

## PATIENT INFORMATION LEAFLET

### **IBURAMIN ZERO 100 mg/1 mg/5 ml suspension** **For oral use only.**

- **Active substance:** Each spoon (5 ml) suspension contains 100 mg ibuprofen and 1 mg chlorpheniramine maleate.
- **Excipients:** Xanthan gum, hydroxypropyl methylcellulose, glycerin, sorbitol (70%) (E420), sodium benzoate (E211), sucrose, polyoxyl 40 castor oil, citric acid monohydrate, strawberry flavor, masking flavor, ammonium glycyrrhizate, microcrystalline cellulose and sodium carboxymethylcellulose (carmellose sodium), ponso 4R (E124) and deionized water.

**Read all of this leaflet carefully before you start using 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, please ask your doctor or pharmacist.*
- *This medicine has been prescribed for you only. Do not pass it on to others.*
- *If you go to a doctor or hospital during the use of this medicine, inform your doctor about this.*
- *Follow the instructions in this leaflet exactly. Do not use **higher or lower** doses than the dose which was recommended for you.*

#### **What is in this leaflet:**

1. *What IBURAMIN ZERO is and what it is used for?*
2. *What you need to know before you use IBURAMIN ZERO?*
3. *How to use IBURAMIN ZERO?*
4. *Possible side effects*
5. *How to store IBURAMIN ZERO?*

#### **1. What IBURAMIN ZERO is and what it is used for?**

- IBURAMIN ZERO is a suspension containing 100 mg ibuprofen and 1 mg chlorpheniramine maleate in each spoon (5 ml) and presented in amber colored 100 ml-glass bottles (Type III) closed with pilfer-proof high-density polyethylene (HDPE) cap and low density polyethylene seal.
- It is used to eliminate or reduce the symptoms of colds, flu and viral upper respiratory tract infections.

## 2. What you need to know before you use IBURAMIN ZERO?

### **Risks related to Cardiovascular System**

- Non-steroidal anti-inflammatory drugs (NSAIDs) may cause a potentially fatal coagulation (KV thrombotic) event, a heart attack (myocardial infarction) and an increased risk of stroke. 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 should not be used (contraindicated) for treatment of pain before surgery performed to improve obstruction in coronary veins (coronary artery by-pass surgery)

### **Risks Related to Digestive System**

Non-steroidal anti-inflammatory drugs (NSAIDs) cause serious adverse events associated with the gastrointestinal system including bleeding, ulceration and perforation of the stomach or intestines, which can 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.

### **DO NOT use IBURAMIN ZERO**

- Not used in children under 2 years
- If you are in the last trimester of pregnancy
- If you have hypersensitivity to ibuprofen, chlorpheniramine or any of the excipients in the product
- If you have previously showed allergic reactions such as asthma, nasal inflammation (rhinitis), or hives (urticaria) against ibuprofen, aspirin, and other NSAIDs
- If you have had a previous gastrointestinal bleeding or perforation because of the mentioned drugs
- If you have had diseases such as recurrent gastrointestinal ulcers, inflammatory bowel diseases (ulcerative colitis, Crohn's disease), gastrointestinal bleeding or you have had them before repetitively
- If you have severe kidney failure
- If you have severe cardiac failure (NYHA Class IV)
- During the period before or after coronary artery by-pass surgery
- Gastrointestinal bleeding or wounds (ulcerations) occur during ibuprofen use
- If you have cerebrovascular bleeding or other active bleeding or if the tendency to bleeding is increased
- If you are using drugs called as monoamine oxidase inhibitors or if not more than 2 weeks have passed over the treatment you had with those drugs

### **Take special care with IBURAMIN ZERO in the following conditions**

- If you have a rhythm disorder in your heart
- If you have epilepsy (seizures) disease
- If you have enlarged prostate
- If you have liver failure
- If you have high intraocular pressure (glaucoma)
- If you have bronchitis, bronchiectasis, asthma
- If you have overworking thyroid gland

- If you have severe hypertension (high blood pressure)
- If you have cardiovascular disease
- It may cause contraction of the respiratory tract (bronchial spasm) if you are an asthma patient or you had a previous asthma attack
- If you previously had gastrointestinal ulcers or other gastrointestinal diseases, these may flare up,
- If you have kidney disease, the kidney functions should be followed up. The risk of kidney function worsening is increased in people, who take ibuprofen and similar NSAIDs for a long time; who have heart failure and liver disorders; who take drugs increasing urine output (diuretics) and antihypertensive drugs belonging to ACE inhibitor class; and who are elderly,
- If you have heart disease or hypertension (high blood pressure); fluid retention and as a result of it swellings (edema) may be observed in various parts of the body
- When ibuprofen and similar drugs are used for especially at high doses (2400 mg/day), these were detected to be related to a small increase in risk of heart attack (myocardial infarction) or stroke. Treatment should be consulted with the physician or the pharmacist in people who have heart or vascular diseases; have previous stroke or have risks for such conditions (high blood pressure, high cholesterol or diabetes disease or smokers)
- Ibuprofen and similar non-steroidal anti-inflammatory drugs (NSAIDs) are used for a long time period (continuous use), although you have not had such a disease before, ulcers, bleeding and perforations may occur in the gastrointestinal tract. The risk of such undesired effects is increased in subjects who have had such a disease before, in elderly people, at high drug doses, and during long-term treatments
- If you realize purple coloring or bruises without unknown origin in your body, consult your physician
- Immediately consult your physician if there are chill, tremor and sudden increase in fever, fatigue, headache and vomiting or neck stiffness; these may be symptoms of a type of brain membrane inflammation (aseptic meningitis)
- If you have redness and rash on your skin

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

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

#### **IBURAMIN ZERO with food and drink**

It can be used on an empty stomach. However, mild indigestion may occur in very few people. If such a condition develops, it will help to take the required dose with some food or milk. Do not use IBURAMIN ZERO with alcohol.

#### **Pregnancy**

*Consult your doctor or pharmacist before using the medicine.*

Use of IBURAMIN ZERO should be avoided during pregnancy whenever possible.

*Consult your doctor or pharmacist immediately if you recognize that you are pregnant during your treatment.*

#### **Breast-feeding**

*Consult your doctor or pharmacist before using the medicine.*

It is not recommended for administration in breastfeeding women.

### **Driving and using machines**

Time to react to certain stimuli can be affected in some patients receiving Ibuprofen. This should be taken into account in case of drive and use of machines that require high attention. Use of high doses may cause side effects such as fatigue and dizziness in central nervous system. This effect may be increased with concomitant alcohol intake.

### **Important information about some of the excipients of IBURAMIN ZERO**

As it contains sorbitol (70%) (E420) and sucrose, if you have been told by your doctor that you have intolerance to some sugars, consult your doctor before taking IBURAMIN ZERO.

Each dose (5 ml) contains 1.875 g sucrose. This should be considered in patients with diabetes.

It may cause nausea and diarrhea due to Polyoxyl 40 castor oil in its composition.

This medicinal product contains less than 1 mmol (23 mg) of sodium per 5 ml; so it actually does not contain sodium.

It may cause allergic reactions due to ponso 4R (E124) in its composition.

### **Using with other medicines**

Because interactions were reported in some patients, when you are having IBURAMIN ZERO treatment you should be careful if you are receiving any of the drugs listed below:

- Aminoglycoside class antibiotics (i.e. gentamicin, kanamycin, streptomycin)
- Drugs used in high blood pressure treatment, e.g. ADE inhibitors, beta-blockers and diuretics
- Cholestyramine used in the treatment of high cholesterol
- Sulphonylurea group drugs used to reduce the blood sugar level
- CYP2C9 inhibitors (e.g. voriconazole, fluconazole), a group of drugs that stop the proteins that are involved in neutralizing drugs in the liver
- 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)
- Some kind of blood pressure medication, Captopril
- 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 in psychiatric disease treatments) and methotrexat (a drug used in rheumatic joint diseases, and in some cancer types)
- Mifepristone (miscarriage drug)
- Tacrolimus and cyclosporine which are drugs used to prevent your body from rejecting the transplanted organ after organ transplant operations
- Blood-diluting drugs called ticlopidine
- Zidovudine used in the treatment of AIDS (HIV infection)
- Alcohol

- Classical antihistamines used in the treatment of allergic diseases (with sedative [calming, quietening] effect)
- Phenytoin containing epilepsy drugs, in anxiety (dismay, fear) treatment or sleep regulating drugs
- MAOIs (used in treatment of psychiatric diseases), drugs lowering blood pressure such as brenthionium, bethanidine, guanethidine, debrisoquine, methyldopa and alpha and beta-adrenergic blocker drugs

*If you currently have been receiving or have recently received any prescription or nonprescription medicine, please notify your doctor or pharmacist about these.*

### **3. How to use IBURAMIN ZERO?**

- **Instructions for appropriate method and dosage/frequency of administration:**

Absorption is accelerated when IBURAMIN ZERO is taken on an empty stomach, but it is recommended to be taken preferably after meals to minimize gastrointestinal side effects.

Unless otherwise recommended by the doctor, it is used as follows;

5 ml in children aged 2-4

7.5 ml in children aged 4-6 years

10 ml in children aged 6-12 years

If necessary, the dose is repeated every 6-8 hours (3-4 times a day). It should not be used more than 4 doses per day.

Undesirable effects can be minimized by using the lowest effective dose required to control symptoms as soon as possible.

- **Route of administration and method:**

IBURAMIN ZERO is for oral administration.

Shake the bottle well before use.

- **Different age groups:**

#### **Use in children:**

Not used in children under 2 years old.

#### **Use in elderly:**

The frequency of adverse effects that may occur in the elderly digestive system is increased. Thus, if it needs to use for elderly patients, the possible smallest effective dose and the shortest duration of treatment should be preferred.

It should be used under medical supervision in patients older than 65 years of age. The maximum daily dose should not exceed 12 mg chlorpheniramine.

- **Special case of use:**

#### **Kidney/Liver/Heart failure:**

If you have kidney, liver or heart failure, you should be careful because the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as IBURAMIN ZERO may result in impaired renal function. In such cases, the dose should be kept as low as possible and kidney functions should be monitored.

*If you have impression that the effect of IBURAMIN ZERO is very strong or weak, tell a 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 about the measure to be taken and opinion on the risks.

Symptoms may include nausea, abdominal pain, vomiting (bloody lines may be present), 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.

*If you take more IBURAMIN ZERO than you should, tell your doctor or pharmacist.*

**If you forget to use IBURAMIN ZERO**

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

If you have forgotten to take your medicine, take it as soon as you remember. However, if it is time for the next dose, do not take the missed dose.

**If you stop using IBURAMIN ZERO**

It is very important to keep taking IBURAMIN ZERO until your doctor tells you to stop. Do not stop treatment even if you feel better. If you do stop, the symptoms may worsen.

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

If you have any further questions on the use of this medicine, please ask your doctor or pharmacist.

**4. Possible side effects?**

Like all medicines, side effects can occur in people sensitive to the contents of IBURAMIN ZERO.

Side effects were listed by frequency as following:

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.

**If you notice any of the following stop taking IBURAMIN ZERO and IMMEDIATELY inform your doctor or go to the nearest emergency department.**

- 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 abdominal pain (stomach ulcers or pancreatitis)
- Yellowing of the eyes and/or skin (liver dysfunction)

- Any blood or black color that look like coffee grounds in stool or vomit (gastrointestinal bleeding)
- Skin bruising, bleeding of the nose and gums, increased incidence of infectious diseases, pale skin and fatigue (bone marrow suppression)
- A disease on the skin, mouth, eyes and around genitals associated with peeling, swelling and blistering of the skin and fever (Steven-Johnson syndrome)
- A disease with red skin rashes of different sizes or with collection of water in mouth and other areas of the body (erythema multiforme)
- A serious disease associated with skin blisters filled with liquid and peeling and loss of the skin (toxic epidermal necrolysis)
- Sudden loss of muscle strength, loss of sensation, visual disorders (stroke)
- Severe headache, stiffness of the neck, nausea, vomiting and decreased level 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)

These are very serious side effects.

If you have any of them, this means you have serious allergy for IBURAMIN ZERO. You may need emergency medical care or hospitalization.

**If you notice any of the followings, immediately inform your doctor or go to the nearest emergency department:**

**Very common:**

- Nervelessness
- Sleepiness (somnolance)

**Common:**

- Headache, dizziness, lack of attention and abnormal coordination
- Blurred vision
- Digestive problems (dyspepsia)
- Diarrhea
- Nausea, vomiting, abdominal pain
- Excessive floating in stomach and intestines (flatulence)
- Decreased or diminished colon motility (constipation)
- Rash
- Fatigue

**Uncommon:**

- Visual defects
- Wound in duodenum (duodenal ulcer)
- Inflammation of the inner membrane of the stomach (gastritis)
- Mouth inflammation prominent by small wounds (oral ulceration)
- Perforation in the stomach or intestines (gastrointestinal perforation)
- Sleeplessness and anxiety (concern, worry)
- Numbness (paresthesia)
- Hearing disorder (decreased or increased hearing)

- Rhinitis (common cold), influenza
- Hemolytic anemia (a type of anemia)
- Respiratory reactions such as asthma, asthma aggravation, narrowing of the respiratory tract (bronchospasm) or distressed breathing (dyspnea)
- Hives (urticaria)
- Itching (pruritus)
- Small hemorrhages on the skin and mucosa (purpura)
- Sensitivity to light (photosensitivity)
- Sudden kidney failure
- Reduction in renal excretion of creatinine

**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 disorder in the inner ear (vertigo)
- Depression
- Inflammation in the eye nerve (Optic neuritis)
- Inflammation in the eye due to a toxic substance (toxic optic neuropathy)
- Dry mouth
- Damage in the liver
- Edema
- Difficult urination in male patients (urinary retention)

**Very rare:**

- Seizures
- Liver failure

**Unknown:**

- Increased excitability and anxiety
- Tremor
- Thickening of sputum
- Inflammation of colon (colitis) and exacerbation of Crohn's disease, a kind of inflammatory bowel disease
- Common redness and flaking (exfoliative dermatitis)
- Muscular twitching, muscle weakness

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

Rarely IBURAMIN ZERO may cause blood disorders and kidney problems. These are very serious side effects. Emergent medical care may be required.

*If you notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.*



## **5. How to store IBURAMIN ZERO?**

*Keep IBURAMIN ZERO in the original package and out of the reach and sight of children.*

Store at room temperature below 25 °C.

### **Use in accordance with expiry date.**

*Do not use IBURAMIN ZERO after the expiry date which is stated on the package.*

Do not use IBURAMIN ZERO, if you notice any defects in the product/package.

### ***Marketing authorization holder:***

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