember it. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for the forgotten tablets.

If you stop taking Isoniazid Atb
Do not discontinue the treatment with Isoniazid Atb unless your doctor will recommend this.
If you have any further questions on the use of this medicine, ask your doctor or your pharmacist.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.
The most common side effects are at the nervous system and liver.
If you experience any of the following side effects contact your doctor as soon as possible:

- **Inflammation of the pancreas, which causes severe pain in the abdomen and back**

(pancreatitis, frequency not known)

- **Severe extensive skin damage (separation of the epidermis and superficial mucous membranes) (toxic epidermal necrolysis, TEN, may affect up to 1 in 1,000 people)**
- **A severe drug reaction that causes rash, fever, inflammation of internal organs, hematologic abnormalities and systemic illness (DRESS syndrome may affect up to 1 in 1,000 people)**
- **Yellowing of the skin or whites of the eyes, or urine getting darker and stools paler, fatigue, weakness, malaise, loss of appetite, nausea or vomiting caused by liver problems (hepatitis, may affect up to 1 in 100 people)**

Other side effects:
- very common: formication and numbness in your hands and feet (peripheral neuropathy). It could be prevented by administration of pyridoxine (vitamin B6);
- uncommon: mental disturbances, toxic psychosis, convulsions, chronic encephalopathy;
- not known: change of serum levels of hepatic enzymes (transaminases); loss of appetite (anorexia), nausea, vomiting, abdominal pains, constipation, ballooning, dry mouth, gastric irritation; decrease in the total number of white and red blood cells (agranulocytosis, anaemia, thrombocytopenia, leukopenia); hypertension; irregular or accelerated heartbeat; **inflammation of blood vessels** (vasculitis); hyperglycaemia, metabolic acidosis, pyridoxine deficiency, pellagra (lack of niacin); confusion, disorientation, hallucinations, dizziness, headache, hyper-reflexes, blurred vision, problems with optic nerve (optic neuritis, atrophy); erythema multiforme, cutaneous eruption (morbilliform, maculopapular, pruritic or exfoliative eruptions), purpura; fever; muscle and joint pains, enlargement of lymph nodes; intractable pain in the shoulder and arm (shoulder-hand syndrome), rheumatic syndrome, Lupus syndrome; urine retention, nephrotoxicity, interstitial nephritis inclusive; gynecomastia.

The frequency of adverse reactions is defined using the following convention:
Very common: may affect more than 1 in 10 people
Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1,000 people
Very rare: may affect up to 1 in 10,000 people
Not known: frequency cannot be estimated from the available data

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system whose details are published on website of National Agency for Medicines and Medical Devices http://www.anm.ro. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Isoniazid Atb

Keep out of the sight and reach of children.

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

Store below 25 °C, in the original package.

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

6. Content of the pack and other information

What Isoniazid Atb contains
- Active substance is isoniazid. Each tablet contains 100 mg of isoniazid.
- Other ingredients: lactose monohydrate, powdered cellulose, sodium starch glycolate, colloidal anhydrous silica, magnesium stearate.

What Isoniazid Atb looks like and contents of the pack
The tablets are white to yellowish white round, flat, glossy tablets.

Folding carton containing 2 PVC/Al blisters of 10 tablets.
Cardboard box containing 150 PVC/Al blisters of 10 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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1 Valea Lupului, 707410 Iaşi, Romania

This leaflet was revised in December 2016.