

MODULE 1.3.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

PROPRIETARY NAME AND DOSAGE FORM:

NUROFEN® for Children SUGAR FREE

Suspension

COMPOSITION:

Each 5 ml contains ibuprofen 100 mg

Other ingredients include: citric acid monohydrate, domiphen bromide, glycerol, maltitol liquid, polysorbate 80, purified water, sodium chloride, sodium citrate, sodium saccharin, orange flavour 2M16014 and xanthan gum.

Sugar free.

Contains sweetener (maltitol 44,5 % w/w and sodium saccharin 0,2 % w/w)

Contains preservatives: domiphen bromide 0,01 % m/v.

PHARMACOLOGICAL CLASSIFICATION

A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

NUROFEN® for Children SUGAR FREE has analgesic, antipyretic and anti-inflammatory properties.

Pharmacokinetic properties

NUROFEN® for Children SUGAR FREE is absorbed rapidly, bound avidly to protein, and undergoes hepatic metabolism (90 % is metabolised to hydroxylate or carboxylate derivatives) and renal excretion of metabolites. The half-life is about 2 hours.

INDICATIONS

For the relief of symptoms of fever, pain and inflammation, associated with cold and flu, a sore throat, earache, headache, dental pain and minor aches and sprains.

CONTRAINDICATIONS

- Hypersensitivity to any of the ingredients of **NUROFEN® for Children SUGAR FREE**, including excipients (see COMPOSITION).
- Use of **NUROFEN® for Children SUGAR FREE** is contra-indicated in patients with heart failure.
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs including **NUROFEN® for Children SUGAR FREE**.
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Severe impairment of liver and renal function.
- Pregnancy in the third trimester (see HUMAN REPRODUCTION).
- Hypersensitivity to Ibuprofen, aspirin or any other non-steroidal anti-inflammatory agent. Because of the possibility of cross-sensitivity due to structural relationships which exist among non-steroidal anti-inflammatory medicines, acute allergic reactions may be more likely to occur in patients who have exhibited allergic reactions to these compounds.
- Aspirin-induced nasal polyps associated with bronchospasm.

- Uncontrolled asthma.
- Children under the age of one year.
- Porphyria.
- Concomitant treatment with lithium (see INTERACTIONS).
- Concomitant treatment with digoxin (see INTERACTIONS).

WARNINGS AND SPECIAL PRECAUTIONS

Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with **NUROFEN® for Children SUGAR FREE** therapy. In view of the **NUROFEN® for Children SUGAR FREE**'s inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including **NUROFEN® for Children SUGAR FREE**, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.

The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of **NUROFEN® for Children SUGAR FREE**, in patients with a history of ulcers, and the elderly (see CONTRAINDICATIONS).

When gastrointestinal bleeding or ulceration occurs in patients receiving **NUROFEN® for Children SUGAR FREE**, treatment with **NUROFEN® for Children SUGAR FREE** should be stopped.

NUROFEN® for Children ORANGE FREE should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

DRESS:

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such **NUROFEN® for Children SUGAR FREE**. Some of these events have been fatal or life threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue **NUROFEN® for Children SUGAR FREE** and evaluate the patient immediately.

Dermatological effects:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported. Patients appear to be at highest risk of 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 **NUROFEN® for Children SUGAR FREE**.

NUROFEN® for Children SUGAR FREE should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Pregnancy:

Regular use of NSAIDs such as **NUROFEN® for Children SUGAR FREE** during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus *in utero*, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased.

Respiratory:

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

Other NSAIDs:

The use of **NUROFEN® for Children ORANGE FREE** with concomitant NSAIDs including cyclooxygenase- 2 selective inhibitors should be avoided (see INTERACTIONS).

SLE and mixed connective tissue disease:

Systemic lupus erythematosus and mixed connective tissue disease, due to increased risk of aseptic meningitis (see SIDE EFFECTS).

Cardiovascular and cerebrovascular effects:

Caution 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 such as **NUROFEN® for Children SUGAR FREE**.

Renal:

There is a risk of renal impairment in dehydrated children and adolescents (CONTRAINDICATIONS AND SIDE EFFECTS).

Hepatic:

Hepatic dysfunction (see CONTRAINDICATIONS AND SIDE EFFECTS).

Gastrointestinal effects (GI):

NSAIDs, such as **NUROFEN® for Children SUGAR FREE**, 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 SIDE EFFECTS).

Gastrointestinal bleeding, peptic ulceration or perforation which can be fatal, has been reported with all NSAIDs including **NUROFEN® for Children SUGAR FREE** at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, peptic ulceration or perforation is higher with increasing **NUROFEN® for Children SUGAR FREE** doses, in patients with a history of peptic ulcer, particularly if complicated with haemorrhage or perforation (see CONTRAINDICATIONS) and in the elderly. These patients should commence treatment on the lowest dose available.

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding).

Caution should be advised in patients receiving concomitant medicines 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 INTERACTIONS).

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

Complications with infections:

Varicella can be at the origin of serious cutaneous and soft tissues infectious complications. NSAIDs such as **NUROFEN® for Children SUGAR FREE** increase the risk of worsening of these infections. Thus, it is advisable to avoid use of **NUROFEN® for Children SUGAR FREE** in case of varicella.

NUROFEN® for Children SUGAR FREE should be discontinued in patients who experience blurred or diminished vision, or changes in colour vision. Patients with collagen disease may be at increased risk of developing aseptic meningitis.

Masking of symptoms of underlying infections:

NUROFEN® for Children SUGAR FREE 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 pain or fever in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Impaired female fertility:

There is limited evidence that medicines which inhibit cyclo-oxygenase/ prostaglandin synthesis such **NUROFEN® for Children SUGAR FREE** as may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

Effects on ability to drive and use machines:

No adverse effects known.

Sugar:

Patients with the rare hereditary condition of maltitol intolerance should not take

NUROFEN® for Children SUGAR FREE.

INTERACTIONS:

NUROFEN® for Children ORANGE FREE should be avoided in combination with:

- **Aspirin:** unless low-dose aspirin not more than 75 mg has been advised by a doctor, as this may increase the risk of adverse reactions (see WARNINGS AND SPECIAL PRECAUTIONS). **NUROFEN® for Children SUGAR FREE** may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly.
- **Other NSAIDs including cyclooxygenase- 2 selective inhibitors:** concomitant use of two or more NSAIDs should be avoided as this may increase the risk of adverse effects (see WARNING AND SPECIAL PRECAUTIONS)

NUROFEN® for Children SUGAR FREE should be used with caution in combination with:

- **Anti-coagulants:** **NUROFEN® for Children SUGAR FREE** may enhance the effects of anti-coagulants, such as warfarin (see WARNING AND SPECIAL PRECAUTIONS).
- **Anti-hypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics:** **NUROFEN® for Children SUGAR FREE** may diminish the effects of these medicines. Diuretics can increase the risk of nephrotoxicity of **NUROFEN® for Children SUGAR FREE**.
- **Corticosteroids:** increased risk of gastrointestinal ulceration or bleeding (see WARNING AND SPECIAL PRECAUTIONS).
- **Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs):** increased risk of gastrointestinal bleeding (see WARNINGS AND SPECIAL PRECAUTIONS).
- **Digoxin:** **NUROFEN® for Children SUGAR FREE** may exacerbate cardiac failure, reduce renal function and increase plasma digoxin levels.

- **Lithium:** there is evidence for potential increases in plasma levels of lithium (see CONTRAINDICATIONS).
- **Methotrexate:** there is a potential for an increase in plasma levels of methotrexate.
- **Ciclosporin:** increased risk of nephrotoxicity.
- **Mifepristone:** **NUROFEN® for Children SUGAR FREE** should not be used for 8-12 days after mifepristone administration as **NUROFEN® for Children SUGAR FREE** can reduce the effect of mifepristone.
- **Tacrolimus:** possible increased risk of nephrotoxicity when **NUROFEN® for Children SUGAR FREE** are given with tacrolimus.
- **Zidovudine:** increased risk of haematological toxicity when **NUROFEN® for Children SUGAR FREE** is given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in haemophiliacs receiving concurrent treatment with zidovudine and **NUROFEN® for Children SUGAR FREE**.
- **Quinolone antibiotics:** animal data indicate that NSAIDs including **NUROFEN® for Children SUGAR FREE** can increase the risk of convulsions associated with quinolone antibiotics. Patients taking **NUROFEN® for Children SUGAR FREE** and quinolones may have an increased risk of developing convulsions.

HUMAN REPRODUCTION:

Pregnancy:

NUROFEN® for Children SUGAR FREE should be avoided during the first and second trimesters of pregnancy.

During the third trimester, the use of **NUROFEN® for Children SUGAR FREE** is contraindicated (see CONTRAINDICATIONS).

Lactation:

NUROFEN® for Children SUGAR FREE is not recommended during breastfeeding as ibuprofen is excreted in breastmilk.

Fertility:

NUROFEN® for Children SUGAR FREE may impair female fertility by an effect of ovulation. This is reversible upon withdrawal of treatment.

DOSAGE AND DIRECTIONS FOR USE:

Use the lowest effective dose for the shortest possible duration of treatment

The dosage of **NUROFEN® for Children SUGAR FREE** is 20 mg/kg of body weight per day given in divided doses.

Do not give to children under 12 months of age unless on prescription from a doctor.

Children:

Pain

Initial dose 5mg/kg body weight.

A second dose of 5 mg/kg may be given after 2 hours if pain is not controlled, thereafter 5 mg/kg every 6 hours.

DO NOT EXCEED 20 mg/kg of body weight per day.

Fever

5 mg/kg of body weight every 6 hours.

DO NOT EXCEED 20 mg/kg of body weight per day.

If fever persists for more than 3 days, a doctor should be consulted.

Using the 5 ml easy dosing syringe:

1. Push the syringe firmly into the plug (hole) in the neck of the bottle.

2. Shake the bottle well.
3. To fill the syringe, turn the bottle upside down. Whilst holding the syringe in place, gently pull the plunger down drawing the liquid to the correct mark on the syringe.
4. Turn the bottle the right way up and remove the syringe from the plug and bottle by gently twisting the syringe.



5. Place the end of the syringe into the child's mouth. Press the plunger slowly down to gently release the liquid.
6. After use replace the cap. Wash the syringe in warm water and allow to dry, store out of the reach of children.

Age	Bodyweight	Daily dosage in 5 ml spoonful
1 - 2 years	7 - 12 kg	2,5 ml (half medicine measure) up to 3-4 times daily
3 - 7 years	14 - 23 kg	2,5 - 5 ml (half to one medicine measure) up to 3-4 times daily
8 - 12 years	25 - 40 kg	10 ml (two medicine measures) up to 3-4 times daily

SIDE-EFFECTS

The following side-effects have been reported:

System organ class	Frequencies	Adverse event
Blood and lymphatic system disorders	Less frequent	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, neutropenia, pancytopenia, eosinophilia and agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.
Immune system disorders	Less frequent	Hypersensitivity reactions with urticaria and pruritus. Severe hypersensitivity reactions, including facial tongue and throat swelling, dyspnoea, tachycardia and hypotension (anaphylaxis, angioedema or severe shock).
	Not known	DRESS reaction.
Nervous system disorders	Less frequent	Headache, aseptic meningitis, dizziness, nervousness, tinnitus, depression, drowsiness, insomnia.
Eye disorders	Less frequent	Blurred vision, changes in visual colour perception, toxic amblyopia.
Cardiac disorders	Not known	Cardiac failure and oedema
Vascular disorders	Not known	Hypertension
Respiratory, thoracic and mediastinal disorders	Not known	Exacerbation of asthma and bronchospasm or dyspnoea.

System organ class	Frequencies	Adverse event
Gastrointestinal disorders	Less frequent	Abdominal discomfort or pain, nausea, diarrhoea, flatulence, constipation, vomiting, GI ulcers (sometimes with bleeding), GI perforation or gastritis.
	Not known	Exacerbation of colitis and Crohn's disease
Hepatobiliary disorders	Less frequent	Hepatotoxicity, abnormalities in liver function tests, hepatitis.
Skin and subcutaneous tissue disorders	Less frequent	Skin rashes, bullous reactions including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis.
	Not known	Acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions.
Renal and urinary disorders	Less frequent	Acute renal failure, cystitis, haematuria, interstitial nephritis, nephrotic syndrome.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms:

In children, the ingestion of more than 400 mg/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.

The most likely symptoms of over dosage are pain in upper, middle region of the stomach and nausea, vomiting and dizziness. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasional 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 clear airway and monitoring of cardiac and vital signs until stable.

If recently taken, washing out the stomach will remove any unabsorbed ibuprofen.

Electrolytes may be corrected by intravenous infusions, if necessary. There is no specific antidote for ibuprofen.

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 bronchospasm.

IDENTIFICATION

An off-white coloured, orange-flavoured syrup suspension.

PRESENTATION

A 100 ml amber coloured, plastic bottle with a child-resistant, tamper-evident polyethylene cap.

STORAGE INSTRUCTIONS

Store below 25 °C.

Keep well closed and protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

31/2.7/0466

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF
REGISTRATION**

Reckitt Benckiser Pharmaceuticals (Pty) Ltd

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