NUROFEN FOR CHILDREN CHEWABLE CAPSULES 100mg

Prescribing Information

1. NAME OF THE MEDICINAL PRODUCT

Nurofen for children chewable capsules 100mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable capsule, contains 100 mg Ibuprofen.

Excipient with known effect:

Glucose, 358.3 mg per chewable capsule

Sucrose, 251.6 mg per chewable capsule

Soya Lecithin, 0.01mg 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 “N100” print in white ink.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the reduction of fever and the relief of 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 short term use only.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

For pain & fever : The daily dosage of Nurofen for children chewable capsules 100mg aged 7 years old and older is 5 to 10 mg/kg ORALLY every 6 to 8 hours as needed MAX 4 doses/day. Children with identical ages can have significantly different weights. Therefore, try to obtain the weight of the child and determine the dosage by weight. Only if you cannot find the child's weight determine the dosage according to age.

Dosing chart

Weight	**Age**	**Dosage**	**Num. of Times in 24 hours**
20-29 kg	7-9 years	1-2 chewable capsules	3-4 times
30-40 kg	10-12 years	2-3 chewable capsules	
>40 kg	>12 years	2-4 chewable capsules	

Doses should be given approximately every 6 to 8 hours, (or with a minimum of 6 hours between each dose if required).
Not suitable for children under 7 years of age.
Adults and Children above 12 years old: Do not take more than 1200mg (12 chewable capsules) in any 24 hour period.
If in children 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. The product should be chewed before swallowing.
For patients with sensitive stomachs the product can be taken with or after food.

4.3 Contraindications

Hypersensitivity to the active substance (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 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).

History of upper 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 – Fertility, Pregnancy and lactation).

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

4.4 Special warnings and precautions for use

Masking of symptoms of underlying infections :
Nurofen for children chewable capsules 100mg 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 chewable capsules 100mg 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.

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 Undesirable effects).
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 Contraindications and Section 4.8 Undesirable effects).
There is a risk of renal impairment in dehydrated paediatric patients.
Hepatic:
Hepatic dysfunction (See section 4.3 Contraindications and Section 4.8 Undesirable effects).
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 Ibuprofen.
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, 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.

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 any time 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 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 aspirin (see section 4.5).

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

Severe skin reactions:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest

risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Ibuprofen should be discontinued at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of Ibuprofen in case of varicella.

Platelet function:

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.

This product contains glucose. Patients with rare hereditary problems of galactose intolerance e.g. galacotosaemia, or 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:

- **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 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.
  In particular, concomitant use of potassium-sparing diuretics may increase the risk of hyperkalaemia.

- **Corticosteroids:** as these may increase the 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 and phenytoin:** There is evidence for potential increases in plasma levels of these medicinal products 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.

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 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.

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.

Rarely, taking NSAIDs after the 20th week of pregnancy may cause impaired renal function of the fetus, which may cause low levels of amniotic fluid (oligohydramnios).

The effects were observed after days to weeks of treatment. However, in rare cases, low levels of amniotic fluid were observed already after 48 hours of taking NSAIDs. In most cases, oligohydramnios passed with the treatment discontinuation.

Using NSAIDs after the 20th week of pregnancy should be limited. If it was decided that the benefit outweighs the risk for the fetus and the treatment with the medicine is essential after the 20th week of pregnancy, the lowest effective dose should be used for the shortest possible period.

Referring the patient to ultrasound scan should be considered, in order to estimate the amount of amniotic fluid when the treatment with therapeutic dosage of these medicines exceeding 5 days and stopping the treatment if low levels of amniotic fluid is detected.

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

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, 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, 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 (see section 4.2).

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.

See section 4.4 regarding female fertility.

4.7 Effects on ability to drive and use machines

Ibuprofen has no expected influence at recommended doses and duration of therapy.

4.8 Undesirable effects

Hypersensitivity reactions have been reported and these may consist of:

(a) Non-specific allergic reactions and anaphylaxis

(b) Respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea

(c) Assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

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

Hypersensitivity reactions:

Uncommon: Hypersensitivity reactions with urticaria and pruritus.

Very rare: severe hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension, (anaphylaxis, angioedema or severe shock).

Exacerbation of asthma and bronchospasm.

Gastrointestinal:

The most commonly observed adverse events are gastrointestinal in nature.

Uncommon: abdominal pain, nausea, dyspepsia

Rare: diarrhoea, flatulence, constipation and vomiting.

Very rare: peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis. Exacerbation of colitis and Crohn's disease (see section 4.4).

Nervous System:
Uncommon: Headache
Very rare: Aseptic meningitis – single cases have been reported very rarely.

Renal:
Very rare: Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Hepatic:
Very rare: liver disorders.

Haematological:
Very rare: Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

Skin:
Uncommon: Various skin rashes
Very rare: Severe forms of skin reactions such as bullous reactions including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis can occur
Frequency not known: Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome). Acute generalised exanthematous pustulosis (AGEP).
Photosensitivity reactions.

Immune System:
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 (See section 4.4)

Cardiovascular and Cerebrovascular:
Oedema, hypertension and cardiac failure, have been reported in association with NSAID treatment.
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).

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

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.

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

ATC code: M01A E01 Propionic acid derivative NSAID

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.

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

The sub-chronic and chronic toxicity of ibuprofen in animal experiments showed up mainly in form of 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 an inhibition of ovulation in rabbits and impaired implantation in various animal species (rabbit, rat, mouse). Experimental studies in rats and rabbits have shown that ibuprofen crosses the placenta. Following administration of maternotoxic doses, an increased rate of malformations (ventricular septal defects) occurred in the progeny of rats.

6. PHARMACEUTICAL P ARTICULARS

6.1 List of excipients

Purified water
Glucose, liquid
Sucrose
Gelatin

Glycerin
Fumaric acid
Citric acid
Sucralose
Natural Orange Flavour*
Acesulfame K
Disodium edentate
Red iron oxide
Yellow iron oxide
*The flavour contains: (R)-p-mentha-1,8-diene (d-limonene), Ethyl acetate and Alpha-Pinene
Capsule printing
Opacode WB White NS-78-18011
Processing Aids
Medium Chain Triglycerides
Isopropyl alcohol
Lecithin ~~(derived from soya)~~
Stearic acid

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Blisters formed of PVC/PE/PVdC/Al packed into cartons.

Each carton contains 12 chewable capsules.

6.6 Special precautions for disposal

No special requirements.

7. MANUFACTURER

Reckitt Benckiser Healthcare International Limited, Nottingham, United Kingdom

8. REGISTRATION HOLDER

Reckitt Benckiser (Near East) Ltd.,
6 Hanagar St., Hod-Hasharon

9. REGISTRATION NUMBER

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