SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ibuprofen 200 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Ibuprofen 200 mg

Excipient with known effect: Lactose 96.4 mg, sucrose 143 mg, sodium benzoate 0.015 mg.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Coated tablet (tablet)
Appearance:
Pink, circular, biconvex, sugar-coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ibuprofen contains the active substance ibuprofen. Ibuprofen belongs to a group of medicines called NSAID (nonsteroidal anti-inflammatory drugs) which work by reducing pain, inflammation and fever.

Ibuprofen is used for the symptomatic treatment of mild to moderate pain including migraine headache period pain and/or fever. In addition, it is used for the symptomatic treatment of pain and inflammation in arthritic diseases (e.g., rheumatoid arthritis), degenerative arthritic conditions (e.g., osteoarthritis) and in painful swelling and inflammation after soft tissues injuries.

In the treatment of non-articular rheumatic conditions, ibuprofen is indicated in periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain. Ibuprofen is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhoea, dental and post-operative pain and for the symptomatic relief of headache including migraine headache.

4.2 Posology and method of administration

For oral administration.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4). During short-term use, if symptoms persist or worsen the patient should be advised to consult a doctor.
The tablets should be swallowed with a drink of water or milk and should be taken preferably with or after food. 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. Ibuprofen tablets should be swallowed whole and not chewed, broken, crushed or sucked on to avoid oral discomfort and throat irritation.

Adults and children over 12 years:
The usual dosage is 600 to 1800 mg spread throughout the day.
Your doctor may choose to increase this depending on what you are being trea ted for; but no more than 2400 mg should be taken in one day.

Children: 20 mg per kg of body weight daily, given in divided doses.
Not recommended for children weighing less than 7 kg. For young children, more suitable formulations are available. In cases of severe juvenile arthritis your doctor may increase the dosage up to 40 mg per kilogram.
Elderly: The elderly are at an increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored for GI bleeding during NSAID therapy. If renal or hepatic function is impaired, dosage should be assessed individually.
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).

4.3 Contraindications

Hypersensitivity to ibuprofen or to any of the excipients.

This drug should not be given to patients with active, or history of re-current ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding) in
the stomach or small intestine (duodenum).

NSAIDs are contra-indicated in patients who have previously shown hypersensitivity
reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen,
aspirin or other NSAIDs.

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, related to previous NSAIDs therapy.

Suffering from significant dehydration (caused by vomiting, diarrhoea or insufficient
fluid intake).

Any active bleeding (including in the brain).

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

4.4 Special warnings and precautions for use

This drug contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the total lactose deficiency or glucose-galactose malabsorption should not take this medication.
Additionally, this drug contains sucrose and therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
This product also contains sodium benzoate which may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

This medicinal product contains a total of 12.788 mg sodium per tablet, equivalent to 0.7 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.
As this medicine contains less than 1 mmol sodium (23 mg) per tablet, it is essentially ‘sodium-free’.
As with other NSAIDs, ibuprofen may mask the signs of infection.
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 the gastrointestinal tract, such as GI haemorrhage or the central nervous system, possibly due to an additive effect. 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 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.
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 reported 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 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 trial data suggest that use of ibuprofen, particularly at a high dose (2400mg

daily) and in long term treatment 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 daily) 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. Similar consideration should be made before initiating longer-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 ibuprofen. 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 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 GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) especially 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 antiplatelet 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-dependant reduction in prostaglandin 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 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 skin reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen should be discontinued at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions or any other sign of hypersensitivity.
Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. To date, the contributing role of NSAIDs in the worsening

of these infections cannot be ruled out. Thus, it is advisable to avoid use of Ibuprofen in case of varicella (see section 4.8).

Impaired female fertility:

The use of ibuprofen may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

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 systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

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.

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 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 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 likely for occasional ibuprofen use (see section 5.1).
Antihypertensives, 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 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 decreased elimination 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. NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Corticosteroids: Increased risk of GI ulceration or bleeding (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 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, NSAIDs should not be used during the first two trimesters of pregnancy or labour unless 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. NSAID 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 (with premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydroamniosis;
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.
Lactation:
In limited studies so far available, NSAIDs can appear in breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

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

4.8 Undesirable effects

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

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
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 forms of skin reactions (e.g., Erythema multiforme, bullous reactions, including 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
Metabolism and nutrition disorders	Not known Not known	Decreased appetite Hypokalemia*
Renal and urinary disorders	Uncommon Very rare Not known Not known	Nephrotoxity in various forms e.g., Tubulointerstitial nephritis, nephrotic syndrome and renal failure Acute renal failure Ureteric colic, dysuria 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.

Infections and infestations: Exacerbation of infection-related inflammations (e.g., development of necrotising fasciitis) coinciding with the use of non-steroidal anti-inflammatory drugs has been described. This is possibly associated with the mechanism of action of the non-steroidal anti-inflammatory drugs. 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, fever or disorientation (see section 4.4). 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. It is to be investigated whether there is an indication for anti-infective/antibiotic therapy.

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 has been observed. Pancreatitis has been reported very rarely.

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, pruritis, urticaria, purpura, angiodema and, less commonly, bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Cardiac disorders and vascular disorders: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.
Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high dose (2400 mg daily), and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

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")

Photosensitivity reactions: Frequency unknown.

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 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, 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, acute renal
failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.
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).

Management
Management should be symptomatic and supportive and include the maintenance of a
clear airway and monitoring of cardiac and vital signs until stable. Within 1 hour of
ingestion of a potentially toxic amount, consider oral administration of activated
charcoal. Alternatively, in adults, gastric lavage should be considered within 1 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 4 hours after ingestion of potentially toxic amounts. If frequent
or prolonged, convulsions should be treated with intravenous diazepam. Give bronchodilators for asthma. Other measures maybe 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, a derivative of propionic acid, has useful anti-inflammatory, analgesic and antipyretic activity. Similar to other propionic acid derivatives such as naproxen and fenoprofen it can cause gastrointestinal erosions (gastric, duodenal and intestinal) in experimental animals. All produce gastrointestinal side effects in man but are usually less severe than with aspirin. The propionic acid derivatives are all effective inhibitors of the cyclo-oxygenase responsible for the biosynthesis of prostaglandins. All of these agents alter platelet function and prolong bleeding time.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. Some 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 likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed following oral administration to man and peak concentrations in plasma are observed after 1 to 2 hours. The half-life in plasma is about 1 to 2 hours.

Ibuprofen is extensively (99%) and firmly bound to plasma proteins but the drug occupies only a fraction of the total drug-binding sites at usual concentrations. Ibuprofen passes slowly into the synovial spaces and may remain there in higher concentration as the concentrations in plasma decline. In experimental animals, ibuprofen and its metabolites pass easily across the placenta. The excretion of ibuprofen is rapid and complete. Greater than 90% of the ingested dose is excreted in the urine as metabolites or their conjugates and no ibuprofen per se is found in the urine. The major metabolites are a hydroxylated and a carboxylated compound.

5.3 Preclinical safety data

Not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Methylcellulose
Sodium Starch Glycollate
Magnesium Stearate
Colloidal Anhydrous Silica

Coating excipients:
Wincoat WT-TR-05034 (Polyvinyl acetate phthalate, Stearic acid)
Ethyl acetate
Purified Talc
Calcium carbonate
Gum Acacia
Winglow WG-02213 pink (sucrose, titanium dioxide, erythrosine aluminium lake, sodium benzoate)
Opaglos 6000P (Yellow Carnauba Wax, White Beeswax, Shellac)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months

6.4 Special precautions for storage

Tube packs - Do not store above 25°C. Keep the container tightly closed. Store in the original container.
Blister packs - Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Polypropylene tubes with low-density polyethylene caps.
Pack sizes: 84, 100, 250 and 500 tablets.
Blister pack comprising of transparent polyvinyl chloride (PVC) with aluminium foil backing
Pack size: 48, 84 tablets
Not all of the pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Steranco Healthcare UK Limited
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8 MARKETING AUTHORISATION NUMBER(S)

PL 60260/0028

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