SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen 200 mg Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200mg Ibuprofen.

Excipients with known effect: 123mg lactose monohydrate and 75mg sucrose per coated tablet.

For the full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Coated tablet

White, capsule-shaped, biconvex, coated tablets with no markings.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For short term symptomatic treatment of mild to moderate pain such as headache, dysmenorrhea (period pain), dental pain, and fever and pain in the common cold.

4.2 Posology and method of administration

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:
200mg – 400mg, up to three times a day as required.
Leave at least four hours between doses of 200mg and six hours between doses of 400mg and do not take more than 1200mg 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 day 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):
200mg – 400mg, up to three times a day as required.
Leave at least four hours between doses of 200mg and six hours between doses of 400mg and do not take more than 1200mg 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 200 mg Coated Tablets with food.

Special patient groups

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 GI 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 section 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).

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 NSAIDs therapy.

Severe hepatic failure, severe renal failure or severe heart failure (NYHA Class IV) (see section 4.4 Special Warnings and Precautions for Use).

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 Pregnancy and lactation).

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 increase risk of hypersensitivity reactions occurring also exists for them on use of Ibuprofen 200 mg Coated Tablets.
- In patients who suffer from hayfever, nasal polyps or chronic obstructive respiratory disorders as an increased risk exists for them of allergic reaction 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 GI and cardiovascular risks below).

The elderly have an increased frequency of adverse reactions to NSAID's 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 200 mg Coated Tablets with concomitant NSAIDs including cyclooxengenase-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 Undesirable effects).

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 section 4.3 Contraindications and section 4.8 Undesirable effects).

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-dependant 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 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 if gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8)

Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events.

The risk of GI 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. misoporstol 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 200 mg 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 200 mg 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 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 200 mg Coated Tablets in case of varicella.

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, 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.

Other notes:
Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after taking/administering Ibuprofen 200 mg Coated Tablets therapy must be stopped. Medically required measures, in line with symptoms, much be initiated by specialist personnel.

In prolonged administration of Ibuprofen 200 mg 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 200 mg 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 on combination of several pain-relieving active substance, 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 sale 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 Interactions with other medicinal products and other forms of interaction

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

Low dose Acetyl salicylic 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 ASA. Ibuprofen should therefore only be used with particular caution in patients who are receiving ASA to inhibit throbocyte aggregation.

Other NSAIDs including salicylates >100mg/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 agent: 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. 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 NSAID's can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increase 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 approximate 80-100% has been shown. Reduction of the ibuprofen does should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high dose ibuprofen is administered with either voriconazole and fluconazole.

Interaction studies have only been performed on adults.

4.6 Fertility, pregnancy and lactation

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.

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal 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 prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss 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

During the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a women attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

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

- the fetus to:

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

- the mother and the neonate, at the end of pregnancy, to:
  - possible prolongation of bleeding time, an anti-aggregating effect with 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.

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.

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 200 mg 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

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)
Not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The most commonly observed adverse reactions are gastrointestinal in nature, Peptic ulcers, perforation or GI 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).

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.
Vary rare: Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of nonsteroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the nonsteroidal anti-inflammatory drugs.

If signs of an infection occur or get worse during use of Ibuprofen 400 mg Film-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 an 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, missed connective-tissue disease) appear to be predisposed.

Blood and Lymphatic System Disorders:
Uncommon: Leucopenia, thrombocytopenia, agranulocutosis, aplastic anemia, and haemolytic anemia. 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 400 mg Film-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.
Vary 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:
Vary rare: Palpitations, cardiac failure, myocardial infarction.

Vascular Disorders:
Vary rare: Arterial hypertension, vasculitis

Respiratory, Thoracic and Mediastinal Disorders:
Uncommon: Asthma, bronchospasm, Dyspnoea.

Gastrointestinal Disorders:
Common: Gastro-intestinal complaints such as dyspepsia, purosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastro-intestinal 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: Tubulointersititial 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 reactions:
Common: fatigue.
Rare: Oedema.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

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. 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

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.

5.1 Pharmacodynamic properties

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

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has proven to be effective via prostaglandandin-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 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 show up mainly in the form of lesions and ulcerations in the gastro-intestinal 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

Core:

Hypromellose

Lactose Monohydrate

Magnesium Stearate

Maize Starch

Sodium Starch Glycollate (Type A)

Silica, Colloidal Anhydrous

Coat:

Sucrose

Talc

Maize Starch

Titanium Dioxide

Carnauba Wax

6.2 Incompatibilities

None.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C. Keep in the original container in order to protect from light and moisture

6.5 Nature and contents of container

Blister packs comprised of 20 µm aluminium foil and 250 µm PVC, enclosed in an outer carton containing 6, 8, 10, 12, 16, 20, 24, 30, 48, 50, 96 or 100 tablets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special precautions.

7. MARKETING AUTHORISATION HOLDER

Galpharm Healthcare Limited
Wrafton
Braunton
Devon
EX33 2DL

8 MARKETING AUTHORISATION NUMBER(S)

PL 16028/0156

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/10/2013

10 DATE OF REVISION OF THE TEXT

05/04/2018