

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nurofen for Children Meltlets 100mg Orodispersible Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each orodispersible table contains ibuprofen 100 mg

Excipients with known effects:

Sodium 1.98 mg (0.09 mmol) per tablet

Aspartame 12 mg per tablet

Sorbitol less than 6 mg per tablet

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Orodispersible tablets

White to off-white round tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Reduction of fever and relief of mild to moderate pain, such as cold and flu symptoms, toothache, headache, sprains and strains and to ease the pain of sore throats and earache.

4.2 Posology and method of administration

Posology

For short term use only.

For pain and fever: The daily dosage of Nurofen for Children Meltlets is 20 to 30 mg of Ibuprofen/kg bodyweight in divided doses.

The recommended dose should not be exceeded.

Not suitable for children weighing less than 20kg.

This can be achieved as follows:

Body weight	Approximate Age	Recommended Dosage
20-30 kg	6 – 9 years	Initial dose 2 tablets, then if necessary 2 tablets every 4 – 6 hours. Do not exceed 6 tablets in a 24 hour period.
31-40 kg	10 -12 years	Initial dose 3 tablets, then if necessary 3 tablets every 4-6 hours. Do not exceed 9 tablets in a 24 hour period.

If in children aged from 6 years and in adolescents this medicinal product is required for more than 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 oral administration. Place a tablet on the tongue, allow it to dissolve and then swallow; no water is required.

4.3 Contraindications

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

Patients who have previously shown hypersensitivity reactions (e.g. asthma, bronchospasm, rhinitis, angioedema or urticaria) in response to ibuprofen, Acetylsalicylic Acid (Aspirin) 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) or other gastrointestinal disorders.

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

Severe heart failure, renal failure or hepatic failure (see section 4.4)

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 duration necessary to relieve symptoms.

If symptoms persist, worsen or new symptoms develop, patients should be advised to consult their doctor.

Do not exceed the stated dose.

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

Gastrointestinal effects: 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).

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 ibuprofen, the treatment should be withdrawn.

Respiratory: Bronchospasm may be precipitated in patients suffering from or with a 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, due to increased risk of aseptic meningitis (see section 4.8).

Cardiovascular and cerebrovascular 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 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. ≤ 1200 mg 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.

Renal: Renal impairment as renal function may deteriorate (see sections 4.3 and 4.8). There is a risk of renal impairment in dehydrated children and adolescents.

Hepatic: Caution is required in treating patients with hepatic impairment (see section 4.3 and 4.8).

Impaired female fertility: See section 4.6.

Severe cutaneous adverse reactions (SCARs):

Serious 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 occurred 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 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 for Children is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital setting, 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 Meltlets in case of varicella.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

It also contains 12 mg aspartame per tablet, which is a source of phenylalanine. Therefore, caution is required with patients with Phenylketonuria or who are intolerant to phenylalanine.

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 platelet 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 ibuprofen use.

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).

Ibuprofen should be used with caution in combination with:

Anti-coagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin or heparin (see section 4.4).

Anti-hypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics: NSAIDs may diminish the effects of these drugs.

In some patients with compromise 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 a coxib 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-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 glomerular filtration rate -GFR and increase plasma cardiac glycoside levels.

Lithium: decreased elimination of lithium.

Methotrexate: decreased elimination of methotrexate.

Ciclosporin: Increased risk of nephrotoxicity with NSAIDs.

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.

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.

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 (positive) 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 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 the pregnancy to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, ibuprofen is contraindicated during the third trimester of pregnancy (see section 4.3 and 5.3).

Breast-feeding

In limited studies, ibuprofen appears in the breast milk in very low concentrations and is unlikely to affect the breast fed infant adversely.

Fertility

Impaired female 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.

4.7 Effects on ability to drive and use machines

No adverse effects known.

4.8 Undesirable effects

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

Adverse events which have been associated with ibuprofen are given below, tabulated by system organ class and frequency.

Frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), very rare ($< 1/10,000$) and 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 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 meningitis ³
Cardiac Disorders	Very rare	Cardiac failure and oedema ⁴
	Not known	Kounis Syndrome

Vascular Disorders	Not known	Hypertension ⁴
Respiratory, Thoracic and Mediastinal Disorders	Not known	Respiratory tract reactivity compromising 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 . Mouth ulceration and gastritis
	Not known	Exacerbation of colitis and Crohn's disease ⁷
Hepatobiliary Disorders	Very rare	Liver disorder
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 ⁸
Investigations	Very rare	Haemoglobin 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

¹Examples 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.

³The 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, single cases of symptoms of aseptic meningitis (such as stiff neck, headache, nausea, vomiting, fever or disorientation) have been observed during treatment with ibuprofen in patients with existing auto-immune disorders (such as systemic lupus erythematosus and mixed connective tissue disease).

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 (for example myocardial infarction or stroke) (see section 4.4).

⁵ The most commonly observed adverse events are gastrointestinal in nature.

⁶ Sometimes fatal

⁷ See section 4.4

⁸Especially in long-term use, associated with increased serum urea and oedema. Also includes papillary necrosis.

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 children ingestion of more than 400mg/kg of ibuprofen may cause symptoms. 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, dizziness, occasionally excitation and disorientation, loss of consciousness 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.

Management

Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable, if necessary correction of serum electrolytes. 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 specific antidote is available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Ibuprofen is a propionic acid derivative, having analgesic, anti-inflammatory and antipyretic activity. The drug's therapeutic effects as a non-steroidal anti-inflammatory drug are thought to result from inhibitory activity on prostaglandin synthesis.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet 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

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring about 2.25 hours after administration of Nurofen For Children Meltlets. The elimination half life is approximately 2 hours. 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. When taken with food, peak plasma levels may be delayed.

Ibuprofen is extensively bound to plasma proteins and diffuses into the synovial fluid.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethylcellulose
Silicon dioxide

Hypromellose
Mannitol (E421)
Aspartame (E951)
Croscarmellose sodium
Magnesium stearate
Strawberry flavour
Contains: flavours
acacia gum
maltodextrin
sorbitol (E420)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The orodispersible tablets are packed in a cold blister pack. The blister pockets are formed from 60 µm PVC/ 45 µm aluminium/ 25 µm polyamide film heat sealed to the 20 µm aluminium foil blister lid. The blister trays are packed in a cardboard carton. Pack sizes: 12 and 18 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA0979/032/005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30 July 2004

Date of last renewal: 30 July 2009

10 DATE OF REVISION OF THE TEXT

January 2025