SUMMARY OF PRODUCT CHARACTERISTICS
IFEN – 200 TABLETS (Ibuprofen Tablets 200 mg)
IFEN – 400 TABLETS (Ibuprofen Tablets 400 mg)

1. NAME OF THE MEDICINAL PRODUCT

IFEN – 200 TABLETS (Ibuprofen Tablets 200 mg)
IFEN – 400 TABLETS (Ibuprofen Tablets 400 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Ibuprofen
IFEN – 200 TABLETS: Each sugar coated tablet contains Ibuprofen BP 200 mg.
IFEN – 400 TABLETS: Each sugar coated tablet contains Ibuprofen BP 400 mg.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sugar coated tablet.
IFEN – 200 TABLETS are reddish pink, circular, biconvex, sugar coated tablets, plain on both sides.
IFEN – 400 TABLETS are reddish pink, circular, biconvex, sugar coated tablets, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ibuprofen is indicated for its analgesic and anti-inflammatory effects in the treatment of rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease), ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies.

In the treatment of non-articular rheumatic conditions, ibuprofen is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain; ibuprofen can also be used in soft tissue injuries such as sprains and strains.

Ibuprofen is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain and for the symptomatic relief of headache including migraine headache.

4.2 Posology and Method of Administration

Posology

For oral administration and short-term use only.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

Adults

200 mg – 400 mg, up to three times a day as required.

Leave at least four hours between doses of 200 mg and six hours between doses of 400 mg and do not take more than 1200 mg in any 24-hour period.

If this medicinal product is required for more than 3 days in the case of fever, or for more than 4 days for the treatment of pain, or if the symptoms do not improve or worsen, a doctor should be consulted.

Adolescents ≥ 40 kg (12 years of age and above)

200 mg – 400 mg, up to three times a day as required.

Leave at least four hours between doses of 200 mg and six hours between doses of 400 mg and do not take more than 1200 mg in any 24-hour period.

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

It is recommended that patients with a sensitive stomach take Ibuprofen Sugar Coated Tablets with food.

Special populations

Paediatric population: Not recommended for adolescents weighing under 40 kg or children under 12 years of age.

Elderly population: The elderly are at increased risk of serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for gastrointestinal bleeding during NSAID therapy. If renal or hepatic function is impaired, dosage should be assessed individually.

Renal impairment: Caution should be taken with ibuprofen dosage in patients with renal impairment. The dosage should be assessed individually. The dose should be kept as low as possible and renal function should be monitored (see sections 4.3 and 4.4).

Hepatic impairment: Caution should be taken with dosage in patients with hepatic impairment. The dosage should be assessed individually and the dose should be kept as low as possible (see section 4.3).

Method of administration

Ibuprofen tablets should be swallowed whole with a glass of water. They should be taken with or after food; patients with a sensitive stomach should take ibuprofen tablets with food. Do not break, crush or chew the tablets. Never change the dose of the medicine without talking to the doctor first. Continue to take the tablets for as long as the doctor recommends.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients who have previously shown hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) associated with

the intake of acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs (NSAIDs).

- Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- History of gastrointestinal bleeding or perforation related to previous NSAID therapy.
- Severe hepatic failure, severe renal failure or severe heart failure (NYHA Class IV) (see section 4.4).
- Patients with cerebrovascular or other active bleeding.
- Patients with blood coagulation disorders.
- Patients with unclarified blood-formulation disturbances.
- Patients with severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).
- Last trimester of pregnancy (see section 4.6).

4.4 Special Warnings and Precautions for Use

Caution is required in patients with certain conditions, which may be made worse:

- Congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria).
- Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).
- Directly after major surgery.
- In patients who react allergically to other substances, as an increased risk of hypersensitivity reactions occurring also exists for them on use of Ibuprofen Sugar Coated Tablets.
- 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 be present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticaria.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see gastrointestinal and cardiovascular risks below).

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

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

Respiratory

Bronchospasm may be precipitated in patients suffering from, or with a previous history of, bronchial asthma or allergic disease.

Other NSAIDs

The use of Ibuprofen Sugar Coated Tablets with concomitant NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided (see section 4.5).

SLE and mixed connective tissue disease

Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).

Renal

Hypertension and/or cardiac impairment, as renal function may deteriorate and/or fluid retention occur. Renal impairment, as renal function may further deteriorate (see sections 4.3 and 4.8).

As with other NSAIDs, long-term administration of ibuprofen has resulted in renal papillary necrosis and other pathologic changes in the kidney. 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 an NSAID may cause a dose-dependent reduction in prostaglandin formation and, in the second place, in renal blood flow, which may cause kidney failure. Those who are at greatest risk of this are patients with renal impairment, heart failure, hepatic dysfunction, the elderly and patients on diuretics or ACE inhibitors.

There is a risk of renal impairment in dehydrated adolescents.

Impaired female fertility

There is limited 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.

Gastrointestinal safety

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease), as these conditions may be exacerbated (see section 4.8).

Gastrointestinal bleeding, ulceration and perforation: Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, 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 NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest possible dose available.

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

Patients with a history of gastrointestinal toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding), particularly in the initial stages of treatment. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid (see section 4.5).

When gastrointestinal bleeding or ulceration occurs in patients receiving Ibuprofen Sugar Coated Tablets, the treatment should be withdrawn.

Skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Ibuprofen Sugar Coated Tablets should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue 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 Sugar Coated Tablets in case of varicella.

Cardiovascular and cerebrovascular effects

Caution (discussion with a doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure, as fluid retention, hypertension 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 ischaemic 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, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Information about some of the ingredients in this medicine

Contains lactose: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Contains sucrose: Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. If a patient has been told by their doctor that they have an intolerance to some sugars, they should contact their doctor before taking this medicinal product.

Sodium methyl parahydroxybenzoate and sodium propyl parahydroxybenzoate: This medicine contains sodium methyl parahydroxybenzoate and sodium propyl parahydroxybenzoate, which may cause allergic reactions (possibly delayed).

Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Other notes

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of a hypersensitivity reaction after taking/administering Ibuprofen Sugar Coated Tablets, therapy must be stopped. Medically required measures, in line with symptoms, must be initiated by specialist personnel. In prolonged administration of Ibuprofen Sugar Coated Tablets, regular checking of the liver values, the kidney function as well as of the blood count is required.

Ibuprofen, the active substance of Ibuprofen Sugar Coated Tablets, may temporarily inhibit the blood platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.

Ibuprofen, as any other NSAID, may mask symptoms of an underlying infectious disease.

In general terms, the habitual intake of painkillers, particularly in combination of several pain relieving active substances, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased under physical strain associated with loss of salt and dehydration. Therefore it should be avoided.

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.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Ibuprofen (like other NSAIDs) should be avoided in combination with:

Low dose acetylsalicylic acid (aspirin): Results of experimental investigation indicate an attenuation of the thrombocyte aggregation-inhibiting effect of acetylsalicylic acid on concomitant administration of ibuprofen. This interaction could reduce the desired protective cardiovascular effect of acetylsalicylic acid. Ibuprofen should therefore only be used with particular caution in patients who are receiving acetylsalicylic acid to inhibit thrombocyte aggregation.

Other NSAIDs including salicylates >100 mg/day: The concomitant administration of several NSAIDs may increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect; the concomitant use of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

The following combinations with ibuprofen should be avoided:

The dicumarol group: NSAIDs may increase the effect of anticoagulants such as warfarin. Experimental studies show that ibuprofen reinforces the effects of warfarin on bleeding time. NSAIDs and the dicumarol group are metabolised by the same enzyme, CYP2C9.

Anti-platelet agents: NSAIDs should not be combined with antiplatelet agents such as ticlopidine due to the additive inhibition of the platelet function (see below).

Methotrexate: NSAIDs inhibit the tubular secretion of methotrexate and some metabolic interaction with reduced clearance of methotrexate may also occur as a result. Accordingly, in high-dose treatment with methotrexate one should always avoid prescribing NSAIDs (see below).

Acetylsalicylic acid: Concomitant administration of ibuprofen and acetylsalicylic acid 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 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).

Cardiac glycosides: NSAIDs can exacerbate heart failure, reduce glomerular filtration and increase plasma cardiac glycoside (e.g. digoxin) levels.

Mifepristone: A decrease of the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of non-steroidal anti-inflammatory drugs (NSAIDs) including acetylsalicylic acid. Limited evidence suggests that co-administration 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 medical termination of pregnancy.

Sulphonylureas: There are rare reports of hypoglycaemia in patients on sulphonylurea medications receiving ibuprofen.

Zidovudine: There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

The following combinations with ibuprofen may require dose adjustment:

NSAIDs can reduce the effect of diuretics and other antihypertensive agents.

NSAIDs may reduce the excretion of aminoglycosides. In children, care should be taken during concomitant treatment with ibuprofen and aminoglycosides.

Lithium: Ibuprofen reduces the renal clearance of lithium, as a result of which serum lithium levels may rise. The combination should be avoided unless frequent checks of serum lithium can be carried out and a possible reduction in the dose of lithium made.

ACE inhibitors and angiotensin-II antagonists: There is an increased risk of acute renal failure, usually reversible, in patients with renal impairment (e.g. dehydrated and/or elderly patients) when treatment with ACE inhibitors or angiotensin-II antagonists is given at the same time as NSAIDs, including selective cyclooxygenase-2 inhibitors. The combination should therefore be given with care to patients with renal impairment, especially elderly patients. Patients should be adequately hydrated and a check of renal function should be considered after the initiation of combination treatment and at regular intervals during treatment (see section 4.4).

Beta-blockers: NSAIDs counteract the antihypertensive effect of beta-adrenoceptor blocking drugs.

Selective serotonin re-uptake inhibitors (SSRIs): SSRIs and NSAIDs each entail an increased risk of bleeding, e.g. from the gastrointestinal tract. This risk is increased by combination therapy. The mechanism may possibly be linked to reduced uptake of serotonin in the platelets (see section 4.4).

Cyclosporine: The concomitant administration of NSAIDs and cyclosporine is thought to be capable of increasing the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney. Accordingly, in the event of combination treatment, renal function must be monitored closely.

Captopril: Experimental studies indicate that ibuprofen counteracts the effect of captopril on sodium excretion.

Colestyramine: The concomitant administration of ibuprofen and colestyramine retards and reduces (by 25%) the absorption of ibuprofen. These drugs should be given at an interval of at least 2 hours.

Thiazides, thiazide-related preparations and loop diuretics: NSAIDs can counteract the diuretic effect of furosemide and bumetanide, possibly through inhibition of prostaglandin synthesis. They can also counteract the antihypertensive effect of thiazides.

Tacrolimus: Concomitant administration of NSAIDs and tacrolimus is thought to be capable of increasing the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney. Accordingly, in the event of combination treatment, renal function should be monitored closely.

Methotrexate: The risk of a potential interaction between an NSAID and methotrexate should also be taken into account in connection with low-dose treatment with methotrexate, especially in patients with renal impairment. Whenever combination treatment is given, renal function should be monitored. Caution should be exercised if both an NSAID and methotrexate are given within

24 hours, as the plasma levels of methotrexate can increase, resulting in increased toxicity (see above).

Corticosteroids: Concomitant treatment gives rise to an increased risk of gastrointestinal ulceration or bleeding.

Antiplatelet drugs: Increased risk of gastrointestinal bleeding (see above).

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs 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 80–100% 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.

Interaction studies have only been performed on adults.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of cardiovascular malformation was increased from less than 1% up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

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 and second trimester of pregnancy, the dose should be kept as low and the duration of treatment as short as possible.

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

The foetus to:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydramnios.

The mother and the neonate, at the end of pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contraction resulting in delayed or prolonged labour.

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

Breast-feeding / lactation

Ibuprofen and its metabolites can pass in low concentrations into the breast milk. No harmful effects to infants are known to date, so for short-term treatment with the recommended dose for pain and fever, interruption of breast-feeding would generally not be necessary.

Fertility

Impaired female fertility: There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

4.7 Effects on Ability to Drive and Use Machines

As central nervous undesirable effects such as tiredness and dizziness may occur on use of Ibuprofen Sugar Coated Tablets at high dosage, the ability to react and the ability to take part actively in road traffic and to operate machines may be impaired in isolated cases. This applies to a greater extent in combination with alcohol.

4.8 Undesirable Effects

Summary of the safety profile

The most commonly observed adverse reactions are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastritis has been observed.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. 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) (see section 4.4).

Tabulated summary of adverse reactions

For the frequency of occurrence of side effects, the following phrases are used: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (≤1/10,000); and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The list of the following undesirable effects comprises all undesirable effects that have become known under treatment with ibuprofen, also those under high dose long-term therapy in rheumatism patients. The stated frequencies, which extend beyond very rare reports, refer to the short-term use of daily doses up to a maximum of 1200 mg ibuprofen for oral dosage forms and a maximum of 1800 mg for suppositories. With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary interindividually.

Infections and infestations

Uncommon: Rhinitis.

Very rare: Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs. If signs of an infection occur or get worse during use of Ibuprofen Sugar Coated Tablets, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for anti-infective/antibiotic therapy. The symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousness clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective tissue disease) appear to be predisposed.

Blood and lymphatic system disorders

Uncommon: Leucopenia, thrombocytopenia, agranulocytosis, aplastic anaemia and haemolytic anaemia. First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising. In such cases the patient should be advised to discontinue the medicine immediately, to avoid any self-medication with analgesics or antipyretics and to consult a physician. The blood count should be checked regularly in long-term therapy.

Very rare: Pancytopenia.

Immune system disorders

Uncommon: Hypersensitivity reactions with skin rashes and pruritus, as well as asthma attacks (possibly with drop in blood pressure), aggravated asthma, bronchospasm, dyspnoea. The patient is to be instructed to inform a doctor at once and no longer to take Ibuprofen Sugar Coated Tablets in this case.

Rare: Anaphylactic reactions.

Very rare: Severe general hypersensitivity reactions. Symptoms could include facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (angioedema or severe shock). If one of these symptoms occurs, which can happen even on first use, the immediate assistance of a doctor is required.

Psychiatric disorders

Uncommon: Insomnia, anxiety.

Rare: Confusional state.

Very rare: Psychotic reaction, depression.

Nervous system disorders

Common: Headache, dizziness.

Uncommon: Paraesthesia, somnolence, sleeplessness, agitation, irritability or tiredness.

Rare: Optic neuritis.

Eye disorders

Uncommon: Visual impairment.

Rare: Toxic optic neuropathy.

Ear and labyrinth disorders

Uncommon: Hearing impairment.

Rare: Tinnitus, vertigo.

Cardiac disorders

Very rare: Palpitations, cardiac failure, myocardial infarction.

Vascular disorders

Very rare: Arterial hypertension, vasculitis.

Respiratory, thoracic and mediastinal disorders

Uncommon: Asthma, bronchospasm, dyspnoea.

Gastrointestinal disorders

Common: Gastrointestinal complaints such as dyspepsia, pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastrointestinal blood losses that may cause anaemia in exceptional cases.

Uncommon: Gastrointestinal ulcers, potentially with bleeding and perforation; ulcerative stomatitis, gastritis.

Very rare: Oesophagitis, pancreatitis, formation of intestinal diaphragm-like structures. The patient is to be instructed to withdraw the medicinal product and to go to a doctor immediately if severe pain in the upper abdomen or melaena or haematemesis occurs.

Not known: Colitis and Crohn's disease.

Hepatobiliary disorders

Uncommon: Hepatitis, jaundice, hepatic function abnormal.

Rare: Liver injury.

Very rare: Hepatic damage, hepatic failure.

Skin and subcutaneous tissue disorders

Common: Rash.

Uncommon: Urticaria, pruritus, purpura, angioedema, photosensitivity reaction.

Very rare: Severe forms of skin reactions such as bullous reactions, including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis, can occur. Alopecia. In exceptional cases, severe skin infections and soft tissue complications may occur during a varicella infection (see also "Infections and infestations").

Not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).

Renal and urinary disorders

Uncommon: Tubulointerstitial nephritis, nephrotic syndrome and renal failure.

Rare: Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood may also occur rarely.

Very rare: Formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency; nephritic syndrome; interstitial nephritis that may be accompanied by acute renal insufficiency. Renal function should therefore be checked regularly.

General disorders and administration site conditions

Common: Fatigue.

Rare: Oedema.

Reporting of suspected adverse reactions

Health care professionals are asked to report any suspected adverse reactions via the https://pv.pharmacyboardkenya.org

4.9 Overdose

In adolescents and adults the dose response effect is not clear cut in overdose. The half-life in overdose is 1.5–3 hours.

Symptoms: Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain or, more rarely, diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Management/treatment: Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam

or lorazepam. Give bronchodilators for asthma. Good urine output should be ensured. Renal and liver function should be closely monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, propionic acid derivatives. **ATC code:** M01A E01

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen reduces inflammatory-related pain, swellings and fever.

Furthermore, ibuprofen reversibly inhibits ADP- and collagen-induced platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid 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 cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic Properties

On oral application, ibuprofen is partly absorbed in the stomach and then completely in the small intestine. Following hepatic metabolism (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90%), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8–3.5 hours; plasma-protein binding is about 99%. Peak plasma levels following oral administration of a normal-release pharmaceutical form (tablet) when taken with food are reached after 1–2 hours.

5.3 Preclinical Safety Data

The subchronic and chronic toxicity of ibuprofen in animal experiments shows up mainly in the form of lesions and ulcerations in the gastrointestinal tract. In vitro and in vivo studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice, no evidence of carcinogenic effects of ibuprofen was found. Ibuprofen led to an inhibition of ovulation in rabbits as well as disturbances of implantation in various animal species (rabbit, rat and mouse).

Experimental studies in rats and rabbits have demonstrated that ibuprofen crosses the placenta. For maternally toxic doses, an increased incidence of malformations (ventricular septal defects) was observed in the progeny of rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

For IFEN – 200 and IFEN – 400 tablets:

Starch (maize), dibasic calcium phosphate, sodium starch glycolate, gelatin, sodium methylparaben, sodium propylparaben, purified talc, magnesium stearate, croscarmellose sodium, sodium lauryl sulphate, Aerosil-200 (colloidal silicon dioxide), calcium carbonate, sucrose, colour erythrosine, white beeswax and carnauba wax.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months.

6.4 Special Precautions for Storage

Store below 30 °C. Protect from light and moisture. Store in the original packing. Keep the container tightly closed.

Keep all medicines out of the reach of children.

6.5 Nature and Contents of Container

Packing of IFEN – 200 TABLETS: Aluminium-PVC blister pack and white plastic jar packing. Blister pack: 10 x 10 tablets. Jar packing: 1000 tablets.

Packing of IFEN – 400 TABLETS: Aluminium-PVC blister pack and white plastic jar packing. Blister pack: 10 x 10 tablets. Jar packing: 500 tablets.

6.6 Special Precautions for Disposal and Other Handling

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

IFEN – 200 TABLETS: 15297/R1

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

IFEN – 200 TABLETS: Date of first authorisation: 2026 September 02

10. DATE OF REVISION OF THE TEXT

2026 September 02