

PATIENT INFORMATION LEAFLET

IBURAMIN ZERO 200 mg/2 mg film-coated tablet

For oral use.

- **Active substance:** Each film coated tablet contains 200 mg ibuprofen and 2 mg chlorpheniramine maleate
- **Excipients:** Microcrystalline cellulose (E460), colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate (obtained from cow milk), magnesium stearate, povidone, polyvinyl alcohol, polyethylene glycol, copovidone, sunset yellow (E110), titanium dioxide (E171), kaolin (E559), sodium lauryl sulfate, pregelatinized starch, talc, corn starch and stearic acid.

Read all of this PATIENT INFORMATION LEAFLET carefully before you start using this medicine because it contains important information for you.

- *Keep this **PATIENT INFORMATION LEAFLET**. You may need to read it again.*
- *If you have any additional questions, please contact your physician or pharmacist.*
- *This medicine has been prescribed personally for you. Do not pass it on to others.*
- *When you go to doctor or hospital while using this medicine, tell your doctor that you are using this medicine.*
- *Please completely follow the instructions in this information leaflet. Do not use higher or lower doses other than what is recommended to you.*

What is in this leaflet:

- 1. What IBURAMIN ZERO and what it is used for?**
- 2. Before you use IBURAMIN ZERO**
- 3. How to use IBURAMIN ZERO**
- 4. Possible side effects**
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1. What IBURAMIN ZERO and what it is used for?

- IBURAMIN ZERO is available in transparent PVC/PVDC/Aluminum folio blisters of 24 film coated tablets. One film coated tablet contains 200 mg ibuprofen and 2 mg chlorpheniramine maleate.
- The tablet is used for the relief of symptoms associated with common cold, flu and other upper respiratory tract infections including fever, headache, runny nose, body aches and pain.

2. Before you use IBURAMIN ZERO

DO NOT USE IBURAMIN ZERO in the following conditions:

Cardiovascular Risks

- Non steroidal anti-inflammatory drugs (NSAIDs) may be associated with increased risk of thrombotic cardiovascular events, myocardial infarction and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

- IBURAMIN ZERO is contraindicated for treatment of peri-operative pain management in the setting of coronary artery by-pass surgery.

Gastrointestinal Risks

- Non steroidal anti-inflammatory drugs (NSAIDs) may be associated with increased risk of serious gastrointestinal adverse events including bleeding, ulceration, gastric or intestinal perforation which may be fatal. These adverse events can occur at any time with or without prior warning symptoms. Elderly patients are at a greater risk for serious gastrointestinal events.

If,

- you are in the last trimester of pregnancy,
- you are hypersensitive (allergic) to ibuprofen, chlorpheniramine or any of the other excipients of this medicine,
- you have previously had allergic reactions such as asthma, nasal inflammation (rhinitis), or hives against ibuprofen, aspirin, and other NSAIDs,
- you have had a previous gastrointestinal bleeding or perforation because of those mentioned medicines,
- you have or previously had diseases such as recurrent gastric-duodenal ulcers, inflammatory bowel diseases (ulcerative colitis, Crohn's disease), gastrointestinal bleeding,
- you have severe hepatic failure,
- you have severe renal failure,
- you have severe heart failure (NYHA class IV),
- you will have or had coronary artery bypass graft surgery (surgery to resolve the blockage of a coronary artery)
- you experience gastrointestinal bleeding or ulceration while using ibuprofen
- you have cerebrovascular (cerebral arteries) bleeding or any other active bleeding,
- You have increased bleeding tendency
- you are using medicines called monoamine oxidase inhibitors used to treat depression or 2 weeks have not yet passed since you stopped taking these medicines

TAKE SPECIAL CARE with IBURAMIN ZERO in the following conditions:

If,

- You have heart rhythm disorders,
- You have epilepsy,
- You have enlarged prostate,
- You have hepatic failure,
- You have increased intraocular pressure
- You have bronchitis, enlarged bronchitis, asthma,
- You have overactive thyroid dysfunction,
- You have serious hypertension (increased blood pressure),

- You have cardiovascular disease,
- You have or previously had asthma; this may cause bronchial spasm.
- You previously had gastric-duodenal ulceration or any other gastrointestinal disease; these conditions may flare up.
- You have kidney disease; monitoring of kidney functions may be required. Risk of kidney dysfunction is increased with the prolonged use of ibuprofen and similar non steroidal anti-inflammatory drugs (NSAIDs), in patients with heart failure and liver failure, with the use of diuretics and ACE inhibitors and in elderly.
- You have a heart disease or high blood pressure; fluid retention in various parts of the body and associated swelling (edema) may occur.
- Prolonged use of ibuprofen and similar drugs at high doses are associated with a small increase in the risk of heart attack (myocardial infarction) and stroke. You have cardiac or vascular diseases, had prior stroke or you think you are at risk of those conditions (e.g. If you have high blood pressure, high cholesterol or diabetes or you smoke) you should consult your doctor or pharmacist about your treatment.
- Prolonged use of ibuprofen and similar non-steroidal anti-inflammatory drugs (NSAIDs) may cause gastrointestinal ulcers, bleeding and perforation even if you have never had such a disease before. The risk of occurrence of this kind of undesirable effects increases in those who have had such a disease before, in elderly, at high doses and with prolonged use.
- If you experience bruising, contusions of unknown origin, consult your doctor.
- Consult your doctor straight away if you experience chills, tremor or sudden increase in fever, fatigue, headache and nausea or neck stiffness; these may be symptoms of a type of inflammation of cerebral cortex (aseptic meningitis).
- You have redness, rash on your skin,

As with other non-steroidal anti-inflammatory drugs (NSAIDs), IBURAMIN ZERO may mask the signs of infection. The administration of the lowest dose effective to relieve the signs of your disease, for the shortest treatment duration will minimize the undesired effects of the drug.

Please consult your doctor even if these warnings apply to you at any time in the past.

Using IBURAMIN ZERO with food and drink

You can take IBURAMIN ZERO on an empty stomach. However, very few people may experience slight indigestion with IBURAMIN ZERO. If such a condition develops, it will help to take the necessary dose with some food or milk. Avoid to drink alcohol while using IBURAMIN ZERO.

Pregnancy

Before using this medicine consult your doctor or pharmacist.

The use of IBURAMIN ZERO should be avoided during pregnancy if possible.

If you notice that you have been pregnant during treatment, consult immediately your doctor or pharmacist.

Breastfeeding

Before using this medicine consult your doctor or pharmacist.

IBURAMIN ZERO is not recommended in breastfeeding women.

Driving and using machinery

Following ibuprofen therapy, the response time of certain patients may be affected. This should be taken into account in situations requiring high attention, such as driving and using machinery. High doses may cause side effects of the central nervous system, such as fatigue and dizziness. This effect may increase with concomitant intake of alcohol.

Important information on some excipients present in IBURAMIN ZERO

This medicinal product contains lactose monohydrate. If you have previously been told by your doctor that you have intolerance to certain sugars, you should consult your doctor before taking this medicinal product.

This medicinal product may cause allergic reactions due to the sunset yellow (E110).

Taking with other medicines

Since interactions have been reported in some patients, you should be careful if you are using any of the following medicines while on IBURAMIN ZERO:

- Aminoglycoside class antibiotics (i.e. Gentamicin, kanamycin, streptomycin);
- ADE inhibitors, beta-blockers and diuretics used to treat high blood pressure,
- Cholestyramine use to treat high cholesterol,
- Sulphonylurea type medicines used to lower the level of blood sugar,
- CYP2C9 inhibitors, a drug group which stops proteins responsible for neutralization of drugs in the liver (i.e voriconazole, fluconazole);
- Drugs preventing blood coagulation (i.e. Warfarin);
- Drugs inhibiting thrombocytes, which provide coagulation (antithrombocyte agents, i.e. aspirin, dipyridamole, clopidogrel) and selective serotonin re-uptake inhibitors used for depression (i.e., fluoxetine, fluvoxamine, paroxetine, sertraline);
- Ginkgo biloba herbal extract;
- Cardiac glycosides used for heart failure (i.e. Digoxin, digitoxin);
- Caution is required when used with captopril, which is a blood pressure medication.
- Quinolone class antibiotics (i.e. ciprofloxacin); seizures (convulsion)
- Other analgesics (other NSAIDs including COX-2 inhibitors i.e. aspirin, naproxen, celecoxib, nimesulide);
- Cortisone group drugs,
- Lithium salts used to treat psychiatric disorders and methotrexate used to treat rheumatic joint diseases and certain forms of cancer);
- Mifepristone (miscarriage drug);
- Tacrolimus and cyclosporine used to prevent the rejection of the organ following transplantation surgeries;
- Ticlopidine used to dilute blood;
- Zidovudine used for the treatment of AIDS (HIV infection);
- Alcohol;
- Classic antihistaminics (with sedative [calming, tranquiliser] effect) used to treat allergic diseases
- Phenytoin containing epilepsy drugs, drugs used to treat anxiety or sleep regulating drugs;
- MAOIs (used to treat psychiatric disorders), drugs lowering blood pressure such as bethanidine, bethanidine, guanethidine, debrisoquine, methyldopa and alpha- and beta-adrenergic blocker drugs

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

3. How to use IBURAMIN ZERO

- **Instructions for proper use and dosage/administration frequency:**

Always take this medicine exactly as described in this leaflet or as your doctor has told you.

Adults and children over 12 years should take 1 or 2 tablets every 4 or 6 hours, without exceeding 6 tablets within 24 hours.

If you are going to undergo any surgical operation and have used this medicine a few days ago, inform your doctor at the beginning of the operation. Unexpected results can be seen in allergy skin tests when using this medicine.

- **Route and method of administration:**

IBURAMIN ZERO is for oral use only.

- **Different age groups:**

Use in children:

Should not be used in children under 12 years old.

In elderly:

IBURAMIN ZERO may increase the risk of gastrointestinal side effects in elderly. Therefore, if it should be used in elderly patients, the smallest effective dose and the shortest duration of treatment should be preferred.

Patients over 65 years of age should be under the supervision of the doctor. The maximum daily dose should not exceed 12 mg of chlorpheniramine.

- **Special populations:**

Kidney/Liver/Heart Failure:

Caution should be exercised in patients with kidney, liver or heart failure because the use of NSAIDs such as IBURAMINE ZERO may result in impaired renal function. In these patients, the dose should be kept as low as possible and renal function should be monitored.

If you have the impression that the effect of IBURAMIN ZERO is too strong or weak, talk with your doctor or pharmacist.

If you use more IBURAMIN ZERO than you should:

If you have used more IBURAMIN ZERO than you should, or if the children have used this medicine by accident, always consult a doctor or nearest hospital for advice and opinion on the risks.

Symptoms may include nausea, abdominal pain, vomiting (bloody lines), headache, ringing in the ears, clouding of consciousness, and uncontrolled eye movements. At high doses, drowsiness, chest pain, palpitation, loss of consciousness, contractions (especially in children), weakness and dizziness, blood in the urine, chills, respiratory problems have been reported.

Sudden (acute) overdose can cause clinical signs of central nervous system stimulation and variable cardiovascular effects. Conservative treatment should be administered in patients with overdose symptoms.

If you used more IBURAMIN ZERO than was prescribed, tell your doctor or pharmacist.

If you forget to use IBURAMIN ZERO

Continue with the next dose at the usual time of intake.

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

Possible effects may occur when you stop taking IBURAMIN ZERO:

It is important that you continue to use IBURAMIN ZERO until your doctor decides to stop your treatment. Do not stop treatment just because you feel better. If you stop IBURAMIN ZERO prematurely, your disease may get worse.

The administration of the lowest dose effective to relieve the signs of your disease, for the shortest treatment duration will minimize the undesired effects of the drug.

Consult your doctor or pharmacist if you have other questions about the use of this medicine.

4. Possible side effects

Like all medicines, IBURAMIN ZERO may cause side effects in patients sensitive to its ingredients.

If any of the following reactions happen, stop taking IBURAMIN ZERO and tell your doctor immediately or contact the casualty department at your nearest hospital:

- Shortness of breath; swelling of your face, lips, tongue, eye lids or throat; severe itching and rash on the skin; palpitations and dizziness resulting from low blood pressure (hypersensitivity – allergy – angioedema - anaphylaxis)
- Wheezing or difficult breathing (asthma attack),
- Decreased blood pressure (hypotension),
- Irregular heart rate, palpitations, chest pain,
- Severe stomach pain (gastric ulcers or pancreatitis)
- Yellowing of the eyes and/or skin (liver dysfunction),
- Blood or dark particles that look like coffee grounds in stool or vomitus (gastrointestinal bleeding),
- Skin bruises, nose and gingival bleeding, increased incidence of infectious diseases, pallor and weakness (bone marrow suppression),
- Severe disease with peeling, swelling, blistering of the skin around the mouth, eyes and genitals and fever (Stevens-Johnson syndrome),
- A disease with blistering and red rash of different sizes in the mouth and other parts of the body (erythema multiforme),
- A serious disease associated with skin blisters filled with liquid and peeling and tissue loss (toxic epidermal necrolysis),
- Sudden loss of muscle strength, loss of sensation, visual disturbances (stroke),
- Severe headache, stiffness of the neck, nausea, vomiting and cloudless of consciousness (aseptic meningitis)
- Seeing or hearing things that are not real (hallucinations)
- A severe skin reaction known as DRESS syndrome may develop. Signs of DRESS are: rash, fever, swelling of lymph nodes and increased eosinophils (a type of white blood cell).

If you experience one of these side effects it means that you are severely allergic to IBURAMIN ZERO. You may need urgent medical attention or to be hospitalized.

Side effects are classified as follows according to their frequency:

Very common: may be seen in at least 1 of 10 patients;

Common: may be seen in less than 1 of 10 patients but in more than 1 of 100 patients

Uncommon: may be seen in less than 1 of 100 patients but in more than 1 of 1,000 patients

Rare: may be seen in less than 1 of 1,000 patients but in more than 1 of 10,000 patients

Very rare: may be seen in less than 1 of 10,000 patients;

Not known: Cannot be estimated from the available data.

Very common:

- Sedation
- Somnolence

Common:

- Headache, dizziness, attention deficit and abnormal coordination
- Blurred vision
- Dyspepsia
- Diarrhea
- Nausea, vomiting, abdominal pain
- Excessive gas in the stomach and the intestines (flatulence)
- Decreased or no bowel movement (constipation)
- Skin rash
- Fatigue

Uncommon:

- Visual impairment
- Duodenal ulcer
- Inflammation of the inner lining of the stomach (gastritis)
- Inflammation of the mouth prominent by small wounds (oral ulceration)
- Gastrointestinal perforation
- Insomnia and anxiety
- Numbness (paresthesia)
- Hearing impairment (decreased, increased hearing)
- Rhinitis (cold, flu)
- Hemolytic anemia (a kind of anemia)
- Respiratory tract reactions such as asthma, worsening of asthma, bronchospasm or difficulty in breathing (dyspnea),
- Hives (urticaria)
- Itching (pruritus)
- Small hemorrhages on the skin and mucosa (purpura)
- Sensitivity to light (photosensitivity)
- Acute kidney disorder
- Reduced excretion of creatinine from the kidneys

Rare:

- Decreased number of white blood cells (leukocyte) (leukopenia)

- Decreased number of cells mediating thrombocyte-blood coagulation (thrombocytopenia)
- Sudden onset, decreased number of white blood cells (agranulocytosis)
- Severe depletion of blood cells (aplastic anemia)
- Ringing in the ears (Tinnitus)
- Dizziness due to a pathology in the inner ear (vertigo)
- Depression
- Inflammation of ophtalmic nerves (optic neuritis)
- Inflammation of ophtalmic nerves due to a toxic substance (toxic optical neuropathy)
- Dry mouth
- Liver damage
- Edema
- Difficulty to urinate (urinary retention)

Very rare:

- Fits
- Hepatic failure

Not known:

- Increased excitability and nightmares
- Tremor
- Thickening of sputum
- Exacerbation of inflammation of the intestine (colitis) and Crohn's disease, a kind of inflammatory bowel disease
- Generalized redness and scaling (exfoliative dermatitis)
- Muscle twitches, muscle weakness

Medicines like IBURAMIN ZERO can cause heart attack (myocardial infarction) or a small increase in the risk of stroke.

Rarely, IBURAMIN ZERO can cause blood disorders and kidney problems. These are all serious side effects. You may need urgent medical attention.

Tell your doctor or pharmacist if you notice any other effects not listed in this leaflet.

Reporting side effects

Please inform your doctor, pharmacist or nurse if you get any side effect whether or not included in this leaflet. In addition, please report the side effect that you are experiencing to Turkish Pharmacovigilance Center (TÜFAM) by clicking to the icon "Reporting Drug Side Effects" at www.tick.gov.tr or call the reporting hotline dialing 0 800 314 00 08. By reporting the side effects, you can help provide more information on the safety of this medicine.

5. How to store IBURAMIN ZERO

Store IBURAMIN ZERO in its original packaging and keep out of the reach and sight of children.

Store at room temperature below 25°C.

Use in compliance with the expiry date.

Use IBURAMIN ZERO before the date of expiry on the label or packaging.

Do not use IBURAMIN ZERO if you notice defects on the product and/or its packaging.

Do not throw away drugs that have expired or are not used! Deliver to the collection system determined by the Ministry of Environment and Urbanism.

Marketing authorization holder:

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