MODULE 1.3.1.1. PROFESSIONAL INFORMATION

SCHEDULING STATUS

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PROPRIETARY NAME AND DOSAGE FORM

NUROFEN® for Children STRAWBERRY

Oral suspension

COMPOSITION:

Each 5 ml contains ibuprofen 100 mg

Other ingredients include: Citric acid monohydrate, glycerol, maltitol, polysorbate 80, purified water, sodium chloride, sodium citrate, sodium saccharin, strawberry flavour 500244E and xanthan gum.

Sugar free

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

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 STRAWBERRY has analgesic, antipyretic and anti-inflammatory properties.

Pharmacokinetic properties

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NUROFEN® for Children STRAWBERRY is absorbed rapidly, bound avidly to protein, and undergoes hepatic metabolism (90 % is metabolized 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 STRAWBERRY**, including excipients (see COMPOSITION).
- Hypersensitivity to Ibuprofen, aspirin or any other non-steroidal anti-inflammatory medicine. 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 STRAWBERRY is contra-indicated in patients with heart failure.
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs including **NUROFEN® for Children STRAWBERRY**
- Active or history of recurrent ulcer/haemorrhage/perforations.
- Severe impairment of liver and renal function.
- Pregnancy in the third trimester (see HUMAN REPRODUCTION).
- Aspirin-induced nasal polyps associated with bronchospasm.

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- 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

The lowest effective dose for the shortest duration necessary to control symptoms should be used (see GI and cardiovascular risks below).

Cardiovascular and cerebrovascular effects:

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 STRAWBERRY** therapy. In view of the **NUROFEN® for Children STRAWBERRY**'s inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with diclofenac after careful consideration.

Gastrointestinal effects:

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

Gastrointestinal bleeding, peptic ulceration or perforation which can be fatal, has been reported with all NSAIDs including **NUROFEN® for Children STRAWBERRY** at any time

during treatment, with or without warning symptoms or a previous history of serious GI events.

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding) When gastrointestinal bleeding or ulceration occurs in patients receiving

NUROFEN® for Children STRAWBERRY 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. 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~~ medicines such as aspirin (see INTERACTIONS).

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

DRESS:

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such **NUROFEN® for Children STRAWBERRY**. 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 STRAWBERRY** 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 fisrt month of treatment.

Severe skin reaction such as acute generalised exanthematous pustulosis (AGEP) has been reported. **NUROFEN® for Children STRAWBERRY** should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity .

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.

NUROFEN® for Children STRAWBERRY should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity (including pyrexia, erythema or many pustules).

Pregnancy:

Regular use of NSAIDs such as **NUROFEN® for Children STRAWBERRY** 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 STRAWBERRY** 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).

Renal:

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

Hepatic: Hepatic dysfunction (see CONTRAINDICATIONS AND SIDE EFFECTS).

Elderly:

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

Complications with infections:

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

NUROFEN® for Children STRAWBERRY 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.

NUROFEN® for Children STRAWBERRY 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 STRAWBERRY** 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 STRAWBERRY**.

INTERACTIONS

NUROFEN® for Children STRAWBERRY should be avoided in combination with:

unless low-dose aspirin not more than 75 mg daily has been advised by a doctor, as this may increase the risk of adverse reactions (see WARNINGS AND SPECIAL PRECAUTIONS).

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

Anti-coagulants: **NUROFEN® for Children STRAWBERRY** 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 STRAWBERRY may diminish the effects of these medicines. Diuretics can increase the risk of nephrotoxicity of **NUROFEN® for Children STRAWBERRY**.

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 STRAWBERRY** 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 STRAWBERRY** should not be used for 8-12 days after mifepristone administration as **NUROFEN® for Children STRAWBERRY** can reduce the effect of mifepristone.

Tacrolimus: possible increased risk of nephrotoxicity when **NUROFEN® for Children STRAWBERRY** are given with tacrolimus.

Zidovudine: increased risk of haematological toxicity when **NUROFEN® for Children STRAWBERRY** 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 STRAWBERRY**.

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

HUMAN REPRODUCTION

Pregnancy:

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

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

Lactation:

NUROFEN® for Children STRAWBERRY is not recommended during breastfeeding as ibuprofen is excreted in breastmilk in very low concentrations.

Fertility:

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

Do not give to children under 12 months of age.

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. A total dose of 20 mg/kg of body weight per day should not be exceeded.

Fever

5 mg/kg of body weight every 6 hours.

A total dose of 20 mg/kg of body weight per day should not be exceeded.

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

Adult:

The initial dose is 400 mg (20 ml), then if necessary 200 mg or 400 mg (10 ml or 20 ml) every four hours. A total dose of 1 200 mg (60 ml) in any 24 hours should not be exceeded.

Using the 5 ml easy dosing syringe:

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

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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

Do not give to children less than 7 kg or 12 months of age, except on the advice of your doctor. Use the lowest effective dose for the shortest possible duration of treatment.

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SIDE-EFFECTS

The following side-effects have been reported:

Table 1: Report side effects for NUROFEN® for Children STRAWBERRY

System organ class	Frequencies	Adverse event
Blood and lymphatic system disorders	Less frequent	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.
Immune system disorders	Less frequent	Hypersensitivity reactions consisting of urticaria and pruritus Severe hypersensitivity reactions. Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).
	Not known	Respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea.
Nervous system disorders	Less frequent	Headache, aseptic meningitis
Cardiac disorders	Not known	Cardiac failure and oedema
Vascular disorders	Not known	Hypertension

System organ class	Frequencies	Adverse event
Gastrointestinal disorders	Less frequent	Abdominal pain, nausea, dyspepsia, diarrhoea, flatulence, constipation and vomiting, peptic ulcer, perforation or gastrointestinal haemorrhage, melaena, haematemesis, sometimes fatal, particularly in the elderly. Ulcerative stomatitis, gastritis.
	Not known	Exacerbation of colitis and Crohn's disease
Hepatobiliary disorders	Less frequent	Liver disorders
Skin and subcutaneous tissue disorders	Less frequent	Various skin rashes, severe forms of skin reactions such as bullous reactions including Stevens- Johnson syndrome, erythema multiforme and toxic epidermal necrolysis can occur.
	Not known	DRESS syndrome, acute generalised exanthematous pustulosis (AGEP), photosensitivity reactions.
Renal and urinary disorders	Less frequent	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.
	Not known	Renal insufficiency

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, diarrhoea, gastrointestinal bleeding. In more serious poisoning, drowsiness, excitation, coma convulsions, metabolic acidosis prolongation of prothrombin time/INR, renal failure, liver damage, and asthma exarcebation may occur.

Management:

Management should be symptomatic and supportive and include the maintenance of clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal of 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, strawberry-flavoured syrup suspension.

PRESENTATION

A 100 ml or 150 ml, amber coloured, plastic bottle with a child-resistant, tamper-evident polyethylene cap.

STORAGE INSTRUCTIONS

Store at or below 25 ºC.

Keep well closed and protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

A40/2.7/0092

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

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