Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nurofen for Children 60 mg Suppositories Age 3 months to 2 years

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains: Ibuprofen 60 mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Suppository
White or yellowy-white cylindrical suppositories

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Reduction of fever and relief of mild to moderate pain, such as teething pain, toothache, headache, sprains and strains and to ease the pain of sore throats and earache.
Relief of pain and fever associated with colds and influenza.

4.2 Posology and method of administration

Posology

For short term use only.

Do not use in children under 3 months of age without medical advice.

The maximum total daily dose of Nurofen for Children 60 mg Suppositories Age 3 months to 2 years is 20-30 mg/Kg of body weight, administered in three to four single doses. This can be achieved as follows:

Age (weight)	Single dose	Daily dose
3-9 months (6.0–8.0 Kg)	1 suppository	3 times a day, leaving 6-8 hours between doses
9 months -2 years (8.0–12.0 Kg)	1 suppository	4 times a day, leaving 6 hours between doses

Do not use this product in children weighing less than 6 kg.

For children aged 3 – 5 months medical advice should be sought if symptoms worsen or not later than 24 hours if symptoms persist. If in children aged from 6 months this medicinal product is required for 3 days, or if symptoms worsen a doctor should be consulted.

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

Method of administration

For rectal use only.

4.3 Contraindications

Patients with severe hepatic failure, severe renal failure or severe heart failure (see section 4.4).

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 or other gastrointestinal disorders).

Hypersensitivity to ibuprofen or to any of the excipients listed in section 6.1.
Patients with a history of hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria), associated with acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs (NSAIDs).

During the last trimester of pregnancy (see section 4.6)

4.4 Special warnings and precautions for use

The use of Nurofen for Children 60mg Suppositories Age 3 months to 2 years with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to relieve symptoms.

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

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 any warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and 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 (aspirin) (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Nurofen for Children 60mg Suppositories Age 3 months to 2 years, 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 their condition may be exacerbated (see section 4.8 – undesirable effects).

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.

Cardiovascular and cerebrovascular effects
Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (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. $\leq$ 1200mg daily) is associated with an increased risk of myocardial infarction.

Cases of Kounis syndrome have been reported in patients treated with Nurofen for Children. 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 is required in patients with renal impairment (see section 4.3) since renal function may deteriorate. In patients with renal impairment, renal function should be monitored as it may deteriorate following the use of NSAIDs.

Caution is required in patients with hepatic impairment (see section 4.3 and 4.8)

Elderly patients are particularly susceptible to the adverse effects of NSAIDs. Prolonged use of NSAIDs in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

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

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) and acute generalised 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 occured within the first month of treatment. If signs and symptoms

suggestive of these reactions appear, ibuprofen should be withdrawn immediately, and an alternative treatment considered (as appropriate).

Masking of symptoms of underlying infections
Nurofen for Children can mask symptoms of infection, which may lead to the 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 Nurofen or Children 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.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. It is advisable to avoid use of Nurofen for Children 60mg Suppositories Age 3 months to 2 years in case of varicella.

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.

Bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease.

Caution is advised in patients with systemic lupus erythematosus as well as those with connective tissue disease (see section 4.8)

Caution is also required in patients with disorders of the anus or rectum.

There is a risk of renal impairment in dehydrated children.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen should be avoided in combination with:

Acetylsalicylic Acid (Aspirin): unless low-dose Acetylsalicylic Acid (Aspirin) (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see section 4.4). Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid (aspirin) on platelets aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding the extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional use (see section 5.1)

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

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

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

Anti-hypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics: 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 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. These interactions should be considered in patients taking ibuprofen concomitantly with ACE inhibitors or angiotensin II antagonists. 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. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Anti-coagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin (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 cardiac glycoside levels.

Lithium: decreased elimination of lithium.

Methotrexate: decreased elimination of methotrexate.

Cyclosporin: increased risk of nephrotoxicity with NSAIDs.

Aminoglycosides: reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations.

Probenecid: reduction in metabolism and elimination of NSAID and metabolites.

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

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 of 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.

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 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 section 4.3 and 5.3).

Breast-feeding
Ibuprofen and its metabolites can pass in very small concentrations (0.0008% of the maternal dose) into the breast milk. No harmful effects to infants are known, so it is not necessary to interrupt breast-feeding for short-term treatment with the recommended dose for mild to moderate pain and fever.

Fertility
See section 4.4 on Special Warnings and Precautions for use regarding female fertility

4.7 Effects on ability to drive and use machines

Nurofen for Children 60mg Suppositories Age 3 months to 2 years has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The list of the following adverse effects relates to those experienced with ibuprofen at OTC doses (maximum 1200mg ibuprofen per day), for short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

Adverse events which have been associated with ibuprofen are given below, tabulated by system organ class and frequency.
The frequencies are defined as follows:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1000 to <1/100)
Rare (≥1/10000 to <1/1000)
Very Rare (<1/10000)
Not known (cannot be estimated from the available data)
Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse Events
Blood and Lymphatic System Disorders	**Very rare**	**Haematopoietic disorders[1]**
Immune System Disorders	**Uncommon**	**Hypersensitivity reactions with urticaria and pruritus[2]**
	Very rare	**Severe hypersensitivity reactions, including facial, tongue and throat swelling, dyspnoea, tachycardia and hypotension (anaphylaxis, angioedema or severe shock)[2]**
Nervous System Disorders	**Uncommon**	**Headache**
	Very rare	**Aseptic meningits[3]**
Cardiac Disorders	**Very rare**	**Cardiac failure and oedema[4]**
	Not known	**Kounis syndrome**
Vascular Disorders	**Very rare**	**Hypertension[4]**
Respiratory, Thoracic and Mediastinal Disorders	**Very rare**	**Respiratory and tract reactivity compromising asthma, aggravated asthma, bronchospasm or dyspnoea[2]**
Gastrointestinal Disorders	**Uncommon**	**Abdominal pain, nausea and dyspepsia[5]**
	Rare	**Diarrhoea, flatulence, constipation and vomiting**
	Very rare	**Peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena and haematemesis[6]. Exacerbation of colitis and Crohn's disease[7]. Mouth ulceration and gastritis.**
Hepatobiliary Disorders	**Very rare**	**Liver disorder[8]** Cholestatic jaundice, hepatitis, elevation of serum enzymes.
Skin and Subcutaneous Tissue Disorders	**Uncommon**	**Skin rash[2]**
	Very rare	**Severe cutaneous adverse reactions (SCARS) (including erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis)[2]**
	Not known	**Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).** Acute generalised exanthematous pustulosis (AGEP). Photosensitivity reactions.
Renal and Urinary Disorders	**Very rare**	**Acute renal failure[9]**
Investigations	**Very rare**	**Haemoglobin decreased, urea renal clearance decreased.**
Infections and infestations	**Very rare**	**Exacerbation of infections related inflammation (e.g. development of necrotizing fasciitis), in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection.**

Description of Selected Adverse Reactions

[1] Examples include anaemia, leucopenia, thrombocytopenia, pancytopenia and agranulocytosis. First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

[2]Hypersensitivity reactions: These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity, including asthma, aggravated asthma, bronchospasm, and dyspnoea, or (c) various skin reactions, including pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses, including toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme.

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

[4]Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke), (see section 4.4).

[5]The adverse events observed most often are gastrointestinal in nature.

[6]Sometimes fatal, particularly in the elderly (see section 4.4).

[7]See section 4.4.

[8]Especially in long-term treatment.

[9]Decrease of urea excretion and oedema can occur. Papillary necrosis, especially in long-term use, and increased serum urea concentrations have been reported.

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

A dose in excess of 200mg/kg carries a risk of causing toxicity.

Symptoms of Overdosing

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, abdominal pain, or more rarely diarrhoea. Tinnitus, headache, nystagmus, blurred vision, hypotension and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as dizziness, drowsiness, loss of consciousness, 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 or overdose may result in renal tubular acidosis and hypokalaemia.

Therapeutic Measure in Overdosing

Patients should be treated symptomatically as required. Use supportive care where appropriate. Management should include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam, Give bronchodilators for asthma, No specific antidote is available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Anti-inflammatory and anti-rheumatic products, non-steroids, propionic acid derivative; ATC Code: M01AE01

Ibuprofen is an NSAID that has demonstrated its efficacy in the common animal experimental inflammation models by inhibition of prostaglandin synthesis. In humans, ibuprofen reduces inflammatory pain, swelling and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

The clinical efficacy of ibuprofen has been demonstrated in fever and in pain associated with headache, toothache and dysmenorrhoea. Furthermore it has been demonstrated in patients with pain and fever associated with cold and flu and in pain models such as sore throat, muscular pain, soft tissue injury, backache.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelets aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic properties

After rectal administration, ibuprofen is absorbed quickly and almost completely, and is rapidly distributed throughout the whole body.Median peak plasma concentrations are seen 0.75 hours after use of a 60 mg suppository.

Ibuprofen is extensively bound to plasma proteins.

Ibuprofen is metabolised in the liver to two major inactive metabolites and these, together with unchanged ibuprofen, are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete. The elimination half life is approximately 2 hours.

No special pharmacokinetic studies have been carried out in children. However, pharmacokinetic parameters of ibuprofen in children are comparable with those in adults.

5.3 Preclinical safety data

The toxicity of ibuprofen in animal experiments was observed as lesions and ulcerations in the gastrointestinal tract. Ibuprofen did not show a mutagenic potential in vitro and was not carcinogenic in rats and mice. Experimental studies have demonstrated that ibuprofen crosses the placenta, but there is not evidence of any teratogenic action.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hard Fat

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PE 40g/m^2/aluminium foil 45µm/lacquer 1.0 g/m^2

Pack size: 10 or 20 Suppositories. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

None.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA0979/032/007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th September 2008

Date of last renewal: 12th September 2013

10 DATE OF REVISION OF THE TEXT

January 2025