SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Tablets 200mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen BP 200.0mg

Excipient(s) with known effect

Sucrose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Rheumatic and muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of cold and influenza.

4.2 Posology and method of administration

Posology

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

Adults, the elderly and children over 12 years: 1 or 2 tablets, up to three times a day as required. The dose should not be repeated more frequently than every four hours and no more than 6 tablets in any 24-hour period.

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

Paediatric population: Do not give to children under 12 years.

Renal impairment:
Patients with mild to moderate renal impairment, (see section 4.4 – Special warnings and precautions for use) and patients with severe renal insufficiency (see section 4.3 – Contraindications).

Hepatic Impairment:
For patients with mild to moderate hepatic impairment (see section 4.4 – Special warnings and precautions for use) and patients with severe hepatic dysfunction (see section 4.3 – Contraindications).

Method of administration

For oral use. It is recommended that patients with sensitive stomachs take Ibuprofen with food. If taken shortly after eating the onset of Ibuprofen may be delayed. To be taken preferably with or after food, with plenty of fluid. Ibuprofen tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

4.3 Contraindications

Ibuprofen is contraindicated in patients with a hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Ibuprofen should not be used in patients who have previously shown hypersensitivity reactions (e.g. asthma, angioedema, rhinitis, or urticaria)

after taking ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.

Ibuprofen is also contraindicated in patients with a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy. Ibuprofen should not be used in patients with active, or history of, recurrent peptic ulcer or gastrointestinal haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Ibuprofen should not be given to patients with conditions involving an increased tendency to bleeding.

Ibuprofen is contraindicated in patients with severe heart failure (NYHA Class IV), hepatic failure and renal failure (see section 4.4).

Ibuprofen is contraindicated during the last trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

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

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 analgesic medication.
Patients with medication overuse headache should not be treated by increasing the dose of the analgesic. In such cases the use of analgesics should be discontinued.
The concomitant consumption of excessive alcohol with NSAIDs, including ibuprofen may increase the risk of adverse effects on gastrointestinal tract, such as GI haemorrhage or the central nervous system, possible due to an additive effect.

Masking of symptoms of underlying infections
Ibuprofen Tablets 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 Ibuprofen Tablets are 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.

The use of Ibuprofen with concomitant NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding (see section 4.5).

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation, which may be fatal (see section 4.2).

Paediatric population
There is a risk of renal impairment in dehydrated children and adolescents.

Gastrointestinal bleeding, ulceration and perforation
GI 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 GI 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 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 aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of gastrointestinal disease, 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 aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Ibuprofen, the treatment should be withdrawn.

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

Respiratory disorders and hypersensitivity reactions
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 NSAIDs have been reports to precipitate bronchospasm, urticaria or angioedema in such patients.

Cardiac, renal and hepatic impairment

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. The habitual concomitant intake of various similar painkillers further increased this risk. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. For these patients, use the lowest effective dose, for the shortest possible duration and monitor renal function especially in long-term treated patients (see also section 4.3).

Ibuprofen should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with ibuprofen administration.

Cardiovascular and cerebrovascular effects:
Appropriate monitoring and advice is required for patients with a history of hypertension and/or mild to moderate congestive heart failure as hypertension, fluid retention and oedema have been reported in association with NSAID therapy.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400mg/day) may be associated with a small increase risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that a low dose ibuprofen (e.g. 1200mg/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, and smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen Tablets. 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.

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, administrations of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state.

Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

SLE and mixed connective tissue disease
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see below and section 4.8).

Severe cutaneous adverse reactions (SCARs)
Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), and 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).

In exceptional cases, 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 in case of varicella.

Haematological effects
Ibuprofen, like other NSAIDs, can interfere with 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 systematic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

Impaired female fertility
The use of Ibuprofen may impair female 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.

Ibuprofen tablets contains sucrose:

- patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

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.

Anti-hypertensives, beta-blockers and diuretics: NSAIDs may reduce the effect of anti-hypertensives, such as ACE inhibitors, angiotensin-II receptor antagonists, beta blockers and diuretics. Diuretics can also increase the risk of nephrotoxicity of NSAIDs.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.
Cholestyramine: The concomitant administration of ibuprofen and cholestyramine may reduce the absorption of ibuprofen in the gastrointestinal tract. However, the clinical significance is unknown.

Lithium: Decreased elimination of lithium.

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

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of NSAIDs. 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.

Other analgesics and cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs, including Cox-2 inhibitors, as this may increase the risk of adverse effects (see section 4.4).

Aspirin (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).

Corticosteroids: Increased risk of gastro-intestinal bleeding and ulceration with NSAIDs (see section 4.4).

Anticoagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).

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.

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

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding with NSAIDs (see section 4.4).

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 haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Aminoglycosides: NSAIDs may decrease the excretion of aminoglycosides.

Herbal extracts: Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.

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.

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 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 losses 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.

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 and 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.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to the following:
- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension)
- renal dysfunction (see above)

the mother and the neonate, at the end of the pregnancy, to:
- possible prolongation of bleeding time an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy (see section 4.3 and 5.3).

Breast-feeding
In the limited studies so far available, NSAIDs can appear in the breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breast-feeding.

Fertility

The use of ibuprofen may impair female fertility and not recommended in women attempting to conceive. See section 4.4.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Gastrointestinal disorders: The most commonly observed adverse events 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, gastrointestinal haemorrhage, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following ibuprofen administration. Less frequently, gastritis, duodenal ulcer, gastric ulcer and gastrointestinal perforation have been observed.

Immune system disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnea, 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).

Cardiac disorders and vascular disorders: Oedema, hypertension and cardiac failure have been reported in associations with NSAID treatment. Clinical studies suggest that use of ibuprofen, particularly at 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).

Infections and infestations: Rhinitis and aseptic meningitis (especially in patients with existing autoimmune disorders, such as systemic lupus erythematosus and mixed connective tissue disease) with symptoms of stiff neck, headache, nausea, vomiting or disorientation (see section 4.4).

Exacerbation of infection-related inflammations 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 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").

The following adverse reactions possibly related to ibuprofen and displayed by MedDRA frequency convention and system organ classification. Frequency groupings are classified according to the subsequent conventions: Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1000 to <1/100), Rare (≥1/10,000 to <1/1000), Very rare (<1/10,000) and Not known (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Adverse Reaction**
Infection and infestation	Uncommon	Rhinitis
	Rare	Meningitis aseptic (see section 4.4)
Blood and lymphatic system disorders	Rare	Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, asplastic anaemia, haemolytic anaemia
Immune system disorders	Uncommon	Hypersensitivity
	Rare	Anaphylactic reaction
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, melaena, haematemesis, gastrointestinal haemorrhage
	Uncommon	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation
	Very rare	Pancreatitis

	Not known	Exacerbation of colitis and Crohn's disease (section 4.4)
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, Steven-Johnson syndrome, and toxic epidermal necrolysis)
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP)
Renal and urinary disorders	Uncommon	Nephrotoxicity in various forms e.g. Tubulointerstitial nephritis, nephrotic syndrome and renal failure
	Not known	Renal tubular acidosis*
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
Metabolism and Nutrition Disorders	Not known	Hypokalaemia*

*Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

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 Yellow Card

Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Toxicity

Signs and symptoms of toxicity have generally not been observed at doses below 100mg/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 400mg/kg or greater.

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 or drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion and loss of consciousness. Nystagmus, metabolic acidosis, hypothermia, renal effects, gastrointestinal bleeding, coma, apnoea, diarrhoea and depression of the CNS and respiratory system have also been rarely reported. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported.

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. Large overdoses are generally well tolerated when no other drugs are being taken.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalized weakness (see section 4.4 and section 4.8).

Management

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: Anti-inflammatory and antirheumatic products, nonsteroidal; propionic acid derivatives.

ATC Code: M01AE01

Ibuprofen is a propionic acid derivative with analgesic, anti-inflammatory and anti-pyretic activity. The drug's therapeutic effects as an NSAID is thought to result from in inhibitory effect on the enzyme cyclo-oxygenase, which results in a marked reduction in prostaglandin synthesis.

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 a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release acetylsalicylic acid dosing (81mg), 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 like for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentration occurring 1-2 hours after administration. Elimination half-life is approximately 2 hours.

Ibuprofen is metabolized in the liver to two inactive metabolites and these together with unchanged ibuprofen are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Ibuprofen is extensively bound to plasma proteins.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica, starch, povidone, croscarmellose sodium, microcrystalline cellulose, alginic acid, magnesium stearate, sodium lauryl sulphate, sucrose, E171, E127, sodium starch glycollate, Opaseal (polyvinyl acetate phthalate, stearic acid (E570)).

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a cool dry place protected from moisture below 25°C.

6.5 Nature and contents of container

Cartons of blister packs containing 12 or 16 tablets.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 55612/0038

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