

**SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET**

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ibuprofen Viatris 200 mg oral suspension in sachet

Ibuprofen Viatris 400 mg oral suspension in sachet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet (10 ml) contains 200 mg ibuprofen.

Each sachet (10 ml) contains 400 mg ibuprofen.

Excipient(s) with known effect

Each sachet (10 ml) contains 2500 mg of maltitol (E 965), 20 mg of sodium benzoate (E 211), 14 mg ethanol, 48 mg of propylene glycol and 17°mg of sodium.

Each sachet (10 ml) contains 5000 mg of maltitol (E 965), 10 mg of sodium benzoate (E 211), 0.0017 mg benzyl alcohol and 58°mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension in sachet.

White or almost white, viscous orange flavoured oral suspension.

White, viscous, strawberry flavoured oral suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<Invented name> is indicated for the short term symptomatic relief of mild to moderate pain and/or fever in adult and children above 6 years old (>20 kg).

4.2 Posology and method of administration

Posology

The treatment should start with the lowest dose anticipated to be effective, which can subsequently be adjusted, depending on the therapeutic response and any undesirable effects (see section 4.4).

Adults and adolescents older than 12 years (≥ 40kg)

The ibuprofen dose depends on the patient's age and body weight. The maximum single daily dose for adults and adolescents should not exceed 400 mg of ibuprofen. More than 400 mg at a time does not give a better analgesic effect.

A total dose should not exceed 1,200 mg ibuprofen in any 24-hour period.

Initial dose, 200 mg or 400 mg ibuprofen. If necessary additional doses of 1 or 2 equivalents (200 mg to 400 mg ibuprofen) can be taken up to 3-4 times a day with an interval of 4 to 6 hours.

If in children and adolescents this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

Body weight	200 mg oral suspension in sachet	400 mg oral suspension in sachet	Frequency	Maximum daily dose
≥ 40kg (Adolescents, adults and the elderly)	1 or 2 sachets (200 mg or 400 mg)	1 sachet (400 mg)	Up to 3 or 4 times daily depending on the single dose	1200 mg ibuprofen

Paediatric population

Children 6-12 years (-20 kg-39 kg)

The maximum total daily dose of ibuprofen is 30 mg per kg of body weight, divided into 3 to 4 single doses with dosing intervals of 6 to 8 hours. The maximum recommended daily dose should not be exceeded.

Age (body weight)	200 mg oral suspension in sachet Single dose	Frequency	Maximum daily dose
6 to 7 years (20-30 kg)	1 sachet (200 mg)	Up to 3 times a day	30 mg per kg of body weight
8 to 12 years (>30 kg)	1 sachet (200 mg)	Up to 4 times a day	30 mg per kg of body weight

<Invented name> 200 mg is not indicated for children under 6 years of age (< 20 kg).

For young children, more suitable formulations are available.

Elderly

No special dose modifications are necessary unless renal or hepatic function is impaired in which case dosage should be assessed individually. Caution should be taken with dosage in this group.

Renal impairment

No dose reduction is required in patients with mild to moderate impairment to renal function (patients with severe renal insufficiency, see section 4.3).

Hepatic impairment

No dose reduction is required in patients with mild to moderate impairment to hepatic function (patients with severe hepatic dysfunction, see section 4.3)

Method of administration

For oral use. The sachet should be mixed before taking by pressing the top and bottom of the sachet with your fingers several times. The contents of the sachet cannot be divided between doses, and the entire contents of the sachet should be used. In order to achieve a faster onset of action, the dose may be taken on an empty stomach. It is recommended that patients with sensitive stomachs take ibuprofen with food.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Ibuprofen should not be given to patients who have experienced asthma, urticaria or allergic-type reactions after taking acetylsalicylic acid or other NSAIDs.
- Severe heart failure (NYHA IV).
- Severe liver failure.
- Severe renal failure (glomerular filtration below 30 mL/min).
- Conditions involving an increased tendency or active bleeding.

- History of gastrointestinal bleeding or perforation related to previous NSAID therapy.
- Active gastric or duodenal ulcer or a history of recurrent gastrointestinal ulcer/bleeding (two or more clear episodes of demonstrable ulceration or bleeding).
- During the third trimester of pregnancy.

4.4 Special warnings and precautions for use

General

Undesirable effects may be minimized using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2 and GI and cardiovascular risks below).

On prolonged use of any painkillers, headache may occur that must not be treated with increased doses of the medicinal product.

Through concomitant consumption of alcohol, active substance-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

Elderly

Elderly patients have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal.

Gastrointestinal Bleeding, ulceration and perforation

NSAIDs should be given with care to patients with a history of peptic ulceration and other gastrointestinal disease since their conditions may be exacerbated (see section 4.3).

Gastrointestinal bleeding, ulceration or perforation has been reported with all NSAIDs at any time during treatment. These adverse events can be fatal and may occur with or without warning symptoms or a previous history of serious gastrointestinal events.

The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing ibuprofen doses in patients with a history of ulcers, particularly if complicated with haemorrhage or perforation, and in the elderly. These patients should commence treatment on the lowest dose available.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, as well as patients requiring concomitant low dose acetylsalicylic acid/aspirin, or for other drugs likely to increase gastrointestinal risk (see section 4.5).

The concomitant administration of ibuprofen and other NSAIDs, including cyclooxygenase-2 (Cox-2) selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding (see section 4.5).

Patients with a history of gastrointestinal disease, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding) in the initial stages of treatment.

Caution should be exercised in patients receiving concomitant medication which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin re-uptake inhibitors or antiplatelet drugs such as acetylsalicylic acid/aspirin (see section 4.5).

If gastrointestinal bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn.

Respiratory disorders

Caution is required if ibuprofen is administered to patients suffering from, or with a previous history of, bronchial asthma, chronic rhinitis or allergic diseases since ibuprofen has been reported to cause bronchospasm, urticaria or angioedema in such patients.

Allergic reactions

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed rarely. At the first signs of hypersensitivity reaction after taking/administering ibuprofen therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Caution is required in patients who have had hypersensitivity or allergic reactions to other substances, as they could be at an increased risk of hypersensitivity reactions occurring with ibuprofen.

Caution is required in patients who suffer from hay fever, nasal polyps or chronic obstructive respiratory disorders as an increased risk exists for them of allergic reactions occurring. These may present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticaria.

Cardiac, renal and hepatic impairment

Caution is required in patients with renal, hepatic or cardiac impairment since the use of NSAIDs may result in deterioration of renal function. The habitual concomitant intake of similar painkillers further increases this risk. For patients with renal, hepatic or cardiac impairment, use the lowest effective dose, for the shortest possible duration (see section 4.3).

400 mg sachets: See also section "Information related to the excipients (benzyl alcohol)".

Cardiovascular and cerebrovascular effects

Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/ day) 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/ day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Cases of Kounis syndrome have been reported in patients treated with <Invented name>. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month. If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate).

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Ibuprofen in case of varicella.

Masking of symptoms of underlying infections

<Invented name> can mask symptoms of infection, which may lead to delayed initiation of

appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When <Invented name> is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Renal effects

Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration. There is a risk of renal impairment especially in dehydrated children adolescents and the elderly.

As with other NSAIDs, long-term administration of ibuprofen has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may cause renal failure. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, ACE inhibitors and the elderly. Discontinuation of NSAIDs therapy is usually followed by recovery to the pre-treatment state.

Haematological effects

Ibuprofen, like other NSAIDs, can inhibit platelet aggregation and prolong bleeding time in normal subjects.

Aseptic meningitis

Aseptic meningitis has been observed on rare occasions in patients on ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

Fertility

There is some evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment (see section 4.6).

Information related to the excipients

200 mg:

Ibuprofen 200 mg contains:

- maltitol (E 965). Patients with rare hereditary problems of fructose intolerance should not take this medicine.
- 20 mg benzoate salt (E211) in each sachet which is equivalent to 2 mg/ml.
- 17 mg sodium per 10 ml sachet, equivalent to 1% of the WHO recommended maximum daily intake of sodium of 2 g for an adult.
- The orange flavouring contains 14 mg of alcohol (ethanol), in each 10 ml sachet. The amount in each sachet of this medicine is equivalent to less than 1 ml of beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.
- 48 mg propylene glycol in each sachet which is equivalent to 4.8 mg/ ml.

400 mg:

Ibuprofen 400 mg contains:

- maltitol (E 965) Patients with rare hereditary problems of fructose intolerance should not take this medicine.
- 10 mg benzoate salt (E 211) in each sachet which is equivalent to 1 mg/ml.
- 58 mg sodium per sachet, equivalent to 3% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
- The strawberry flavouring contains 0.0017 mg benzyl alcohol in each 10 ml sachet. Benzyl alcohol may cause allergic reactions. Due to the risk of accumulation and toxicity (metabolic

acidosis) associated with high volumes of benzyl alcohol, caution should be used in pregnant, breast-feeding patients or patients with liver or kidney disease. (see “Cardiac, renal and hepatic impairment” above and section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken in patients treated with any of the following drugs as interactions have been reported in some patients.

Other NSAIDs including cyclooxygenase-2 selective inhibitors

Concomitant use with other NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided due to the potential for additive effects (see section 4.4).

Cardiac glycosides

NSAIDs may exacerbate heart failure, reduce glomerular filtration rate and increase plasma levels of cardiac glycosides.

Corticosteroids

Increased risk of gastrointestinal ulceration or bleeding with NSAIDs.

Anticoagulants

NSAIDs may enhance the effects of anticoagulants, such as warfarin.

Antiplatelet-agents and selective serotonin-reuptake inhibitors (SSRIs) (e.g. clopidogrel and ticlopidine)

Increased risk of gastrointestinal bleeding with NSAIDs

Acetylsalicylic acid

As with other products containing NSAIDs, concomitant administration of ibuprofen and acetylsalicylic acid/aspirin is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid/aspirin on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Lithium

NSAIDs may decrease elimination of lithium.

Anti-hypertensive, beta-blockers and diuretics

NSAIDs may diminish the effect of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor, beta-blocker or angiotensin-II antagonist and agents that inhibit cyclooxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Methotrexate

NSAIDs may inhibit the tubular secretion of methotrexate and reduce clearance of methotrexate.

Cyclosporine

Increased risk of nephrotoxicity with NSAIDs.

Tacrolimus

Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine

Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthrosis and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Quinolone antibiotics

Animal data indicate that NSAID's can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAID's and quinolones may have an increased risk of developing convulsions.

CYP2C9 inhibitors

Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S (+)-ibuprofen exposure by approximately 80 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

Sulfonylureas

NSAIDs may potentiate the effects of sulfonylurea medications. There have been rare reports of hypoglycaemia in patients on sulfonylurea medications receiving ibuprofen.

Cholestyramine

The concomitant administration of ibuprofen and cholestyramine may reduce the absorption of ibuprofen in the gastrointestinal tract. However, the clinical significance is unknown.

Aminoglycosides

NSAIDs may decrease the excretion of aminoglycosides.

Herbal extracts

Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.

Mifepristone

A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of NSAIDs including acetylsalicylic acid. Limited evidence suggests that coadministration of NSAIDs on the day of prostaglandin administration does not adversely influence the effects of mifepristone or the prostaglandin on cervical ripening or uterine contractility and does not reduce the clinical efficacy of medicinal termination of pregnancy.

4.6 Fertility, pregnancy and lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy. In animals, the administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation losses and embryo/fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

From the 20th week of pregnancy onward, ibuprofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following

treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first or second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to ibuprofen for several days from gestational week 20 onward. Ibuprofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

400 mg sachets: Ibuprofen Mylan 400 mg oral suspension in sachet also contains benzyl alcohol and due to the risk of accumulation and toxicity (metabolic acidosis) associated with high volumes of benzyl alcohol, caution should be used in pregnant women. See also section 4.4 “Information related to the excipients (benzyl alcohol)”.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the fetus to the following:

- Cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension)
- Renal dysfunction, which may progress to renal failure with oligohydramnios (see above).

At the end of pregnancy, prostaglandin synthesis inhibitors may expose the mother and the neonate to the following:

- Possible prolongation of bleeding time
- Inhibition of uterine contractions, which may result in delayed or prolonged labor.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy.

Breastfeeding

200 mg sachets: Ibuprofen is excreted in breast milk, but with therapeutic doses during short term treatment the risk for influence on infant seems unlikely. If, however, longer treatment is prescribed, early weaning should be considered.

400 mg sachets: Ibuprofen is excreted in breast milk, but with therapeutic doses during short term treatment the risk for influence on infant seems unlikely. However, Ibuprofen Mylan 400 mg oral suspension in sachet contains benzyl alcohol and due to the risk of accumulation and toxicity (metabolic acidosis) associated with high volumes of benzyl alcohol, caution should be used in breastfeeding women (see sections 4.4 “Information related to the excipients (benzyl alcohol)”). If, however, longer treatment is prescribed, early weaning should be considered.

Fertility

The use of ibuprofen may impair fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered (see section 4.4).

4.7 Effects on ability to drive and use machines

Following treatment with ibuprofen, the reaction time of patients may be affected. This should be taken into account where increased vigilance is required, e.g. when driving a car or operating machinery. This applies to a greater extent in combination with alcohol. Undesirable effects such as dizziness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The following adverse reactions possibly related to ibuprofen are displayed by MedDRA frequency convention and system organ classification. Frequency groupings are classified according to the subsequent conventions: very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), Uncommon ($\geq 1/1,000$ to $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1,000$), Very rare ($< 1/10,000$) and Not known (cannot be estimated from the available data).

System organ class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Rhinitis
	Rare	Meningitis aseptic (see section 4.4)
Blood and lymphatic system disorders	Rare	Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia (first signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising)
Immune system disorders	Uncommon	Hypersensitivity
	Rare	Anaphylactic reaction (symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock)
Psychiatric disorders	Uncommon	Insomnia, anxiety
	Rare	Depression, confusional state
Nervous system disorders	Common	Headache, dizziness
	Uncommon	Paraesthesia, somnolence
	Rare	Optic neuritis
Eye disorders	Uncommon	Visual impairment
	Rare	Toxic optic neuropathy
Ear and labyrinth disorders	Uncommon	Hearing impaired, tinnitus, vertigo
Respiratory, thoracic and mediastinal disorders	Uncommon	Asthma, bronchospasm, dyspnoea
Gastrointestinal disorders	Common	Dyspepsia, diarrhoea, nausea, vomiting, abdominal pain, flatulence, constipation, melena, hematemesis, gastrointestinal haemorrhage
	Uncommon	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation
	Very rare	Pancreatitis
	Not known	Exacerbation of colitis and Crohn's disease
Hepatobiliary disorders	Uncommon	Hepatitis, jaundice, hepatic function abnormal
	Very rare	Hepatic failure
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria, pruritus, purpura, angioedema, photosensitivity reaction
	Very rare	Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis)

	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute generalised exanthematous pustulosis (AGEP), Fixed drug eruption
Renal and urinary disorders	Uncommon	Nephrotoxicity in various forms, e.g. tubulointerstitial nephritis, nephrotic syndrome and renal failure
General disorders and administration site conditions	Common	Fatigue
	Rare	Oedema
Cardiac disorders	Very rare	Cardiac failure, myocardial infarction (also see section 4.4)
	Not known	Kounis syndrome
Vascular disorders	Very rare	Hypertension

The pattern of adverse events reported for ibuprofen is similar to that for other NSAIDs.

Gastrointestinal disorders

The most commonly observed adverse events are gastrointestinal in nature. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melena, haematemesis, ulcerative stomatitis, gastrointestinal haemorrhage and exacerbation of colitis and Crohn's disease (see section 4.3) have been reported following ibuprofen administration. Less frequently, gastritis, duodenal ulcer and gastric ulcer and gastrointestinal perforation have been observed.

A transient sensation of burning in the mouth or throat may occur with ibuprofen suspension or ibuprofen granules

Immune system disorders

Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, very rarely, erythema multiforme, bullous dermatoses (including Stevens-Johnson syndrome and toxic epidermal necrolysis).

Infections and infestations

Exacerbation of skin infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDs has been described. If signs of an infection occur or get worse during use of Ibuprofen the patient is therefore recommended to go to a doctor without delay.

Skin and subcutaneous tissue disorders

In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections and infestations" and section 4.4).

Cardiac and vascular disorders

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400mg/ day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via **the national reporting system** listed in [Appendix V](#).

4.9 Overdose

Toxicity

Signs and symptoms of toxicity have generally not been observed at doses below 100 mg/kg in children or adults. However, supportive care may be needed in some cases. Children have been observed to manifest signs and symptoms of toxicity after ingestion of 400 mg/kg or greater. In serious poisoning metabolic acidosis may occur.

Symptoms

Most patients who have ingested significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours.

The most frequently reported symptoms of overdose include nausea, vomiting, abdominal pain, lethargy and drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnea and depression of the CNS and respiratory system have also been rarely reported. Cardiovascular toxicity, including hypotension, bradycardia and tachycardia, has been reported. In cases of significant overdose, renal failure and liver damage are possible. Prolonged use at higher than recommended doses or overdose may result in renal tubular acidosis and hypokalaemia. Large overdoses are generally well tolerated when no other drugs are being taken.

Treatment

There is no specific antidote for ibuprofen overdose. Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. If necessary, serum electrolyte balance should be corrected. For the most current information, contact the local poison control centre.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, nonsteroidal; propionic acid derivatives, ATC code: M01AE01

Ibuprofen is a propionic acid derivative nonsteroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory and anti-pyretic effects. The drug's therapeutic effects are thought to result from its inhibitory effect on the enzyme cyclooxygenase, which results in a marked reduction in prostaglandin synthesis. These properties provide symptomatic relief of inflammation, pain and fever.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid/aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid/aspirin cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Ibuprofen is a racemic mixture of [+]S- and [-]R-enantiomers.

Absorption

Ibuprofen is rapidly absorbed from the gastrointestinal tract with a bioavailability of 80-90%. Peak serum concentrations occur one to two hours after administration of immediate release formulations. Studies including a standard meal show that food does not markedly affect total bioavailability.

Distribution

Ibuprofen is extensively bound to plasma proteins (99%). Ibuprofen has a small volume of distribution being about 0.12-0.2 L/kg in adults.

Biotransformation

Ibuprofen is rapidly metabolized in the liver through cytochrome P450, preferentially CYP2C9, to two primary inactive metabolites, 2-hydroxyibuprofen and 3-carboxyibuprofen. Following oral ingestion of the drug, slightly less than 90% of an oral dose of ibuprofen can be accounted for in the urine as oxidative metabolites and their glucuronic conjugates. Very little ibuprofen is excreted unchanged in the urine.

Elimination

Excretion by the kidney is both rapid and complete. The elimination half-life of immediate release formulations is approximately two hours. The excretion of ibuprofen is virtually complete 24 hours after the last dose.

Special populations

Elderly

Given that no renal impairment exists, there are only small, clinically insignificant differences in the pharmacokinetic profile and urinary excretion between young and elderly.

Paediatric population

The systemic exposure of ibuprofen following weight adjusted therapeutic dosage (5 mg/kg to 10 mg/kg bodyweight) in children aged 1 year or over, appears similar to that in adults.

Children 3 months to 2.5 years appeared to have a higher volume of distribution (L/kg) and clearance (L/kg/h) of ibuprofen than did children >2.5 to 12 years of age.

Renal impairment

For patients with mild renal impairment, increased plasma level of (S)-ibuprofen, higher AUC values for (S)-ibuprofen and increased enantiomeric AUC (S/R) ratios as compared with healthy controls have been reported. In end-stage renal disease patients receiving dialysis the mean free fraction of ibuprofen was about 3% compared with about 1% in healthy volunteers. Severe impairment of renal function may result in accumulation of ibuprofen metabolites. The significance of this effect is unknown. The metabolites can be removed by haemodialysis (see sections 4.2, 4.3 and 4.4).

Hepatic impairment

Alcoholic liver disease with mild to moderate hepatic impairment did not result in substantially altered pharmacokinetic parameters.

In cirrhotic patients with moderate hepatic impairment (Child Pugh's score 6-10) treated with racemic ibuprofen an average 2-fold prolongation of the half-life was observed and the enantiomeric AUC ratio (S/R) was significantly lower compared to healthy controls suggesting an impairment of metabolic inversion of (R)-ibuprofen to the active (S)-enantiomer (see sections 4.2).

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol

Maltitol liquid E965

Xanthan gum

Citric acid

Sodium citrate

Sodium benzoate E211
Sodium saccharin
Purified water

200 mg only:

Microcrystalline cellulose
Polysorbate 80
Orange flavour containing propylene glycol and ethanol

400 mg only:

Sodium chloride
Hypromellose
Strawberry flavour containing benzyl alcohol
Thaumatococcus E957

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

200 mg:

Carton containing 20 and 40 PET/Alu/PE/PET/PE sachets of 10 ml.

400 mg:

Carton containing 10 and 20 PET/Alu/PE/PET/PE sachets of 10 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2026-01-02

[To be completed nationally]