PROFESSIONAL INFORMATION FOR NUROFEN COLD AND FLU

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

NUROFEN COLD AND FLU Tablets

2. QUALITITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains ibuprofen 200 mg and pseudoephedrine hydrochloride 30 mg.

Sugar free

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets

Yellow, film coated tablet with CN printed in black on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NUROFEN COLD AND FLU is indicated for the relief of symptoms of colds and flu, including aches and pains, headaches, fever, sore throat, blocked nose and sinuses.

4.2 Posology and method of administration

Posology

Adults and children over 12 years: Initial dose: 2 tablets taken with water, then if necessary, 1 or 2 tablets every 4 to 6 hours. Do not exceed 6 tablets in any 24 hours.

If symptoms persist for more than 3 days, consult your doctor.

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

Paediatric population: Not to be given to children under 12 years (see section 4.3).

Method of administration

For oral administration with water

4.3 Contra-indications:

- Hypersensitivity to ibuprofen, pseudoephedrine or any of the excipients in the product.
- Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema, or urticaria) in response to acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs.
- NUROFEN COLD AND FLU is not recommended for use in children under the age of 12 years.
- NUROFEN COLD AND FLU should not be given to patients receiving monoamine oxidase inhibitors (MAOI) therapy or within 14 days of ceasing such therapy (see section 4.5)
- NSAIDs should not be given to patients with history of gastrointestinal bleeding or perforation (PUBs) related to previous NSAID use.
- Active or history of recurrent ulcer, haemorrhage or perforations.
- Severe coronary heart disease and cardiovascular disorders. Severe hypertension.
- Use of NSAID's is contraindicated in patients with heart failure, renal failure or hepatic failure (see section 4.4)

- Pregnancy and lactation (see section 4.6). Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus.

4.4 Special warnings and precautions for use

- NUROFEN COLD AND FLU should not be used without consulting a doctor or pharmacist if you are presently taking monoamine oxidase inhibitors or other medicines for depression, psychiatric or emotional conditions or hypertension.
- NUROFEN COLD AND FLU should not be given to patients with cardiovascular disease, hypertension, diabetes, hyperthyroidism, phaeochromocytoma, closed angle glaucoma, prostatic enlargement, occlusive vascular disorders or aneurysms.
- Anginal pain may be precipitated in patients with angina pectoris.
- 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 NSAID therapy.
- Asthma sufferers should only take NUROFEN COLD AND FLU after consulting their doctor.
- Caution is advised in those patients who are receiving coumarin anticoagulants or undergoing anaesthesia with haloginated anaesthetics.
- Patients who are sensitive to aspirin should not be given NUROFEN COLD AND FLU.
- **Elderly**: The elderly have an increased frequency of adverse reactions to NSAID's, especially gastrointestinal bleeding and perforation (PUBs) which may be fatal.
- The risk of gastrointestinal bleeding or perforation (PUBs) is higher with increasing doses of NSAID's, in patient with a history of ulcers, and the elderly.
- When gastrointestinal bleeding or ulceration occurs in patients receiving an NSAID treatment, treatment with NSAID's should be stopped.

- NSAID's 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.
- Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens Johnson syndrome, and toxic epidermal necrolysis have been reported. NSAID use should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity
- Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with ibuprofen and pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of Nurofen Cold & Flu should be discontinued and appropriate measures taken if needed.
- Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis (see section 4.8).
- Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other systems or ischaemic colitis develop.
- NUROFEN COLD AND FLU should be used with care in patients with impaired renal function (see section 4.3 and 4.8).
- Hepatic dysfunction (see sections 4.3 and 4.8)
- NUROFEN COLD AND FLU 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.

- To be used with caution in combination with antihypertensives including adrenergic neurone blockers & Beta blockers (see section 4.5). The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.
- To be used with caution with other sympathomimetic agents such as decongestants, appetite suppressants and amphetamine-like psycho-stimulants (see section 4.5).
- If hallucinations, restlessness, or sleep disturbances are experienced whilst taking NUROFEN COLD AND FLU, use of the product should be discontinued.
- Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.
- **Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) :**

  Drug Reaction witj Eosinophilia and Systemic Symptoms (DRESS) has been reportd in patients taking NSADIs such as NUROFEN COLD AND FLU. Some of these events have been fatal or life-threatening. DRESS typically, althought not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Ther clinical manifestations may include hepatitis, nephritis, haematologocal abnormalities, myocarditis, or myosiditis. Somestimes 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 COLD AND FLU and evaluate the patient immediately.

- Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus (see sections 4.3 and 4.6).

4.5 Interactions with other medicines and other forms of interaction

NSAIDs: Use of two or more NSAID's concomitantly could result in an increase in side effects.

Corticosteroids: Interaction between NSAID's and corticosteroids can cause an increased risk of gastrointestinal ulceration or bleeding (PUBs).

Anti-coagulants: The interaction between NSAID's and anti-coagulants may enhance the effect of anti-coagulants such as warfarin.

Anti-platelet agents and selective serotonin re-uptake inhibitors SSRIs: The interaction between NSAID's and anti-platelet agents and selective serotonin re-uptake inhibitors (SSRI's) can increase the risk of gastrointestinal bleeding.

Acetylsalicylic Acid (Aspirin): Unless low-dose Acetylsalicylic Acid (aspirin) (not above 75mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see section 4.4).

Antihypertensives and diuretics: NSAIDS and pseudoephedrine may diminish the effects of these medicines. Diuretics- can increase the risk of nephrotoxicity of NSAIDs.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Sympathomimetics such as pseudoephedrine may increase risk of dysrhythmias.

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

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 effects 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 of 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.

Monoamine oxidase inhibitors (MAOIs) and/or Reversible inhibitors of monoamine oxidase A (RIMAs): should not be given to patients receiving MAOI therapy or within 14 days of stopping treatment: increased risk of hypertensive crisis.

Ergot alkaloids (ergotamine & methysergide): increased risk of ergotism.

Other sympathomimetic agents such as decongestants, amphetamine-like psychostimulants and appetite suppressants: pseudoephedrine may potentiate their effects. Risk of hypertension (see section 4.3)

Oxytocin: risk of hypertension.

Anticholinergics: the effect of pseudoephedrine may be diminished/enhanced by tricyclic antidepressants.

Guanethidine, reserpine and methyldopa: the effect of pseudoephedrine may be diminished.

Moclobemide: risk of hypertensive crisis

4.6 Fertility, pregnancy and lactation

NUROFEN COLD AND FLU is contraindicated in pregnancy and breastfeeding.

Pregnancy

Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/foetal renal dysfunction and premature closure of the foetal ductus arteriosus.

Breast feeding:

Although ibuprofen appears in breast milk in very low concentrations, significant amounts of pseudoephedrine are secreted into breast milk and the use of NUROFEN COLD AND FLU during lactation should be avoided.

4.7 Effects on ability to drive and use machines

Since adverse reaction such as drowsiness has been reported in patients taking NUROFEN COLD AND FLU, patients should not drive, use machinery or perform any tasks that require concentration.

4.8 Undesirable effects

a) Summary of the safety profile

Most commonly observed adverse events are gastrointestinal in nature. Dyspepsia, gastro-intestinal intolerance, peptic ulceration and gastrointestinal bleeding/perforation may occur and is sometimes fatal.

b) Tabulated list of adverse reactions

Adverse events which have been associated with Ibuprofen and sympathomimetics including pseudoephedrine are given below, listed by system organ class and frequency.

System Organ Class	Frequency	Adverse Event
Blood and Lymphatic System Disorders	Less frequent	Haematopoietic disorders[1], agranulocytosis, thrombocytopenia
Immune System Disorders	Less frequent	Hypersensitivity with urticaria and pruritus[2], Severe hypersensitivity reactions including facial, tongue and throat swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock)[2]
Psychiatric Disorders	Not known	Insomnia, anxiety, restlessness, agitation, hallucination, nervousness, depression, drowsiness, giddiness
Nervous System Disorders	Less frequent	Headache, tremors Aseptic meningitis[3], muscular weakness

System Organ Class	Frequency	Adverse Event
Cardiac Disorders	Not known	Cardiac failure and oedema[4], sweating, tachycardia, arrhythmia, palpitations.
Vascular Disorders	Not known	Hypertension[4]
Respiratory, Thoracic and Mediastinal Disorders	Not known	Respiratory tract reactivity including exacerbation of asthma, bronchospasm or dyspnoea[2].
Gastrointestinal Disorders	Less frequent	Abdominal pain, nausea and dyspepsia[5] Diarrhoea, flatulence, constipation and vomiting Peptic ulcers, gastrointestinal perforation or gastrointestinal haemorrhage, melaena, haematemesis[6]. Mouth ulceration and gastritis.
	Not known	Dry mouth, exacerbation of colitis and Crohn's disease[7], ischaemic colitis.
Hepatobiliary Disorders	Less frequent	Liver disorders, abnormalities of liver function tests

System Organ Class	Frequency	Adverse Event
Skin and Subcutaneous Tissue Disorders	Not known	Hyperhidrosis Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) Severe skin reactions, including acute generalized exanthematous pustulosis (AGEP) Photosensitivity reactions
	Less frequent	Skin rashes[2] Bullous reactions, including Stevens-Johnson syndrome, erythema multiforme and toxic epidermal necrolysis[2]
Musculoskeletal and connective tissue disorders	Not known	Muscular weakness, tremors,
Renal and Urinary Disorders	Less frequent	Acute reversible renal failure[8]
	Not known	Urinary retention, difficulty in micturition
General and Administration	Not known	Chest pain, irritability, thirst

Site Conditions		
System Organ Class	**Frequency**	**Adverse Event**
Metabolism and Nutrition Disorders	Not known	Decreased Appetite
Investigations	Less frequent	Haemoglobin decreased
Eye disorders	Not known	Ischaemic optic neuropathy, blurred vision,
Ear and labyrinth disorders	Not known	Tinnitus

c) Description of Selected Adverse Reactions

[1] Examples include anaemia, leucopenia, thrombocytopenia, pancytopenia and agranulocytosis. 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 reaction and anaphylaxis, (b) respiratory tract reactivity including asthma, aggravated asthma, bronchospasm and dyspnoea, or (c) various skin reactions, including pruritis, urticaria, purpura, angioedema and, more rarely, severe forms of skin reactions such as exfoliative and bullous dermatoses (including toxic epidermal necrolysis can occur, Stevens-Johnson Syndrome and erythema multiforme).

[3] The pathogenic mechanism of drug-induced aseptic meningitis is not fully understood. However, the available data suggest that NSAID-related meningitis develops in individuals rendered susceptible by an underlying autoimmune disorder who were previously sensitized or

had a natural immunity to the drug. 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 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).

[5] The adverse events observed most often are gastrointestinal in nature.

[6] Sometimes fatal, particularly in elderly.

[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 medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms

Symptoms include headache, nausea, vomiting, thirst, anxiety, restlessness, irritability, fever, sinus tachycardia, sweating, dilated pupils, blurred vision, hallucinations, muscular weakness, tremors, hypertension, supraventricular and ventricular arrhythmia, convulsions, coma and respiratory depression.

Treatment

Treatment consists of correction of serum electrolytes. Symptomatic and supportive measures should be undertaken, particularly for control of cardiovascular and respiratory symptoms.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic Properties

Category and class: A 5.8 Preparations for the common cold, including nasal decongestants and antihistaminics.

Pharmacotherapeutic Group: Anti-inflammatory and antirheumatic products, propionic acid derivatives. Ibuprofen combinations. ATC Code: M01AE51

Ibuprofen is a non-steroidal compound with analgesic, anti-inflammatory and anti-pyretic properties.

Pseudoephedrine is a sympathomimetic agent and produces a vasoconstrictor effect.

Pseudoephedrine is used as a nasal and bronchial decongestant which acts by vasoconstriction to reduce oedema and nasal swelling.

5.2 Pharmacokinetic Properties

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1-2 hours after administration. The elimination half- life is approximately two hours.

Ibuprofen is metabolised in the liver to two major inactive metabolites and these together with unchanged ibuprofen are excreted by the kidney either as such or as conjugates. Excretion by the kidney is both rapid and complete.

Ibuprofen is extensively bound to plasma proteins.

Pseudoephedrine is absorbed from the gastrointestinal tract and is largely excreted in the urine unchanged, together with small amounts of a hepatic metabolite. It has an elimination half-life of several hours, which may be reduced by acidifying the urine.

5.3 Preclinical safety

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline

Croscarmellose sodium

Povidone

Calcium phosphate

Magnesium stearate

Hypromellose

talc

Mastercote yellow FA 01 56 (solids)

Black printing ink

Isopropyl alcohol

Water purified

Industrial methylated spirit

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

Cartons containing 12 and 24 blister packed tablets.

6.6 Special precautions for disposal and other handling

Not applicable

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Reckitt Benckiser Pharmaceuticals (Pty) Ltd

8 Jet Park Road

Elandsfontein

1601

8. REGISTRATION NUMBER:

Z/5.8/256

9. DATE OF FIRST OF AUTHORISATION/RENEWAL OF THE AUTHORISATION

1 June 1992

10. DATE OF REVISION OF THE TEXT

01 September 2023

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