Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nurofen Rapid Relief Max 400 mg soft capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 400 mg ibuprofen

Excipients with known effect:
Each soft capsule contains soya lecithin, 72.59 mg sorbitol (E420) and 0.60 mg Ponceau 4R (E124).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soft capsule

Red, oval-shaped soft capsule with NURO400 printed in white ink. Each capsule is approximately 10mm in width and approximately 15.5 mm in length.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medical product is indicated in adults and adolescents weighing from 40 kg (12 years of age and above) for the short-term symptomatic treatment of mild to moderate pain such as headache, period pain, dental pain and fever and pain associated with the common cold.

4.2 Posology and method of administration

Posology
For short-term use only.

Undesirable effects may be minimised by using the lowest effective dose for the shortest possible duration necessary to control symptoms (see section 4.4).
Adults and adolescents weighing from 40 kg (12 years of age and above). Initial dose is one capsule (400 mg). Then, if necessary, additional doses of one capsule (400 mg) should be taken. The dosing interval should be at least 6 hours. The maximum recommended daily dose of three capsules (1200 mg) should not be exceeded in any 24-hour period.

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

Special patient groups

Paediatric Population:

This medicinal product is not intended for use in adolescents under 40 kg body weight or children under 12 years of age.

Elderly:
No special dose adjustment is required. Because of the possible undesirable-effect profile (see section 4.4), the elderly should be monitored particularly carefully.

Renal insufficiency:
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 insufficiency (see section 5.2):
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:
For oral use. Capsules should not be chewed.

If taken shortly after eating, the onset of action of Nurofen Rapid Pain Relief Max 400 mg Soft Capsules may be delayed. If this happens the patient should not take more Nurofen Rapid Pain Relief Max 400 mg Soft Capsules than recommended within section 4.2 (posology) or until the correct re-dosing interval has passed.

It is recommended that patients with a sensitive stomach take Nurofen Rapid Pain Relief Max 400 mg Soft Capsules with food.

4.3 Contraindications

- Hypersensitivity to the active substance, peanut or soya, or to any of the excipients listed in section 6.1.
- In patients with a history of hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) associated with the intake of acetylsalicylic acid (ASA) or other non-steroidal anti-inflammatory drugs (NSAIDs).
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Patients with severe hepatic failure, severe renal failure, or severe heart failure (NYHA Class IV). See also section 4.4.
- In patients with cerebrovascular or other active bleeding.
- In patients with unclarified blood-formation disturbances.
- In patients with severe dehydration (e.g. caused by vomiting, diarrhoea or insufficient fluid intake).
- During the last trimester of pregnancy (see Section 4.6).

4.4 Special warnings and precautions for use

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

Caution is required in patients with certain conditions, which may be made worse:

- systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).
- congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria).
- gastrointestinal disorders and chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease) (see section 4.8).
- hypertension and/or cardiac impairment (see section 4.3 and 4.8).
- renal impairment as renal function may deteriorate (see sections 4.3 and 4.8).
- hepatic dysfunction (see sections 4.3 and 4.8).
- directly after major surgery.
- in patients who show allergic reactions to other substances, as they are also at a higher risk of hypersensitivity reactions when using <Product name to be completed nationally>
- in patients who suffer from hay fever, nasal polyps, chronic obstructive respiratory disorders, or have a history of allergic disease, as an increased risk exists for them of allergic reactions occurring. These may present as asthma attacks (so-called analgesics asthma). Quincke's oedema or urticaria.

Masking of symptoms of underlying infections
<Product name to be completed nationally> 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 <Product name to be completed nationally> 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.

Gastrointestinal (GI) safety
The use with concomitant NSAID's, including cyclo-oxygenase-2 specific inhibitors, increases risk of adverse reactions (see section 4.5) and should be avoided.

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

Gastrointestinal (GI) bleeding, ulceration or perforation
Gastrointestinal (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 GI events.
When GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses and 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, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).
Patients with a history of GI toxicity, particularly the 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 (SSRI's) or anti-platelet agents such as acetylsalicylic acid (See section 4.5).

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).

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. It is advisable to avoid use of <Product name to be completed nationally> in case of varicella.

Cardiovascular and cerebrovascular effectsCaution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.

Clinical studies data suggest that use of ibuprofen, particularly at high doses (2400 mg daily) may be associated with a small increased risk of arterial thrombotic events (e.g. 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.
Careful consideration should also be exercised before initiating long-term treatment for 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 [product name]. 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.

Other notes
Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of a hypersensitivity reaction after taking/administering <Product name to be completed nationally> therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

Ibuprofen, the active substance of <Product name to be completed nationally> may temporarily inhibit the blood-platelet function (thrombocyte aggregation). Therefore, it is recommended to monitor patients with coagulation disturbances carefully.

In prolonged administration of <Product name to be completed nationally> regular checking of the liver values, the kidney function, as well as of the blood count, is required.

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

The habitual intake of painkillers, particularly the combination of several painkillers, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy). This risk may be increased by salt loss and dehydration.

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 NSAID's.

There is some evidence that drugs which inhibit cyclo-oxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment (see section 4.6).

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

This medicinal product contains 72.59 mg sorbitol in each capsule.
Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

This medicinal product contains Ponceau 4R (E124). It may cause allergic reactions.

This medicinal product contains soya lecithin. Patients who are allergic to peanut or soya, should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicylic acid (low dose):
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).

Other NSAIDs, including cyclooxygenase-2 selective inhibitors:
The concomitant administration of several NSAIDs may increase the risk of gastrointestinal ulcers and bleeding due to a synergistic effect. The concomitant use of ibuprofen with other NSAIDs should therefore be avoided (see section 4.4).

Digoxin, phenytoin, lithium:
The concomitant use of Nurofen Rapid Pain Relief Max 400 mg Soft Capsules with digoxin, phenytoin or lithium preparations may increase serum levels of these medicinal products. A check of serum-lithium, serum-digoxin and serum-phenytoin levels is not as a rule required on correct use (maximum over 4 days).

Corticosteroids:
Corticosteroids as these may increase the risk of adverse reactions, especially of the gastrointestinal tract (gastrointestinal ulceration or bleeding). (see Section 4.4)

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

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

Probenecid and sulfinpyrazone:
Medicinal products that contain probenecid or sulfinpyrazone may delay the excretion of ibuprofen.

Diuretics, ACE inhibitors, betareceptor-blocker and angiotensin-II antagonists:
NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor, betareceptor-blocker or angiotensin-II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Potassium sparing diuretics:
The concomitant administration of Nurofen Rapid Pain Relief Max 400 mg Soft Capsules and potassium-sparing diuretics may lead to hyperkalaemia.

Methotrexate:
The administration of Nurofen Rapid Pain Relief Max 400 mg Soft Capsules within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.

Cyclosporine:
The risk of a kidney-damaging effect due to cyclosporine is increased through the concomitant administration of certain nonsteroidal anti-inflammatory drugs. This effect also cannot be ruled out for a combination of cyclosporine with ibuprofen.

Tacrolimus:
The risk of nephrotoxicity is increased if the two medicinal products are administered concomitantly

Zidovudine:
There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen. Increased risk of haematological toxicity when NSAIDs are given with zidovudine.

Sulfonylureas:
Clinical investigations have shown interactions between nonsteroidal anti-inflammatory drugs and antidiabetics (sulphonylureas). Although interactions between ibuprofen and sulphonylureas have not been described to date, a check of blood-glucose values is recommended as a precaution on concomitant intake.

Quinolone antibiotics:
Animal data indicate that NSAID's can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAID's and quinolones may have an increased risk of developing convulsions.

Mifepristone:
NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

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 and fluconazole.

4.6 Fertility, pregnancy and lactation

Pregnancy:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies raise concern about an increased risk of miscarriage and of cardiac malformation and gastroschisis after 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, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

From the 20th week of pregnancy onward, ibuprofen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore,during the first and second trimester of pregnancy, ibuprofen should not be given unless clearly necessary. If ibuprofen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to ibuprofen for several days from gestational week 20 onward. Ibuprofen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

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

- the foetus to:- 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).

Breast-feeding:
Ibuprofen and its metabolites can pass in low concentrations into the breast milk. No harmful effects to infants are known to date, so for short-term treatment with the recommended dose for pain and fever interruption of breast-feeding would generally not be necessary.

Fertility:
There is some evidence that drugs which inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment (see section 4.4).

4.7 Effects on ability to drive and use machines

This medicine has no or negligible influence on the ability to drive and use machines. Patients who experience dizziness, drowsiness, vertigo or visual disturbances while they are taking ibuprofen, should avoid driving or using machinery. Single administration or short term use of ibuprofen does not usually warrant the adoption of any special precautions. This applies to a greater extent in combination with alcohol.

4.8 Undesirable effects

The list of the following undesirable effects comprises all undesirable effects that have become known under treatment with ibuprofen, also those under high-dose long-term therapy in rheumatism patients. The stated frequencies, which extend beyond very rare reports, refer to the short-term use of daily doses up to a maximum of 1200 mg ibuprofen for oral dosage forms and a maximum of 1800 mg for suppositories.

Please note that within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

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)

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

		nonsteroidal anti-inflammatory drugs. If signs of an infection occur or get worse during use of Nurofen Rapid Pain Relief Max 400 mg Soft Capsules, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an anti-infective/antibiotic therapy. The symptoms of aseptic meningitis with neck stiffness, headache, nausea, vomiting, fever or consciousness clouding have been observed under ibuprofen. Patients with autoimmune disorders (SLE, mixed connective-tissue disease) appear to be predisposed.
Blood and Lymphatic System Disorders	Very rare	Disturbances to blood formation (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranuloctosis). The first signs may be fever, sore throat, superficial wounds in the mouth, influenza-like complaints, severe lassitude, nosebleeds and skin bleeding. In such cases the patient should be advised to discontinue the medicine immediately, to avoid any self-medication with analgesics or antipyretics and to consult a physician. The blood count should be checked regularly in long-term therapy.
Immune system disorders (Hypersensitivity)	Uncommon	Hypersensitivity reactions with urticaria and pruritus, as well as asthma attacks (possibly with drop in blood pressure).
	Very rare	Severe general hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock). Exacerbation of asthma and bronchospasm.
Psychiatric disorders	Very rare	Psychotic reactions, depression
Nervous System Disorders	Uncommon	Central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness
Eye disorders	Uncommon	Visual disturbances
Ear and labyrinth disorders	Rare	Tinnitus, hearing impaired
Cardiac Disorders	Very rare	Palpitations, heart failure, myocardial infarction
	Not known	Kounis syndrome
Vascular disorders	Very rare	Arterial hypertension, vasculitis
Gastrointestinal Disorders	Common	Gastro-intestinal complaints such as dyspepsia, pyrosis, abdominal pain, nausea, vomiting, flatulence, diarrhoea, constipation and slight gastro-intestinal blood losses that may cause anaemia in exceptional cases
	Uncommon	Gastrointestinal ulcers, potentially with bleeding and perforation. Ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4), gastritis
	Very rare	Oesophagitis, pancreatitis, formation of intestinal diaphragm-like strictures. The patient is to be instructed to withdraw the medicinal product and to go to a doctor immediately if severe pain in the upper abdomen or melaena or haematemesis occurs.
Hepatobiliary Disorders	Very rare	Hepatic dysfunction, hepatic damage, particularly in long-term therapy, hepatic failure, acute hepatitis
Skin and Subcutaneous Tissue Disorders	Uncommon	Various skin rashes
	Very rare	Severe cutaneousadverse reactions (SCARs) (including Erythema multiforme, exfoliativedermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis), alopecia. In

		exceptional cases, severe skininfections and soft-tissue complications may occur during a varicella infection(see also "Infections and infestations").
	Not Known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions
Renal and Urinary Disorders	Rare	Kidney-tissue damage (papillary necrosis) and elevated uric acid concentrations in the blood may also occur rarely. Elevated urea concentrations in the blood.
	Very rare	Formation of oedemas, particularly in patients with arterial hypertension or renal insufficiency, nephrotic syndrome, interstitial nephritis that may be accompanied by acute renal insufficiency. Renal function should therefore be checked regularly.
Investigations	Rare	Decreased haemoglobin levels

With the following adverse drug reactions, it must be accounted for that they are predominantly dose-dependent and vary interindividually.

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 has been observed. Particularly the risk of gastrointestinal bleeding occurring is dependent on the dose range and the duration of use.

Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

Hypersensitivity reactions have been reported and these may consist of:
(a) non-specific allergic reactions and anaphylaxis
(b) respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea
(c) various skin reactions, e.g. pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme)
The patient is to be instructed to inform a doctor at once and to stop taking Nurofen Rapid Pain Relief Max 400 mg Soft Capsules if they experience any of the above.

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

In adolescents and adults, the dose response effect is not clear cut. The half-life in overdose is 1.5-3 hours

Symptoms
Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as dizziness, drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. Prolonged use at higher the recommened doses or overdose may result in renal tubular acidosis and hypokalaemia.
In serious poisoning, metabolic acidosis may occur and the prothrombin time/ INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure, and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Management

Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.
No special antidote is available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids; propionic acid derivative
ATC Code: M01A E01

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that in the conventional animal-experiment inflammation models has proven to be effective via prostaglandin-synthesis inhibition. In humans, ibuprofen reduces inflammatory-related pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits ADP – and collagen – induced platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low-dose acetylsalicylic acid on platelets 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 (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

Absorption
On oral administration, ibuprofen is partly absorbed in the stomach and then completely in the small intestine. In a pharmacokinetic study, the time to peak plasma levels (median Tmax) for normal-release ibuprofen tablets was 90 minutes; for [Product name to be completed nationally] soft capsules the time was 40 minutes. An average Cmax is achieved in half the time taken for [Product name to be completed nationally] compared with normal-release pharmaceutical form (tablets).

Distribution
Peak plasma levels following oral administration of a normal-release pharmaceutical form (tablet) are reached after 1 - 2 hours. Ibuprofen is absorbed rapidly from the gastrointestinal tract following oral administration. Ibuprofen is detected in the plasma for more than 8 hours after administration of Nurofen Rapid Pain Relief Max 400 mg Soft Capsules. Plasma-protein binding is about 99 %.

Elimination
Following hepatic metabolism (hydroxylation, carboxylation, conjugation), the pharmacologically inactive metabolites are completely eliminated, mainly renally (90 %), but also with the bile. The elimination half-life in healthy individuals and those with liver and kidney diseases is 1.8 - 3.5 hours.

5.3 Preclinical safety data

The subchronic and chronic toxicity of ibuprofen in animal experiments was observed principally as lesions and ulcerations in the gastro-intestinal tract. *In vitro* and *in vivo* studies gave no clinically relevant evidence of a mutagenic potential of ibuprofen. In studies in rats and mice no evidence of carcinogenic effects of ibuprofen was found. Ibuprofen led to inhibition of ovulation in rabbits as well as disturbance of implantation in various animal species (rabbit, rat, mouse). Experimental studies have demonstrated that ibuprofen crosses the placenta, for maternally toxic doses, an increased incidence of malformations (e.g. ventricular septal defects) was observed. In animal studies, it has been observed that the use of NSAIDs, known to inhibit prostaglandin synthesis, may increase the incidence of dystocia and delayed parturition.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Fill:
Macrogol (minimum 85% purity) (E1521)
Potassium hydroxide (E525)

Soft Capsule Shell:
Gelatin (E441)
Sorbitol Liquid (E420) , partially dehydrated
Ponceau 4R (E124)
Purified water

Printing Ink:
Opacode WB white NSP-78-180002 (consisting of Titanium Dioxide (E171), Propylene Glycol (E1520), SDA 35A Alcohol (Ethanol & Ethyl acetate), Isopropyl alcohol, Polyvinyl acetate phthalate, Purified water, Macrogol/PEG MW400 (E1521) and Ammonium hydroxide 28% (E527)

Processing Aids:
Soya Lecithin (E322)

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 package in order to protect from moisture.

6.5 Nature and contents of container

Opaque PVC/PVdC-Al blisters containing 10, 20, 24, 30 or 40 soft capsules. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Ireland Ltd
7 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0979/085/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th August 2023

10 DATE OF REVISION OF THE TEXT

May 2025