MARKETING AUTHORISATION NO: 1136/2008/01-02 Annex 1
Leaflet

PACKAGING LEAFLET: INFORMATION FOR THE USER

Isoniazid Atb 300 mg tablets
Isoniazid

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 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 any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. WHAT ISONIAZID ATB 300 mg IS AND WHAT IT IS USED FOR
ISONIAZID ATB 300 mg contains isoniazid as active substance that belongs to the group of medicines used in treatment of tuberculosis. It is an antibiotic used in combination with other drugs for tuberculosis treatment.
- treatment of active pulmonary or extra-pulmonary tuberculosis
- treatment of symptomatic tuberculosis on primo-infection;
- tuberculosis prophylaxix;
- 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;

2. BEFORE YOU TAKE ISONIAZID ATB 300 MG

Do not take ISONIAZID ATB 300 mg
- You are allergic (hypersensitive) to isoniazid or any of the other ingredients of the medicine;
- You have severe hepatic failure or you have a yellow staining of the skin and the whites of the eyes (jaundice).

Take special care with ISONIAZID ATB 300 mg

- In case of hepatic failure your doctor will reduce the doses;

Before starting the treatment with isoniazid your doctor will recommend a 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 biological samples, then resume treatment for tuberculosis.

Your doctor will individualize the treatment relating to your clinical condition.
- If you have a severe kidney disease;
- If you have diabetes (characterized by high blood glucose) – because the glycaemia 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 or feet (peripheral neuropathy). Your doctor could ask a neurological investigation;
- 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");
- In case of children.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines you buy without a prescription.

- Combination of Isoniazid Atb with pyrazinamide can cause an increase of hepatotoxicity. The treatment with Isoniazid Atb should be discontinued in case of occurrence of hepatitis. The same effect can occur in case of enzymatic inductors (e.g. rifampicin, barbiturates);

- It is not recommended the concomitant administration of Isoniazid Atb and:
  1. carbamazepine (increase in serum level of carbamazepine accompanied by overdosage signs as inhibition of hepatic metabolism of carbamazepine)
  2. or disulfiram (behavioural and coordination disorders);

- Isoniazid Atb may enhance the effect of phenytoin and inhibits primidone metabolism;

- Salts and aluminium hydroxide may reduce gastrointestinal absorption of isoniazid. Take Isoniazid Atb at least 2 hours before or after any aluminium containing compounds, 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 (by increasing the isoniazid hepatic metabolism and decreasing the glucocorticoids metabolism).

- Isoniazid Atb may decrease ketoconazole serum levels. The time interval between the administrations of the two antibiotics must be at least 12 hours, if possible. Serum level of ketoconalzole should be well monitored and dosage increases should be made if necessary;

- Concomitant administration of Isoniazid Atb with stavudine may increase the risk of peripheral neuropathy by accumulating of the side effects;

- In some patients, concomitant administration of Isoniazid Atb with ethionamide may cause maniac outbursts, acute delirium or depression.

Taking ISONIAZID ATB 300 mg with food and drink

Ethanol consumption increases the risk of hepatic disorders during the treatment with Isoniazid Atb.

Pregnancy and breast-feeding
Talk to your doctor or pharmacist for advice before taking any 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 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. Breast-feeding is not recommended during the treatment with isoniazid to prevent possible neurological side effects in infant.

Effects on ability to drive and use machines
No specific statement, but unlikely to affect the ability to drive or use machinery. However, in case of the neurological reactions occurrence, caution should be taken.

3. HOW TO TAKE ISONIAZID ATB 300 mg

Always take Isoniazid Atb 300 mg exactly as your doctor has told you, in association with other anti-tuberculosis medications and for the prescribed length of time. You should check with your doctor or pharmacist if you are not sure.
Treatment with Isoniazid Atb should be followed throughout the period recommended by your doctor.
Treatment and prophylaxis of tuberculosis are carried out according to National Tuberculosis Control Programme.
Adults: The recommended dose is 5-10 mg isoniazid / kg daily and 10-15 mg for intermittent therapy regimens.
Maximum dosage (mg) of Isoniazid Atb is 300 mg in treatment regimen 7/7 and 900 mg in treatment regimen 3/7.
Children: The recommended dose is 5-10 mg isoniazid / kg daily at the beginning of treatment, not exceed 300 mg / day.
Elderly: low doses are not necessary.
In case of liver failure it will reduce the dose.
In case of severe renal insufficiency, it is recommended not exceed 300 mg isoniazid daily. 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 Atb will be given at the end of haemodialysis session.
Isoniazid Atb 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 Atb is used in chemoprophylaxis. In prevention, Isoniazid Atb is 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.

If you take more ISONIAZID ATB 300 mg than you should
Nausea, vomiting, dizziness, blurred vision, hallucinations may occur after ½ -3 hours if you take more Isoniazide Atb 300 mg than you should. It can be installed coma with involuntary contraction of

muscles (convulsions) and deficiency of oxygen at the blood and tissue level (hypoxia), which can be fatal.
In case of overdose 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 300 mg
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 300 mg
Do not discontinue the treatment with Isoniazid Atb unless your doctor will recommend this.

If you have any further questions, ask your doctor or your pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Isoniazid Atb can cause side effects, although not everybody gets them.
The frequency of adverse reactions of isoniazid is not defined. The most common side effects are at the nervous system and liver.

- Numbness, formication in your hands or feet (peripheral neuropathy). It could be prevented by administration of pyridoxine (vitamin B6);
- Peripheral Nerve Disorders (neuritis);
- Muscle weakness;
- Hyper-reflexia;
- Euphoria;
- Insomnia;
- Seizures;
- Behavioural disorders: mania, acute delirium or depression may occur;
- Liver inflammation, sometimes acute (hepatitis), with or without yellowing of the skin and eyes (jaundice);
- Hyperbilirubinemia, transaminases;
- Transient rash, red spots on the skin (purpura);
- Gynecomastia (breast enlargement in men);
- Hyperglycemia, metabolic acidosis, pyridoxine deficiency;
- Poor nutrition due to loss of appetite (anorexia), nausea, vomiting, abdominal pain, constipation;
- Decrease in the total number of white and red blood cells (agranulocytosis, anemia, thrombocytopenia);
- Increase in the number of a type of white blood cell (eosinophilia);
- Hypertension;
- Palpitations, tachycardia;
- Inflammation of the blood vessels (vasculitis);
- Blurred vision, decreased visual acuity, optic neuritis and atrophy;
- Fever;
- Painful urination (dysuria);
- Muscle and joint pain;
- Enlargement of lymph nodes;
- Intractable pain in the shoulder and arm (shoulder-hand syndrome);
- Constipation or diarrhoea.

If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE ISONIAZID ATB 300 mg

Keep out of the reach and sight of children.

Do not use Isoniazid Atb 300 mg 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. FURTHER INFORMATION

What ISONIAZID ATB 300 mg contains
- Active substance is isoniazid. Each tablet contains 300 mg of isoniazid.
- Other ingredients: microcrystalline cellulose, sodium starch glycolate, colloidal anhydrous silica, magnesium stearate.

What ISONIAZID ATB 300 mg looks like and contents of the pack
The tablets are white to yellowish white round, flat, glossy tablets with median line on one side.

Outer carton containing 3 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
Antibiotice S.A.
1 Valea Lupului, 707410 Iasi, Romania, EU

If you have any questions about this medicine please contact the local representatives of the Marketing Authorisation Holder.

This leaflet was last approved in May, 2012.