# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Nurofen for Children Orange Flavoured 100mg Chewable Capsule, Soft

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable capsule, soft contains 100 mg Ibuprofen.

Excipient with known effect:
Glucose, 358.3 mg per chewable capsule
Sucrose, 251.6 mg per chewable capsule
Soya Lecithin, 0.01 mg per chewable capsule

Sodium, 0.027 mg per chewable capsule

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Chewable capsule, soft.

An orange, square shaped chewable soft gelatin capsule with a “N100” print in white ink. Typical dimensions of the soft gelatin capsule are approximately 5 to 8 mm in width and approximately 15 to 17 mm in diagonal length.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

The medicinal product is indicated in children from 20 kg body weight (7 years of age) to 40 kg body weight (12 years of age).
For the reduction of fever and the relief of the symptoms of colds and influenza and mild to moderate pain, such as a sore throat, dental pain, earache, headache, minor aches and sprains.

### 4.2 Posology and method of administration

**Posology**
For oral administration and short term use only.

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

In children ibuprofen is dosed depending on body weight, as a rule with 5 to 10 mg/kg body weight as a single dose. The maximum daily dosage of Nurofen for

Children is 20-30 mg/kg bodyweight. The recommended daily dose can be achieved as follows:

| Child Body Weight (kg) | Age (Years) | Single dose | Maximum daily dose |
|---|---|---|---|
| 20-29 | 7-9 | 200 mg ibuprofen (corresponding to 2 capsules) | 600 mg ibuprofen (corresponding to 6 capsules) |
| 30-40 | 10-12 | 300 mg ibuprofen (corresponding to 3 capsules) | 900 mg ibuprofen (corresponding to 9 capsules) |

Doses should be given approximately every 6 to 8 hours (or with a minimum of 6 hours between each dose) if required.

Do not use in children under 7 years of age or in children weighing less than 20 kg.

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

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

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

**Method of administration**
For oral administration.

The product should be chewed before swallowing. No water needed

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

History of gastrointestinal bleeding or perforation, related to previous NSAID therapy.

Severe heart failure (NYHA Class IV), severe renal failure or severe hepatic failure (See section 4.4).

Last trimester of pregnancy (See section 4.6).

This medicinal product contains soya lecithin. If you are allergic to peanuts or soya do not use this medicinal product.

Cerebrovascular or other active bleeding.

Unclarified blood-formation disturbances.

Severe dehydration (caused by vomiting, diarrhoea or insufficient fluid intake).

## 4.4 Special warnings and precautions for use

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

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

*Respiratory:*
Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergic disease.

*Other NSAIDs:*
The use of Ibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

*SLE and mixed connective tissue disease:*
Systemic lupus erythematosus and mixed connective tissue disease - increased risk of aseptic meningitis (see section 4.8)

*Porphyrin metabolism:*
Caution is required in patients with congenital disorder of porphyrin metabolism (e.g. acute intermittent porphyria)

*Renal:*
Renal impairment as renal function may further deteriorate (See section 4.3 and Section 4.8)
There is a risk of renal impairment in dehydrated children.

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.

In general terms, the habitual intake of painkillers, particularly on combination of several pain-relieving active substances, may lead to permanent renal damage with the risk of renal failure (analgesic nephropathy).

*Hepatic:*
Hepatic dysfunction (See section 4.3 and Section 4.8)

*Surgery:*
Caution is required directly after major surgery.

*Allergy:*
Caution is required in patients who react allergically to other substances, as an increased risk of hypersensitivity reactions occurring also exists for them on use of Nurofen for Children.

In patients who suffer from hayfever, nasal polyps or chronic obstructive respiratory disorders as an increased risk exists for them of allergic reactions occurring. These may present as asthma attacks (so-called analgesic asthma), Quincke's oedema or urticaria.

Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after using Nurofen for Children therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.

*Cardiovascular and cerebrovascular effects:*
Cases of Kounis syndrome have been reported in patients treated with Nurofen for Children Orange Flavoured 100mg Chewable Capsule, Soft. 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.

Caution (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 suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. $\leq$ 1200 mg/day) is associated with an increased risk of arterial thrombotic events. Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided. Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required

*Impaired female fertility:*
There is limited evidence that drugs which inhibit cyclo-oxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

*Gastrointestinal:*
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).

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk (see below and 4.5).

Patients with a history of 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 acetylsalicylic acid (see section 4.5).

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

*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).

*Platelet function:*
As NSAIDs can interfere with platelet function, they should be used with caution in patients with idiopathic thrombocytopenic purpura (ITP) and bleeding diathesis.

In prolonged administration of Nurofen for Children, 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.

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

Masking of symptoms of underlying infections:
This medicinal product 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 this medicine 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.

This product contains glucose. Patients with rare hereditary problems of glucose-galactose malabsorption should not take this medicine.

This product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

## 4.5 Interaction with other medicinal products and other forms of interaction

**Ibuprofen should be avoided in combination with:**

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

- **Acetylsalicylic acid**
Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects. Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

**Ibuprofen should be used with caution in combination with:**

- **Anticoagulants**: NSAIDS may enhance the effects of anti-coagulants, such as warfarin (See section 4.4).

- **Antihypertensives (ACE inhibitors, beta-receptor-blockers and angiotensin II antagonists) and diuretics**: NSAIDs may diminish the effect of these drugs. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
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, beta-receptor-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.
In particular, concomitant use of potassium-sparing diuretics may increase the risk of hyperkalaemia.

- **Corticosteroids**: Increased risk of 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).

- **Cardiac glycosides**: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels. The concomitant use of Nurofen for Children with digoxin preparations may increase serum level of digoxin. A check of serum digoxin is not as a rule required on correct use (maximum over 3 days).

- **Lithium and phenytoin**: There is evidence for potential increases in plasma levels of lithium when co-administered with ibuprofen. If used correctly, monitoring of the plasma concentrations of lithium or phenytoin is usually not needed.

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

- **Methotrexate**: There is a potential for an increase in plasma methotrexate.

- **Ciclosporin**: Increased risk of nephrotoxicity.

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

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

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

- **Oral hypoglycemic agents**: Inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

- **Aminoglycosides:** NSAIDs may reduce the excretion of aminoglycosides. Children: Care should be taken with concomitant treatment with ibuprofen and aminoglycosides.

- **CYP2C9 Inhibitors:** Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors) an increased S(+)-ibuprofen exposure by approximately 80 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9

inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development.

Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformations and gastroschisis after use of prostaglandin synthesis inhibitors 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 closure of the ductus arteriosus and pulmonary hypertension);

- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis (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 section 4.3).

Breastfeeding

Ibuprofen and its metabolites pass only in low concentrations into breast milk. Since harmful effects to infants have not become known to date, interruption of breast-feeding is usually not necessary during short-term treatment with the recommended dose.

Fertility
There is some evidence that drugs which inhibit cylooxygenase/prostglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

## 4.7 Effects on ability to drive and use machines

Nurofen for Children has no or negligible influence on the ability to drive and use machines.

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

Adverse events which have been associated with Ibuprofen are given below, listed by system organ class and frequency. Frequencies are defined as:

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)

Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

The adverse events observed most often are gastrointestinal in nature. Adverse events are mostly dose-dependent, in particular the risk of occurrence of gastrointestinal bleeding which is dependent on the dosage range and duration of treatment. 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.

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 daily), may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

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 for Children, the patient is therefore recommended to go to a doctor without delay. It is to be investigated whether there is an indication for an antimicrobial/antibiotic therapy.

The blood count should be checked regularly in long-term therapy.

The patient is to be instructed to inform a doctor at once and no longer to take Nurofen for Children if one of the symptoms of hypersensitivity reactions occurs, which can happen even on first use, the immediate assistance of a doctor is required.

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.

| System Organ Class | Frequency | Adverse Events |
|---|---|---|
| Infections and infestations | Very rare | Exacerbation of infection-related inflammations (e.g. development of necrotising fasciitis), in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection |
| Blood and Lymphatic System Disorders | Very rare | Haematopoietic disorders (anaemia, leukopenia, thrombocytopenia, pancytopenia, agranuloctosis). The first signs may be fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, nose and skin bleeding and bruising. In such cases, the patient should be advised to discontinue this medicinal product, to avoid any self-medication with analgesics or antipyretics and to consult a physician. |
| Immune System Disorders | | Hypersensitivity reactions consisting of [1] |
| | Uncommon | Urticaria and pruritus |
| | Very rare | Severe hypersensitivity reactions.Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaophylaxis, angioedema or severe shock). Exacerbation of asthma |
| | Not Known | Respiratory tract reactivity comprising asthma, bronchospasm or dyspnoea |
| Psychiatric disorders | Very rare | Psychotic reactions, depression |
| Nervous System Disorders | Uncommon | Central nervous disturbances such as headache, dizziness, sleeplessness, agitation, irritability or tiredness |
| | Very rare | Aseptic meningitis[3] |
| Eye disorders | Uncommon | Visual disturbances |
| Ear and labyrinth disorders | Rare | Tinnitus |
| Cardiac Disorders | Very rare<br><br>Not known | Cardiac failure, palpitations and oedema myocardial infarction<br><br>Kounis syndrome |

| System Organ Class | Frequency | Adverse Events |
|---|---|---|
| Vascular Disorders | Very rare | Hypertension, vasculitis |
| Gastrointestinal Disorders | Common | Gastrointestinal complaints such as abdominal pain, nausea and dyspepsia. Diarrhoea, flatulence, constipation, heartburn, vomiting and slight gastro-intestinal blood losses that may cause anaemia in exceptional cases. |
| | Uncommon | Gastrointestinal ulcers, perforation or GI bleeding, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4), gastritis |
| | Very rare | Oesophagitis, formation of intestinal diaphragm-like strictures, pancreatitis. |
| 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 cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis)<br>Alopecia |
| | Not known | Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).<br>Acute generalised exanthematous pustulosis (AGEP)<br>Photosensitivity reactions |
| Renal and Urinary Disorders | Rare<br><br><br>Not known | Kidney-tissue damage (papillary necrosis) and elevated urea concentrations in the blood may also occur rarely; elevated uric acid concentrations in the blood.<br>Ureteric colic, dysuria |

| System Organ Class | Frequency | Adverse Events |
|---|---|---|
| | | Renal tubular acidosis* |
| | 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. |
| Investigations | Rare | Decreased haemoglobin levels |
| Metabolism and Nutrition Disorders | Not Known | Decreased Appetite<br>Hypokalaemia |

Description of Selected Adverse Reactions

[1]Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reaction and anaphylaxis, (b) respiratory tract activity 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 toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme).

[2]The pathogenic mechanism of drug-Induced aseptic meningitis is not fully understood. However, the available data on NSAID-related aseptic meningitis points to an immune reaction (due to a temporal relationship with drug intake, and disappearance of symptoms after drug discontinuation). Of note, single cases of symptoms of aseptic meningitis (such as stiff neck, headache, nausea, vomiting, fever or clouding of consciousness ) have been observed during treatment with ibuprofen in patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease).

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: **www.mhra.gov.uk/yellowcard** or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

In children ibuprofen doses in excess of 400mg/kg may cause symptoms of toxicity whilst a risk of toxic effects should not be excluded with a dose above 100 mg/kg. In adults the dose response effect is less 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 drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. 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. 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. 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.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

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

Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans ibuprofen reduces inflammatory pain, swellings and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

The clinical efficiency of ibuprofen has been demonstrated in the symptomatic treatment of mild to moderate pain such as pain through toothache, headache, and in the symptomatic treatment of fever.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg 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

On oral application, ibuprofen is already partly absorbed in the stomach and then completely in the small intestine. Peak plasma levels occur 1-2 hours after

administration of ibuprofen in solid oral immediate-release formulation. Following hepatic metabolisation (hydroxylation, carboxylation), 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, plasma-protein binding about 99%.

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

The pharmacokinetic parameters of ibuprofen in children are comparable with those in adults.

### 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.

Following administration of maternotoxic doses, an increased incidence of malformations (ventricular septal defects) occurred in the progeny of rats.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Gelatin
Purified water
Glucose, liquid
Sucrose
Fumaric acid (E297)
Sucralose
Citric acid (E330)
Acesulfame K (E950)
Disodium edetate
Glycerol
Orange Flavour
Red iron oxide (E172)
Yellow iron oxide (E172)

*Capsule printing*
Titanium dioxide (E171),
Propylene glycol,
HPMC 2910/hypromellose 3cP (E464)

*Processing Aids*
Medium Chain Triglycerides
Lecithin (derived from soya)
Stearic acid

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months.

### 6.4 Special precautions for storage

Do not store above 25°C.

### 6.5 Nature and contents of container

Blisters formed of PVC/PE/PVdC/Al packed into cartons.
Each carton may contain 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, or 32 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 Healthcare (UK) Ltd

103-105 Bath Road, Slough, Berkshire, SL1 3UH, UK

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0723

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14/07/2025

## 10 DATE OF REVISION OF THE TEXT

14/07/2025