MODULE 1.3.1.1. APPROVED PROFESSIONAL INFORMATION FOR NUROFEN FOR CHILDREN ORANGE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

NUROFEN® for Children Orange

Each 5ml suspension contains 100 mg of Ibuprofen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each 5 ml contains ibuprofen 100 mg

Contains sugar: maltitol 2226,0 mg per 5 ml

Contains sweetener sodium saccharin 10,0 mg per 5ml

Contains preservatives: domiphen bromide 0,5 mg per 5 ml

3. PHARMACEUTICAL FORM:

Suspension

An off-white, orange flavoured, syrupy suspension

4. CLINICAL PARTICULARS:

4.1. Therapeutic 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.

4.2. Posology and method of administration

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

The dosage of **NUROFEN® for Children Orange** 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:

- Push the syringe firmly into the plug (hole) in the neck of the bottle.
- Shake the bottle well.
- 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.
- Turn the bottle the right way up and remove the syringe from the plug and bottle by gently twisting the syringe.

- Place the end of the syringe into the child's mouth. Press the plunger slowly down to gently release the liquid.
- 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

Method of administration:

Oral

4.3. Contraindications

- Hypersensitivity to any of the ingredients of **NUROFEN® for Children Orange**, including excipients (see section 6.1).

- 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.
- Use of **NUROFEN® for Children Orange** is contra-indicated in patients with heart failure.
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs including **NUROFEN® for Children Orange.**
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Severe impairment of liver and renal function
- Pregnancy in the third trimester (see section 4.6.
- Aspirin-induced nasal polyps associated with bronchospasm.
- Uncontrolled asthma.
- Children under the age of one year (see section 4.2).
- Porphyria.
- Concomitant treatment with lithium (see section 4.5).
- Concomitant treatment with digoxin (see section 4.5).

4.4. Special warnings and 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 Orange** therapy. In view of the **NUROFEN® for Children Orange**'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 Orange**, 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 Orange**, in patients with a history of ulcers, and the elderly (see section 4.3).

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

NUROFEN® for Children Orange 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 Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such **NUROFEN® for Children Orange**. 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. Eosinophillia 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 Orange** 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 thefirst month of treatment. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to **NUROFEN® for Children Orange**. **NUROFEN® for Children Orange** 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 Orange** 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** 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 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 Orange**.

Renal:

There is a risk of renal impairment in dehydrated children and adolescents (see **sections 4.3 and 4.8**).

Renal tubular acidosis and hypokalaemia:

Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of ibuprofen at higher than recommended doses. Presenting signs and symptoms included reduced level of consciousness and generalised weakness. Ibuprofen induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

Hepatic:

Hepatic dysfunction (see **sections 4.3 and 4.8).**

Gastrointestinal effects (GI):

NSAIDs, such as **NUROFEN® for Children Orange**, 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**).

Gastrointestinal bleeding, peptic ulceration or perforation which can be fatal, has been reported with all NSAIDs including **NUROFEN® for Children Orange** 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 Orange** doses, in patients with a history of peptic 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 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 **section 4.5**).

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 Orange** increase the risk of worsening of these infections. Thus, it is advisable to avoid use of **NUROFEN® for Children Orange** in case of varicella.

NUROFEN® for Children Orange 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 Orange 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 Orange** as may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

Sugar:

Patients with the rare hereditary condition of maltitol intolerance should not take **NUROFEN® for Children Orange**.

4.5. Interaction with other medicines and other forms of interaction

NUROFEN® for Children Orange 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 **section 4.4**). **NUROFEN® for Children Orange** 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 **sections 4.4**)

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

- **Anti-coagulants**: **NUROFEN® for Children Orange** may enhance the effects of anti-coagulants, such as warfarin (see **section 4.4**).
- **Anti-hypertensives** (**ACE inhibitors and Angiotensin II Antagonists) and diuretics**: **NUROFEN® for Children Orange** may diminish the effects of these medicines. Diuretics can increase the risk of nephrotoxicity of **NUROFEN® for Children Orange.**
- **Corticosteroids**: increased risk of gastrointestinal ulceration or bleeding (see **section 4.4**).
- **Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs)**: increased risk of gastrointestinal bleeding (see **section 4.4**).
- **Digoxin**: **NUROFEN® for Children Orange** 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 **section 4.3**).
- **Methotrexate**: there is a potential for an increase in plasma levels of methotrexate.
- **Ciclosporin**: increased risk of nephrotoxicity.
- **Mifepristone**: **NUROFEN® for Children Orange** should not be used for 8-12 days after mifepristone administration as **NUROFEN® for Children Orange** can reduce the effect of mifepristone.
- **Tacrolimus**: possible increased risk of nephrotoxicity **NUROFEN® for Children Orange** is given with tacrolimus**.**
- **Zidovudine**: increased risk of haematological toxicity when **NUROFEN® for Children Orange** 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 Orange.**

- **Quinolone antibiotics**: animal data indicate that NSAIDs including **NUROFEN® for Children Orange** can increase the risk of convulsions associated with quinolone antibiotics. Patients taking **NUROFEN® for Children Orange** and quinolones may have an increased risk of developing convulsions.

4.6. Fertility, pregnancy and lactation

Pregnancy:

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

During the third trimester, the use of **NUROFEN® for Children Orange** is contraindicated (see **section 4.3**).

First and second trimester

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies raise concern about 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 %. 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 Orange** 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. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to **NUROFEN® for Children Orange** for several days from gestational week 20 onward. **NUROFEN® for Children Orange** should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

Second and third trimester:

During the third trimester of pregnancy, 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 hydro-amniosis.

At the end of pregnancy, the mother and the neonate may be exposed 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.

Therefore, **NUROFEN® for Children Orange** is contraindicated in the last trimester of pregnancy and should be avoided during the first six months of pregnancy.

Lactation:

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

Fertility:

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

4.7. Effects on ability to drive and use machines

NUROFEN® for Children Orange may cause blurred vision and dizziness, and therefore may have a negative influence on the ability to drive vehicles or operate machinery.

4.8. Undesirable 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,

System organ class	Frequencies	Adverse event
		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.
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.
	Not known	Renal tubular acidosis[1]
Metabolism and	Not known	Hypokalaemia[1]

System organ class	Frequencies	Adverse event
nutrition disorders		

[1]Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the ibuprofen component at higher than recommended doses.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

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.

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 **sections 4.4** and **section 4.8**).

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.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

A 2.7 Antipyretic or antipyretic and anti-inflammatory analgesics.

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

5.2. Pharmacokinetic properties

NUROFEN® for Children Orange 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.

6. PHARMACEUTICAL PARTICULARS:

6.1. List of excipients

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

6.2. Incompatibilities

N/A

6.3. Shelf life

36 months

6.4. Special precautions for storage

Store at or below 25 ºC.

Keep well closed and protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of containers

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

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

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Reckitt Benckiser Pharmaceuticals (Pty) Ltd.

8 Jet Park Road, Elandsfontein, 1601

South Africa

Consumer Care Line: 0861 11 1100

8. REGISTRATION NUMBER:

31/2.7/0466

9. DATE OF AUTHORISATION

Date of initial approval: 28 June 2000

10. DATE OF REVISION OF THE TEXT:

19 June 2025

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