Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Brufen 600mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 600 mg of ibuprofen.

Excipient(s) with known effect: each tablet contains 40mg of lactose monohydrate.

For the full list of the excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

A white, pillow-shaped, film-coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Brufen is indicated in the symptomatic management of various arthroses such as rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease) and osteoarthritis, fibrositis, ankylosing spondylitis and other muscular syndromes, such as low back pain, soft tissue trauma and various inflammations of tendon, joint capsules and ligaments.

Brufen is also used as an analgesic in the relief of mild to moderate pain.

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 and adolescents older than 12 years (≥ 40kg) The recommended dosage of Brufen is 1200-1800 mg daily in divided doses. Some patients can be maintained on 600-1200 mg daily. The total daily dose should not exceed 2400 mg.

Paediatric population
Brufen 600mg film-coated tablets are not suitable for use inchildren under 12 years of age.

Elderly
No specific dosage modifications are required for elderly patients, unless renal or hepatic function is impaired, in which case, dosage should be assessed individually.

NSAIDs should be used with particular caution in elderly patients who are more prone to adverse events. The lowest dose compatible with adequate safe clinical control should be employed. (See also Section 4.4). Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

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

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

Method of administration

In order to achieve a faster onset of action, the dose may be taken on an empty stomach. It is recommended that patients with sensitive stomachs take ibuprofen with food.
Take Brufen tablets with plenty of fluid. Brufen tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

4.3 Contraindications

- Known hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Brufen should not be given to patients who have experienced asthma, urticarial or allergic-type reactions after taking acetylsalicylic acid/asprin or other NSAIDs.
- Severe heart failure (NYHA IV).
- Severe liver failure.
- Severe renal failure (glomerular filtration below30mL/min).
- Conditions involving an increased tendency or active bleeding.
- History of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- Active, or history of recurrent peptic ulceration or gastrointestinal haemorrhage (defined as two or more distinct episodes of proven ulceration or bleeding).
- During the third trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

General
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2).

Patients treated with NSAIDs long-term should undergo regular medical supervision to monitor for adverse events.

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

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.

The use of Brufen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the potential for additive effects.

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

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

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

Gastrointestinal bleeding, ulceration and perforation

NSAIDs should be given with care to patients with a history of peptic ulceration and other gastrointestinal disease since their conditions may be exacerbated (see section 4.2).

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 acetylsalicylic acid/aspirin, or other drugs likely to increase gastrointestinal risk (See below and section 4.5).

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

Patients with a history of GI disease, particularly when elderly, should report any unusual abdominal symptoms (especially GI 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/aspirin (See section 4.5).

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

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

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice arerequired for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

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

Cases of Kounis syndrome have been reported in patients treated with Brufen. 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 Brufen 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 Brufen has resulted in renal papillary necrosis and other renal pathological changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause a dose-dependent reduction in prostaglandins formation and, secondarily, in renal blood flow, which may cause renal failure. Patients at greatest risk of this

reaction are those with impaired renal function, heart failure, liver dysfunction, those who are taking diuretics and ACE inhibitors and the elderly.
Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state.

Haematological effects
As NSAIDs can interfere with platelet function and may prolong bleeding time, Brufen should be used with caution in patients with intracranial haemorrhage and bleeding diathesis.

Dermatological effects

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

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

Masking of symptoms of underlying infections
Brufen 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 Brufen is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Aseptic meningitis
Aseptic meningitis has been observed on rare occasions in patients with Brufen therapy. Although it is probably more unlikely 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.

Information related to excipients
Brufen 600mg film-coated tablets contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medication.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially sodium free.

4.5 Interaction with other medicinal products and other forms of interaction

It is considered unsafe to take NSAIDs in combination with warfarin or heparin unless under direct medical supervision.

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

Concomitant use of ibuprofen with:	**Possible effects:**
Other NSAIDs including cyclooxygenase-2 selective inhibitors	Concomitant use with other NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the potential for additive effects
Cardiac glycosides	NSAIDs may exacerbate heart failure, reduce glomerular filtration rate and increase plasma levels of cardiac glycosides
Corticosteroids	Increased risk of gastrointestinal ulceration or bleeding with NSAIDs
Anticoagulants	NSAIDs may enhance the effects of anticoagulants, such as warfarin
Antiplatelet agents & selective serotonin-reuptake inhibitors (SSRIs), e.g. clopidogrel and ticlopidine	Increased risk of gastrointestinal bleeding with NSAIDs
Acetylsalicylic acid/aspirin	As with other products containing NSAIDs, concomitant administration of ibuprofen and acetylsalicylic acid/aspirin is not generally recommended

	because of the potential of increased adverse effects. Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid/aspirin on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular long-term use of ibuprofen may reduce the cardioprotective effect of low-dose aspirin (acetylsalicylic acid) cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1)
Lithium	NSAIDs may decrease elimination of lithium
Anti-hypertensive, beta-blockers and diuretics	NSAIDs may 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
Methotrexate	NSAIDs may inhibit the tubular secretion of methotrexate and reduce clearance of methotrexate.
Cyclosporine	Increased risk of nephrotoxicity with NSAIDs
Tacrolimus	Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus
Zidovudine	Increased risk of haematological toxicity with NSAIDs are given with zidovudine. There is evidence of an increased risk of hemarthrosis and hematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen
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 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.
Sulfonylureas	NSAIDs may potentiate the effects of sulfonylrea medications. There have been rare reports of hypoglycaemia in patients on sulfonylurea medications receiving ibuprofen.
Cholestyramine	The concomitant administration of ibuprofen and cholesytramine may reduce the absorption of ibuprofen in the gastrointestinal tract. However, the clinical significance is unknown.
Aminoglycosides	NSAIDs may decrease the excretion of aminoglycosides.
Herbal extracts	Ginkgo biloba may potentiate the risk of bleeding with NSAIDs.
Mifepristone	A decrease in the efficacy of the medicinal product can theoretically occur due to the antiprostaglandin properties of NSAIDs including acetylsalicylic acid. Limited evidence suggests that coadministration of NSAIDs on the day of prostaglandin administration does not adversely influence the effects of mifepristone or the prostaglandin on cervical ripening or uterine contractility and does not reduce the clinical efficacy of medicinal termination of pregnancy.

4.6 Fertility, pregnancy and lactation

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.

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy. In animals, the administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and

post-implantation losses and embryo/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 or second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to ibuprofen for several days from gestational week 20 onward. Ibuprofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

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

- 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 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 sections 4.3 and 5.3).

Labour and delivery

Administration of ibuprofen is not recommended during labour and delivery. The onset of labour may be delayed and the duration increased with a greater bleeding tendency in both mother and child.

Breastfeeding
In limited studies to date, ibuprofen appears in breast milk in very low concentrations. Brufen is not recommended for use in nursing mothers.

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. Following treatment with ibuprofen, the reaction time of patients may be affected. This should be taken into account where increased vigilance is required e.g. when driving a car or operating machinery. This applies to a greater extent in combination with alcohol.

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, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following 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 ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, very rarely, erythema multiforme, bullous dermatoses (including Stevens-Johnson syndrome and toxic epidermal necrolysis).

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

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

Cardiac disorders and vascular disorders
Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment. Clinical studies suggest that use of ibuprofen, particularly at 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 following are adverse reactions possibly related to ibuprofen, 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 (≥1/1,000 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).

System organ class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Rhinitis
	Rare	Meningitis aseptic (see section 4.4)
Blood and lymphatic system disorders	Rare	Leukopenia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia
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, melena, hematemesis, gastrointestinal haemorrhage
	Uncommon	Gastritis, duodenal ulcer, gastric ulcer, mouth ulceration, gastrointestinal perforation
	Very Rare	Pancreatitis
	Not known	Exacerbation of Colitis and Crohn's disease
Hepatobiliary disorders	Uncommon	Hepatitis, jaundice, hepatic function abnormal
	Very Rare	Hepatic failure
Skin and subcutaneous tissue	Common	Rash
	Uncommon	Urticaria, pruritus, purpura, angioedema, photosensitivity reaction
	Very Rare	Severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis).
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Acute generalised exanthematous pustulosis (AGEP), Fixed Drug Eruption
Renal and urinary disorders	Uncommon	Nephrotoxicity in various forms, e.g. Tubulointerstitial

		nephritis, nephrotic syndrome and renal failure
General disorders and administration site conditions	Common	Fatigue
	Rare	Edema
Cardiac disorders	Very Rare	Cardiac failure, myocardial infarction (see also section 4.4)
	Not known	Kounis syndrome
Vascular disorders	Very Rare	Hypertension

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 HPRA Pharmacovigilance Website: www.hpra.ie

4.9 Overdose

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

Symptoms
Most patients who have ingested significant amounts of ibuprofen will manifest symptoms within 4 to 6 hours. The most frequently reported symptoms of overdose include nausea, vomiting, abdominal pain, lethargy and drowsiness. Central nervous system (CNS) effects include headache, tinnitus, dizziness, convulsion, and loss of consciousness. Nystagmus, hypothermia, renal effects, gastrointestinal bleeding, coma, apnea and depression of the CNS and respiratory system have also been rarely reported. Cardiovascular toxicity, including hypotension, bradycardia and tachycardia, has been reported. In cases of significant overdose, renal failure and liver damage are possible.
In serious poisoning, metabolic acidosis may occur.
Large overdoses are generally well tolerated when no other drugs are being taken.
Prolonged use at higher than recommended doses or overdose may result in renal tubular acidosis and hypokalaemia.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: Anti-inflammatory and anti-rheumatic products, non-steroidal, propionic acid derivatives.

ATC Code: M01AE01

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

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

5.2 Pharmacokinetic properties

Ibuprofen is a racemic mixture of [+]S- and [-]R-enantiomers.
Studies including a standard meal, show that food does not markedly affect total bioavailability.

Absorption
Ibuprofen is rapidly absorbed from the gastrointestinal tract with a bioavailability of 80-90%. Peak serum concentrations occur one to two hours after administration of immediate release formulations.

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

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

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

Special populations

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

Paediatric population
The systemic exposure of ibuprofen following weight adjusted therapeutic dosage (5mg/kg to 10mg/kg bodyweight) in children aged 1 year or over, appears similar to that in adults. Children 3 months to 2.5 years appeared to have a higher volume of distribution (L/kg) and clearance (l/kg/h) of ibuprofen than did children >2.5 to 12 years of age.

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

Hepatic impairment
Alcoholic liver disease with mild to moderate hepatic impairment did not result in substantially altered pharmacokinetic parameters.
In cirrhotic patients with moderate hepatic impairment (Child Pugh's score 6-10) treated with racemic ibuprofen, an average 2-fold prolongation of the half-life was observed and the enantiomeric AUC ratio (S.R) was significantly lower compared to healthy controls, suggesting an impairment of metabolic inversion of (R)-ibuprofen to the active (S)-enantiomer (see sections 4.2, 4.3 and 4.4).

5.3 Preclinical safety data

There are no preclinical data of relevance for the safety assessments, apart from what has already been taken into account.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core: microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, anhydrous colloidal silica, sodium laurilsulphate, magnesium stearate
Tablet Coating:hypromellose, talc, titanium dioxide E171

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original pack in order to protect from moisture.

6.5 Nature and contents of container

Blister pack comprising of transparent polyvinyl chloride (PVC) or polyvinyl chloride /polyvinylidene (PVC/PVDC) film with aluminium foil backing.

Pack size: 60 tablets.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Viatris Healthcare Limited
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Mulhuddart
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8 MARKETING AUTHORISATION NUMBER

PA23355/012/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 June 1982

Date of last renewal: 01 June 2007

10 DATE OF REVISION OF THE TEXT

February 2026