

Instructions for medical use of the medicinal product

IBUFENE

100 MG/5 ML, ORAL SUSPENSION

Trade name

IBUFENE, 100 MG/5 ML, ORAL SUSPENSION

International non-proprietary name (INN)

Ibuprofen

Composition

Each 5 ml contains:

active ingredients: Ibuprofen 100 mg

inactive ingredients: propylene glycol, glycerine, methylparaben, propylparaben, sorbitol liquid, polysorbate 80, orange flavour, sucrose, aerosol 200, xanthan, purified water.

Dosage form

Oral pediatric suspension.

White or off-white viscous suspension with characteristic orange odor and bitterly-sweet taste.

Pharmacological group

Nonsteroidal anti-inflammatory drugs (NSAIDs).

ATC code

M01AE01

Pharmacological properties

Pharmacodynamic properties

The mechanism of action of ibuprofen, a propionic acid derivative from the group of non-steroidal anti-inflammatory drugs (NSAIDs), is due to inhibition of prostaglandin synthesis - mediators of pain, inflammation and hyperthermic reaction. Indiscriminately blocks cyclooxygenase 1 (COX-1) and cyclooxygenase 2 (COX-2), due to which it inhibits the synthesis of prostaglandins. In addition, ibuprofen reversibly inhibits platelet aggregation. It has analgesic, antipyretic and anti-inflammatory effects. Analgesic effect is most pronounced in inflammatory pain. The effect of the medicinal product lasts up to 8 hours.

Pharmacokinetic properties

Absorption

High, quickly and almost completely absorbed from the gastrointestinal tract (GIT) (plasma protein binding is 90%). After taking the medicinal product on an empty stomach in adults, ibuprofen is detected in the blood plasma after 15 minutes, the maximum concentration (C_{max}) of ibuprofen in the blood plasma is reached after 60 minutes. Taking the drug with food can increase the time to reach the maximum concentration (T_{Cmax}) to 1-2 hours.

Elimination

The half-life (T_{1/2}) is 2 hours. Slowly penetrates into the joint cavity, lingers in the synovial fluid, creating higher concentrations in it than in the blood plasma. After absorption, about 60% of the pharmacologically inactive R-form is slowly transformed into the active S-form. It is metabolized in the liver. It is excreted by the kidneys (in unchanged form no more than 1%) and, to a lesser extent, with bile.

In limited studies, ibuprofen was found in breast milk in very low concentrations.

Indication

Ibufene suspension is indicated for children from 6 months to 12 years, but for infants 3-6 month only after medical prescription, taking into account baby's weight over 5 kg.

As antipyretic: acute respiratory diseases, flu, paediatric infections, post-vaccination period, and diseases which proceed with high temperature.

As analgesic: mild to moderate pain such as: dentation, headache, toothache, earache, throat ache, traumatic and postoperative pains, neuralgia and migraine.

As anti-inflammatory: juvenile rheumatoid arthritis, osteoarthritis, bursitis, tendovaginitis.

Dosage and administration

Dosage depends on children age and weight (see table below).

Single dose of *Ibufene suspension* varies between 5-10 mg/kg per body weight, maximum daily dose is 30 mg/kg per body weight. *Ibufene suspension* can be given 3-4 times during 24 hours.

The medicine is effective until 8 hours.

Age	Average weight	Single dose	Maximum daily dose
3-6 month		By medical advise	
6 month – 1 year	7-10 kg	2.5 ml (50 mg)	200 mg
1-3 year	10-16 kg	2.5-5 ml (50-100 mg)	300 mg
4-6 year	18-22 kg	7.5 ml (150 mg)	450 mg
7-9 year	24-28 kg	10 ml (200 mg)	600 mg
10-12 year	30-36 kg	15 ml (300 mg)	900 mg

It is not recommended to use *Ibufene suspension* for more than 5 days as analgesic. And for more than 3 days as antipyretic.

Contraindications

- Hypersensitivity to ibuprofen or any of the components of the medicinal product;
- A complete or incomplete combination of bronchial asthma, recurrent nasal and paranasal polyposis, and intolerance to acetylsalicylic acid or other NSAIDs;
- Bleeding or perforation of a gastrointestinal ulcer in the anamnesis caused by the use of NSAIDs;
- Erosive and ulcerative diseases of the gastrointestinal tract (including peptic ulcer of the stomach and duodenum, Crohn's disease, ulcerative colitis) or ulcerative bleeding in the active phase or in the anamnesis (two or more confirmed episodes of peptic ulcer disease or ulcerative bleeding);
- Severe liver failure or liver disease in the active phase;
- Severe renal insufficiency (creatinine clearance < 30 ml/min), confirmed hyperkalemia;
- Decompensated heart failure, the period after coronary artery bypass grafting;
- Cerebrovascular or other bleeding;
- Hemophilia and other blood clotting disorders (including hypocoagulation), hemorrhagic diathesis;
- Pregnancy over 20 weeks;
- Sucrase/isomaltase deficiency, fructose intolerance, glucose-galactose malabsorption;
- Taking other NSAIDs as an analgesic or aspirin at a daily dose above 75 mg;
- Child's body weight up to 5 kg;
- Children under 3 months.

With caution

If there are conditions listed in this section, consult a doctor before using the medicinal product.

Simultaneous administration of other NSAIDs, a history of a single episode of gastric ulcer or ulcerative bleeding of the gastrointestinal tract, gastritis, enteritis, colitis, the presence of *Helicobacter pylori* infection, ulcerative colitis; bronchial asthma or allergic diseases in the acute stage or in the anamnesis - the development of bronchospasm is possible; severe somatic diseases, systemic lupus erythematosus or mixed connective tissue disease (Sharpe syndrome) – increased risk of aseptic meningitis; chickenpox; renal failure, including dehydration (creatinine clearance 30-60 ml/min), fluid retention and edema, liver failure, arterial hypertension and/or heart failure, cerebrovascular diseases, dyslipidemia/hyperlipidemia, diabetes mellitus, peripheral arterial disease, blood diseases of unknown etiology (leukopenia, anemia); concomitant administration of other medicinal product that may increase the risk of ulcers or bleeding, in particular, oral glucocorticosteroids (including prednisolone), anticoagulants (including warfarin), selective serotonin reuptake inhibitors (including citalopram, fluoxetine, paroxetine, sertraline) or antiplatelet agents (including acetylsalicylic acid, clopidogrel); pregnancy less than 20 weeks, breastfeeding period, old age.

Pregnancy and lactation

Pregnancy

NSAIDs should not be used in women starting from the 20th week of pregnancy due to the possible development of oligohydramnios and/or kidney pathology in newborns (neonatal renal dysfunction).

Lactation

There is evidence that ibuprofen in small amounts can enter breast milk without any negative consequences for the health of an infant.

Fertility

No information available.

Interaction with other medicinal products and other forms of interaction

Concomitant use of ibuprofen with the following medications should be avoided:

1. Acetylsalicylic acid: with the exception of low doses of acetylsalicylic acid (no more than 75 mg per day) prescribed by a doctor, since combined use may increase the risk of adverse reactions. When used simultaneously, ibuprofen reduces the anti-inflammatory and antiplatelet effect of acetylsalicylic acid (an increase in the incidence of acute coronary insufficiency is possible in patients receiving low doses of acetylsalicylic acid as an antiplatelet agent after starting to take ibuprofen).
2. Other NSAIDs including cyclooxygenase-2 selective inhibitors: avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects.

Ibuprofen should be used with caution in combination with:

3. Anticoagulants and thrombolytic drugs: NSAIDs may enhance the effect of anticoagulants, particularly warfarin and thrombolytic product.
4. Antihypertensive agents (ACE inhibitors and angiotensin II antagonists) and diuretics: NSAIDs may reduce the effectiveness of drugs in these groups. Diuretics and ACE inhibitors may increase the nephrotoxicity of NSAIDs.
5. Glucocorticosteroids: increased risk of gastrointestinal ulceration and gastrointestinal bleeding.
6. Antiplatelet agents and selective serotonin reuptake inhibitors: increased risk of gastrointestinal bleeding.
7. Cardiac glycosides: concomitant administration of NSAIDs and cardiac glycosides may lead to worsening of heart failure, decreased glomerular filtration rate and increased plasma concentrations of cardiac glycosides.
8. Lithium preparations: there is evidence of the possibility of an increase in the concentration of lithium in the blood plasma during the use of NSAIDs.
9. Methotrexate: there is evidence that plasma methotrexate concentrations may increase with the use of NSAIDs.
10. Cyclosporine: increased risk of nephrotoxicity with concomitant administration of NSAIDs and cyclosporine.

11. Mifepristone: NSAIDs should not be started earlier than 8-12 days after taking mifepristone, as NSAIDs may reduce the effectiveness of mifepristone.
12. Tacrolimus: when NSAIDs and tacrolimus are co-administered, the risk of nephrotoxicity may increase.
13. Zidovudine: concomitant use of NSAIDs and zidovudine may result in increased hematotoxicity. There is evidence of an increased risk of hemarthrosis and hematomas in HIV-positive patients with hemophilia who received concomitant treatment with zidovudine and ibuprofen.
14. Quinolone antibiotics: patients receiving concomitant treatment with NSAIDs and quinolone antibiotics may have an increased risk of seizures.

Special instructions

It is recommended to take the drug for the shortest possible course and in the minimum effective dose necessary to eliminate symptoms.

During long-term treatment, it is necessary to monitor the peripheral blood picture and the functional state of the liver and kidneys. If symptoms of gastropathy appear, careful monitoring is indicated, including esophagogastroduodenoscopy, a complete blood count (determination of hemoglobin), and a stool test for occult blood. If it is necessary to determine 17-ketosteroids, the medicinal product should be discontinued 48 hours before the study. During the treatment period, it is not recommended to take ethanol.

The medicinal product does not contain dyes.

Patients with renal impairment should consult a physician before using the medicinal product, as there is a risk of deterioration in renal function. Patients with hypertension, including a history of hypertension and/or chronic heart failure, should consult a doctor before using the medicinal product, since the drug may cause fluid retention, increased blood pressure and edema.

The use of NSAIDs in patients with chickenpox may be associated with an increased risk of developing severe purulent complications of infectious and inflammatory diseases of the skin and subcutaneous fat (for example, necrotizing fasciitis). In this regard, it is recommended to avoid using the medicinal product in case of chickenpox.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported rarely in association with the use of NSAIDs. Patients are thought to be most susceptible to developing these reactions early in therapy; onset of the reaction in the vast majority of cases occurs within the first month of treatment.

The use of NSAIDs containing ibuprofen may cause severe skin reactions such as acute generalized exanthematous pustulosis (AGEP). Ibuprofen should be discontinued at the first appearance of signs and symptoms of serious skin reactions such as skin rash, mucous membrane lesions, or any other signs of hypersensitivity.

The use of NSAIDs containing ibuprofen may mask the symptoms of an infectious disease, which may lead to a delay in the initiation of appropriate treatment and thereby complicate the course of the disease. If *Ibufene suspension* for children is used for fever or pain relief due to infection, it is recommended to monitor

the infectious disease. In a hospital setting, the patient should seek medical attention if symptoms persist or worsen.

In patients with bronchial asthma or an allergic disease in the acute stage, as well as in patients with a history of bronchial asthma/allergic disease, the medicinal product may provoke bronchospasm. Concomitant use of ibuprofen and other NSAIDs, including (selective COX-2 inhibitors) should be avoided.

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg daily) is associated with an increased risk of myocardial infarction.

There is a risk of renal impairment in dehydrated children.

NSAIDs should be used with caution in patients with gastrointestinal diseases (ulcerative colitis, Crohn's disease), as taking this medicinal product may lead to an exacerbation of these conditions.

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with NSAIDs at any time during treatment, with or without warning symptoms, with or without a history of serious gastrointestinal disease. The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated by bleeding or perforation, and in the elderly. These patients should be started on the lowest available dose of the medicinal product.

Patients with a history of gastrointestinal toxicity, particularly elderly patients, should report any unusual gastrointestinal symptoms (especially gastrointestinal bleeding), particularly in the early stages of treatment. If gastrointestinal bleeding or ulceration occurs in patients receiving ibuprofen, treatment should be discontinued.

The medicinal product contains Glycerol, which may cause headache, upset stomach and diarrhea.

The medicinal product contains Methylparaben and Propylparaben, which may cause allergic reactions (including delayed).

The medicinal product contains Sorbitol, and if you have an intolerance to some sugars, consult your doctor before taking this medicinal product.

The medicinal product contains Sucrose (each 5 ml contains 1750 mg), and if you have an intolerance to some sugars, consult your doctor before taking this medicinal product.

Effects on ability to drive and use machines

Patients who experience dizziness, drowsiness, confusion, or visual disturbances while taking ibuprofen should avoid driving or operating machinery.

Undesirable effects

The risk of adverse effects can be minimized if the medicinal product is taken in a short course, at the minimum effective dose necessary to eliminate symptoms.

Adverse effects are predominantly dose-dependent.

The following adverse effects have been reported with short-term use of ibuprofen at doses not exceeding 1200 mg/day.

Other adverse effects may occur when treating chronic conditions and with long-term use.

The frequency of adverse effects was assessed based on the following criteria: very common ($\geq 1/10$), common ($\geq 1/100$ and $<1/10$), uncommon ($\geq 1/1000$ and $<1/100$), rare ($\geq 1/10,000$ and $<1/1000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data).

<i>System/Organ/Class</i>	<i>Frequency of occurrence</i>	<i>Undesirable effects</i>
<i>Blood and Lymphatic System Disorders</i>	<i>very rare ($< 1/10,000$)</i>	haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia and agranulocytosis) The first symptoms of such disorders are fever, sore throat, superficial ulcers on the oral mucosa, flu-like symptoms, severe weakness, unexplained bleeding and bruising
<i>Immune System Disorders</i>	<i>uncommon ($\geq 1/1000$ and $<1/100$)</i>	hypersensitivity reactions - non-specific allergic reactions (itching, urticaria)
	<i>very rare ($< 1/10,000$)</i>	severe hypersensitivity reactions, including swelling of the face, tongue and larynx, dyspnea, tachycardia, hypotension (anaphylaxis, angioedema or severe anaphylactic shock), exfoliative and bullous dermatoses
	<i>not known</i>	airway hyperreactivity including asthma, bronchospasm or dyspnea, medicinal product hypersensitivity syndrome, acute generalized exanthematous pustulosis (AGEP)
<i>Skin and Subcutaneous Tissue Disorders</i>	<i>uncommon ($\geq 1/1000$ and $<1/100$)</i>	various forms of skin rashes
	<i>very rare ($< 1/10,000$)</i>	exfoliative and bullous dermatoses, including toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme
	<i>not known</i>	medicinal product reaction with eosinophilia and systemic symptoms (medicinal product hypersensitivity syndrome - DRESS), acute generalized exanthematous pustulosis (AGEP), photosensitivity reactions
<i>Gastrointestinal Disorders</i>	<i>uncommon ($\geq 1/1000$ and $<1/100$)</i>	abdominal pain, nausea, dyspepsia
	<i>Rare ($\geq 1/10,000$ and $<1/1000$)</i>	diarrhea, flatulence, constipation, vomiting
	<i>very rare ($< 1/10,000$)</i>	peptic ulcer, perforation or gastrointestinal bleeding, melena, hematemesis, ulcerative stomatitis, gastritis
	<i>not known</i>	exacerbation of ulcerative colitis and Crohn's disease
<i>Liver and Urinary Disorders</i>	<i>very rare ($< 1/10,000$)</i>	liver dysfunction
<i>Renal and Urinary Disorders</i>	<i>very rare ($< 1/10,000$)</i>	acute renal failure (compensated and decompensated), especially with prolonged use, in combination with an increase in the concentration of urea in the blood plasma and the appearance of edema, papillary necrosis
<i>Nervous System Disorders</i>	<i>uncommon ($\geq 1/1000$ and $<1/100$)</i>	headache
	<i>very rare ($< 1/10,000$)</i>	aseptic meningitis (isolated cases of symptoms of aseptic meningitis such as stiff neck, headache, nausea, vomiting, fever and disorientation have been observed during treatment with ibuprofen in patients with autoimmune diseases (systemic lupus erythematosus and mixed connective tissue disease))
<i>Cardiovascular disorders</i>	<i>not known</i>	heart failure, peripheral edema, with prolonged use increased risk of thrombotic complications (eg myocardial infarction or stroke), increased blood pressure
<i>Respiratory, thoracic and mediastinal disorders</i>	<i>not known</i>	bronchial asthma, bronchospasm, dyspnea
<i>Laboratory indicators</i>	hematocrit or hemoglobin (may decrease)	
	bleeding time (may increase)	

	plasma glucose concentration (may decrease)
	creatinine clearance (may decrease)
	plasma creatinine concentration (may increase)
	activity of "liver" transaminases (may increase)

Overdose

In children, overdose symptoms may occur after taking a dose exceeding 400 mg/kg body weight.

In adults, the dose-dependent effect of overdose is less pronounced.

The half-life of the in overdose is 1.5-3 hours.

Symptoms

Symptoms may include nausea, vomiting, epigastric pain or, less commonly, diarrhea, tinnitus, headache and gastrointestinal bleeding.

In more severe cases, manifestations from the central nervous system are observed: drowsiness, rarely - agitation, convulsions, disorientation, coma. In cases of severe poisoning, metabolic acidosis and an increase in prothrombin time, renal failure, liver tissue damage, decreased blood pressure, respiratory depression and cyanosis may develop. In patients with bronchial asthma, an exacerbation of this disease is possible.

Management

Treatment should be symptomatic, with mandatory maintenance of airway patency, ECG and vital signs monitoring until the patient's condition is normalized. Oral administration of activated charcoal or gastric lavage within 1 hour after taking a potentially toxic dose of ibuprofen is recommended. If ibuprofen has already been absorbed, alkaline drinks may be prescribed to eliminate the acidic derivative of ibuprofen by the kidneys, and forced diuresis. Frequent or prolonged convulsions should be stopped by intravenous diazepam or lorazepam. If bronchial asthma worsens, bronchodilators are recommended.

Nature and contents of container

Glass bottle of 100 ml with measuring cup.

Special precautions for storage

Store below 25°C.

Keep out of reach of children.

Shelf life

3 years.

Use within 6 months after first opening.

Legal status

OTC medicine.

Manufacturer and marketing authorization holder

«Medical Horizon» Ltd

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