1 NAME OF THE MEDICINAL PRODUCT

Nurofen for Children Orange Baby
Nurofen for Children 3 months to 9 years Orange
Nurofen for Children Cold, Pain and Fever Orange Flavour 100mg/5mL Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ibuprofen 100 mg/5ml (equivalent to 2.0% w/v).

Excipients with known effect:

Maltitol Liquid: 2226 mg (2.26 g) per 5 ml

Wheat Starch* (contains gluten) 11 mg per 5 ml

For the full list of excipients, see section 6.1.
*present within orange flavouring

3 PHARMACEUTICAL FORM

Oral suspension.
An off-white, orange-flavoured, syrupy suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prescription and OTC: For the fast and effective reduction of fever, including post immunisation pyrexia and the fast and effective relief of the symptoms of colds and influenza and mild to moderate pain, such as a sore throat, teething pain, toothache, headache, minor aches and sprains.

4.2 Posology and method of administration

Posology

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

The recommended daily dose of the product is 20 – 30 mg per kg of body weight, divided into equal doses, with dosing intervals of 6 to 8 hours. Leave at least 4 hours between doses and do not take more than the recommended dose in 24 hours. The recommended dose should not be exceeded.

Using the spoon or syringe dosing device provided this can be achieved as follows:

Age	Body weight (kg)	Recommended Dosage
Infants 3-6 months weighing more than 5 kg	5-7.6	one 2.5ml dose may be taken 3 times in 24 hours
Infants 6-12 months	7.7-9	one 2.5ml dose may be taken 3 to 4 times in 24 hours
Children 1-3 years	10-16	one 5ml dose may be taken 3 times in 24 hours
Children 4-6 years	17-20	7.5ml (5ml +2.5ml spoonful) may be taken 3 times in 24 hours
Children 7-9 years	21-30	two 5ml doses may be taken 3 times in 24 hours

Not suitable for children under 3 months of age.

Do not use this product in children weighing less than 5 kg.

For infants aged 3-6 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 more than 3 days, or if symptoms worsen a doctor should be consulted.

Special patient groups:
• For children with Juvenile Rheumatoid Arthritis: The usual daily dose of up to 30 to 40 mg per kg of body weight, in three to four divided doses may be taken.
• For post-immunisation pyrexia: One 2.5 ml dose followed by one further 2.5 ml dose 6 hours later if necessary. Do not exceed two 2.5ml doses in 24 hours. If the fever is not reduced, consult a doctor.

Method of administration

For oral administration.

For patients with sensitive stomachs the product can be taken with or after food.

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, rhinitis, angioedema or urticaria) in response to ibuprofen, acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs (NSAIDs).

Active or a 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 NSAIDs therapy.

Severe hepatic failure, renal failure or heart failure (See section 4.4, Special warnings and precautions for use).

Last trimester of pregnancy (See section 4.6 Pregnancy and lactation).

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, due to increased risk of aseptic meningitis (see section 4.8)

Cardiovascular and cerebrovascular effects:

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 (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 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. ≤ 1200mg daily) is associated with an increased risk of myocardial infarction.

Renal:

Renal impairment as renal function may further deteriorate (See section 4.3 Contraindications and Section 4.8 Undesirable effects)

There is a risk of renal impairment in dehydrated children (See section 4.3 and 4.8)

Hepatic:

Hepatic dysfunction (See section 4.3 and 4.8)

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 effects:

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their conditions may be exacerbated (see section 4.8).

Gastrointestinal 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.

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.

<u>Severe cutaneous adverse reactions (SCARs)</u>

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 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.

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

This medicine 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.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. Thus, it is advisable to avoid use of Nurofen for Children in case of varicella.

This product contains Maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine. This medicinal product contains 9.08 mg sodium per 5 ml, equivalent to 0.45% of the WHO recommended maximum daily intake of 2 g of sodium for an adult.

The label will include:

Read the leaflet before use.

Warning: do not take more medicine than the label tells you to.

Do not give this product if the child:

- is under 3 months old or weighs less than 5 kg
- has (or has had two or more episodes of) a stomach ulcer, perforation or bleeding
- is allergic to ibuprofen or any other ingredient of the product, aspirin or other related painkillers, or fructose
- is taking other NSAID painkillers, or aspirin with a daily dose above 75mg

Consult a doctor or pharmacist before use for:

- someone who has or had asthma, diabetes, high cholesterol, high blood pressure, a stroke, heart, liver, kidney or bowel problems; is dehydrated; has chicken pox
- smokers
- pregnant, breastfeeding or women trying to get pregnant
- elderly

You must consult a doctor if symptoms persist or worsen, or if the medicine is needed:

- for more than 24h for a child of 3 to 6 months
- for more than 3 days for a child over 6 months

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 aspirin (not above 75mg 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 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 (see section 5.1).

- *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)

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 and Angiotensin II Antagonists) and diuretics: NSAIDs may diminish the effect of these drugs. 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 GFR and increase plasma glycoside levels.

Lithium: There is evidence for potential increases in plasma levels of lithium.

Methotrexate: There is a potential for an increase in plasma levels of 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 (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, Nurofen for Children 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, Nurofen for Children should not be given unless clearly necessary. If Nurofen for Children 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 Nurofen for Children for several days from gestational week 20 onward. Nurofen for Children 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), which may progress to renal failure with oligo-hydroamniosis;

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, Nurofen for Children is contraindicated during the third trimester of pregnancy.

Breast-feeding

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

Fertility

See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

None expected at recommended doses and duration of therapy.

4.8 Undesirable effects

The following list of adverse effects relates to those experienced with ibuprofen at OTC doses (maximum 1200 mg 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 (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000), 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. The most commonly observed adverse events are gastrointestinal in nature.

System Organ Class	Frequency	Adverse Events
Blood and Lymphatic System Disorders	Very rare	Haematopoietic disorders, anaemia, leucopenia, thrombocytopenia, pancytopenia and agranulocytosis[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	Not known Not known	Cardiac failure and oedema[4] Kounis syndrome
Vascular Disorders	Not known	Hypertension[4]
Respiratory, Thoracic and Mediastinal Disorders	Not known	Respiratory tract reactivity comprising 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. 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) (Stevens-Johnson Syndrome, erythema multiforme, exfoliative dermatitis and toxic epidermal necrolysis[2])
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Acute generalized exanthematous pustulosis (AGEP) Photosensitivity reactions
Renal and Urinary Disorders	Very rare	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema[8]

Investigations	Very rare	Haemoglobin decreased
Infections and infestations	Not known	Exacerbation of infections related inflammation has been described, in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection.

Description of Selected Adverse Reactions

[1] 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, 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 2400 mg 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.

[7] See section 4.4.

[8] Especially 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 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 ingestion of more than 400 mg/kg 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, 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.

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.

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: Antinflammatory and anti-rheumatic products,

non-steroids, propionic acid derivative; **ATC Code:** M01AE01

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.

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 dosing (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 use.

Clinical evidence demonstrates that:

- 5 mg/kg of ibuprofen can provide up to 6 hour fever relieving effect

- 6 mg/kg of ibuprofen and above can provide up to 8 hour fever relieving effect
- 5 mg/kg of ibuprofen and above can provide up to 8 hour pain relieving effect

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body. The excretion is rapid and complete via the kidneys.

Maximum plasma concentrations are reached 45 minutes after ingestion if taken on an empty stomach. When taken with food, peak levels are observed after 1 to 2 hours. These times may vary with different dosage forms.

The half-life of ibuprofen is about 2 hours.

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

5.3 Preclinical safety data

There are no preclinical safety data of relevance to the consumer.

6.1 List of excipients

Citric acid
Sodium citrate
Sodium chloride
Sodium saccharin
Domiphen bromide
Purified water
Polysorbate 80
Maltitol liquid
Xanthan gum
Orange flavour (contains natural & artificial flavourings, maltodextrin (wheat starch (contains gluten)), modified starch E1450 (maize), Arabic gum E414) Glycerol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

100 ml - 3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Amber-coloured polyethylene terephthalate (PET) bottle with a child-resistant closure fitted with a low density polyethylene liner. The bottle contains 100 ml of product. A double-ended spoon with measures of 2.5 ml and 5 ml will be provided.
OR
Amber-coloured polyethylene terephthalate (PET) bottle with a child-resistant closure fitted with a low density polyethylene liner. The bottle contains 100 ml of product. A syringe composed of a polypropylene barrel and a PE piston with measures of 2.5 ml and 5 ml will be provided.

Not all pack sizes will be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Healthcare (UK) Ltd
Slough
SL1 4AQ

8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0668

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

5 August 2004

10 DATE OF REVISION OF THE TEXT

06/02/2025