SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen Tablets BP 600 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 600 mg of Ibuprofen.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet

Pink coloured capsule shaped film coated tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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

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

4.2 Posology and method of administration

Posology:

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

***Adults*:**

The recommended dosage of Ibuprofen is 1200-1800mg daily in divided doses. Some patients can be maintained on 600-1200mg daily. In severe or acute conditions, it can be advantageous to increase the dosage until the acute

phase is brought under control, provided that the total daily dose does not exceed 2400mg in divided doses.

***Elderly*:**
The elderly are at increased risk of the serious consequences of adverse reactions. If NSAIDs are 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.

In Juvenile Rheumatoid Arthritis, up to 40mg/kg of body weight daily in divided doses may be taken.

Tablets are not suitable for children under the age of 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 administration. It is recommended that patients with sensitive stomachs take Ibuprofen with food. If taken shortly after eating, the onset of action 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

Hypersensitivity to Ibuprofen or to any of the excipients listed in section 6.1.
Ibuprofen should not be used in patients with active, or history of recurrent Peptic ulcer/ gastrointestinal haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

NSAIDs (ibuprofen) are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin or other non-steroidal anti-inflammatory drugs.

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

Severe heart failure (NYHA Class IV), hepatic failure and renal failure (see section 4.4)

During the last trimester of pregnancy (see section 4.6).

History of gastrointestinal bleeding or perforation, relating to previous NSAIDs therapy.

4.4 Special warnings and precautions for use

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

***Other NSAIDs*:**
As with other NSAIDs, ibuprofen may mask the signs of infection.

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

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 analgesic should be discontinued.

The concomitant consumption of excessive alcohol with NSAIDs, including ibuprofen may increase the risk of adverse effects on the gastrointestinal tract, such as GI haemorrhage or the central nervous system, possibly due to an additive effect.

***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).

***Respiratory disorders and hypersensitivity reactions*:**
Caution is required if administered to patients suffering from, or with a previous history of bronchial asthma, chronic rhinitis or allergic diseases since NSAIDs have been reported to cause bronchospasm, urticaria or angioedema in such patients.

***Cardiovascular, 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 increases 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 are required 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 (2400mg/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, particularly of myocardial infarction.

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 (2400mg/day) should be avoided.

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

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, GI toxicity, 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 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 gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (see section 4.8)

Renal effects:

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

As with other NSAIDs, long-term administration of ibuprofen has resulted in renal papillary necrosis and other renal pathologic changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of 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 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 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.

***Haematological effects*:**
Ibuprofen, like other NSAIDs, can interfere with platelet aggregation and has been shown to prolong bleeding time in normal subjects.

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

***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.

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

Masking of symptoms of underlying infections:
Ibuprofen 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 is administered for fever or pain relief in relation to infection, monitoring of infection is advised.

In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

Important information regarding the ingredients in this medicine

Lactose: This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium: 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

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

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

***Acetylsalicylic acid*:** As with other products containing NSAIDs, 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).

***Anti-hypertensives, beta blockers and diuretics*:** Reduced anti-hypertensive effect of ACE inhibitors, beta-blockers, angiotensin-II receptor antagonists, and diuretics.

***Diuretics*:** Reduced diuretics effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

***Cardiac glycosides*:** NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma 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 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 medicinal termination of pregnancy.

***Corticosteroids*:** Increased risk of gastrointestinal ulceration or bleeding with NSAIDs (see section 4.4)

***Anticoagulants*:** NSAIDs may enhance the effects of anticoagulants, 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 medications 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 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 absolute risk for 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, 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 the following:

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

Breast-feeding:

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

Fertility:

See section 4.4 Special warnings and precautions for use, regarding female fertility.

4.7 Effects on ability to drive and use machines

Undesirable effects such 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 and 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 dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme).

***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), and in long term treatment, may be associated with a small increased risk of arterial thrombotic events such as myocardial infarction or stroke (see section 4.4).

***Infections and infestations*:** Rhinitis and reports of aseptic meningitis (especially in patients with existing auto-immune disorders such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever 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 to a doctor without delay.

***Skin and subcutaneous disorders*:** Very rare: In exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection (see also "Infections an 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 (≥1/1,000 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, haemolytic anaemia
Immune system disorders	Uncommon	Hypersensitivity
	Rare	Anaphylactic reaction
Metabolism and Nutrition disorders	Not known	Hypokalaemia*
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
Hepatobiliary disorders	Uncommon	Hepatitis, jaundice, hepatic function abnormal
	Very Rare	Hepatic failure
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria, pruritus, purpura, Angioedema
	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), photosensitivity reaction
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

*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 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 Website:

www.mhra.gov.uk.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 400 mg/kg or greater.

***Symptoms*:**

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

The most frequently reported symptoms of overdose include nausea, vomiting, lethargy, drowsiness, abdominal pain.

Central nervous system (CNS) effects include Tinnitus, headache, 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.

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. Disorientation, excitation, fainting and cardiovascular toxicity, including hypotension, bradycardia and tachycardia have been reported. In cases of significant overdose, renal failure and liver damage are possible. 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 generalised weakness (see section 4.4 and section 4.8).

***Therapeutic measures*:**

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. 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 anti-rheumatic products, non-steroidal, Propionic acid derivatives.
ATC code: M01AE

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 its 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 aspirin on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400mg 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

Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body. The excretion is rapid and complete via the kidneys.
Maximum plasma concentrations are reached 45 minutes after ingestion if taken on an empty stomach. Ibuprofen is extensively bound to plasma proteins. When taken with food, peak levels are observed after 1 to 2 hours. These times may vary with different dosage forms.

Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete.

The elimination half-life of ibuprofen is approximately 2 hours.

No significant differences in pharmacokinetic profile are observed in the elderly.

In limited studies ibuprofen appears in the breast milk in very low concentrations.

5.3 Preclinical safety data

No data of relevance which is additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Maize Starch
Microcrytalline Cellulose
Croscarmellose Sodium
Povidone
Colloidal Silicon Dioxide
Alginic Acid
Sodium Lauryl Sulfate
Sodium Starch Glycolate
Magnesium Stearate
Hydroxypropylcellulose
Hydroxypropylmethylcellulose
Polyethylene Glycol 400
Erythrosine Aluminium Lake (E127)
Titanium Dioxide (E171)

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original container. Keep the container tightly closed.

Blister packs: Do not store above 25ºC. Store in the original package.

6.5 Nature and contents of container

PP or HDPE tablet containers of 50, 56, 84, 100, 250 or 500 tablets.

or

Plastic tablet containers of 50 tablets.

or

Blister packs comprised of Aluminium foil (20µm) and PVC (250µm) enclosed in an outer carton containing 84 tablets.

6.6 Special precautions for disposal

Non applicable.

7 MARKETING AUTHORISATION HOLDER

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Berkhamsted
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HP4 1EG
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8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first Authorisation: 22 September 2000

Date of Renewal of Authorisation: 13 October 2008

10 DATE OF REVISION OF THE TEXT

10/01/2024