NEW ZEALAND DATA SHEET

1. PRODUCT NAME

NUROFEN® Cold and Flu with Decongestant Tablets
Ibuprofen 200mg and pseudoephedrine hydrochloride 30mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The active ingredients in NUROFEN® Cold and Flu with Decongestant Tablets are Ibuprofen 200mg and pseudoephedrine hydrochloride 30mg.

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Nurofen Cold and Flu with Decongestant Tablet is a round tablet with a yellow-coloured film-coating inscribed with a black logo of a letter 'N' in a letter 'C''.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the temporary relief of the symptoms of colds and flu with associated congestion, including aches and pains, headaches, fever, sore throat, runny nose, blocked nose and sinuses.

4.2 Dose and method of administration

Adults and children 12 years and over:
Initial dose of 2 tablets then, if necessary, 1 or 2 tablets every 4 hours. Not to be given to children under 12 years.

Do not exceed 6 tablets in any 24 hour period.
Do not use for a period of more than three days at a time except on medical advice, in which case the patient should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment.

Children:
Do not use in children under 12 years.

4.3 Contraindications

- Known hypersensitivity to ibuprofen, pseudoephedrine hydrochloride or any of the excipients (see section 6.1).
- Hypersensitivity (e.g. asthma, rhinitis or urticaria) to aspirin or other non-steroidal anti-inflammatory drugs.
- Use with concomitant NSAIDs including cylco-oxygenase-2 specific inhibitors.
- Current receipt or receipt within the last two weeks, of therapy with monoamine oxidase inhibitors.
- As with other non-steroidal anti-inflammatory agents, ibuprofen should not be used in patients with active or a history of gastrointestinal bleeding or in the presence of peptic ulceration.
- History of ulcerative colitis, Crohn's disease, recurrent peptic ulceration or gastrointestinal hemorrhage (defined as two or more distinct episodes of proven ulceration or bleeding).

- Severe heart failure (NYHA IV).
- Severe liver failure.
- Severe renal failure (glomerular filtration below 30 mL/min).
- Conditions involving an increased tendency or active bleeding.
- Patients with serious coronary heart disease or cardiovascular disorders, heart failure, kidney or liver disease, tachycardia, hypertension, angina pectoris, hyperthyroidism, diabetes, phaeochromocytoma, closed angle glaucoma, prostatic enlargement, undergoing treatment of perioperative pain in setting of coronary artery bypass surgery (CABG).
- During the last trimester of pregnancy

4.4 Special warnings and precautions for use

Nurofen Cold and Flu with Decongestant should be administered with caution, and at the lowest effective dose, in patients with a history of gastrointestinal haemorrhage or ulcer, asthma and particularly those with aspirin-sensitive asthma and in patients with hepatic, renal or cardiac impairment. In patients with renal impairment, renal function should be monitored since it may deteriorate following the use of any NSAID.

Through concomitant consumption of alcohol, NSAID-related undesirable effects, particularly those that concern the gastrointestinal tract or the central nervous system, may be increased on use of NSAIDs.

Cardiovascular and cerebrovascular effects

Observational studies have indicated that NSAIDs may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day), 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 (≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with cardiovascular disease, history of atherosclerotic cardiovascular disease or cardiovascular risk factors may also be at greater risk.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Patients should be advised to remain alert for such cardiovascular events, even in the absence of previous cardiovascular symptoms. Patients should be informed about signs and/or symptoms of serious cardiovascular toxicity and the steps to take if they occur.

Fluid retention, hypertension and oedema have been reported in association with NSAID therapy. Patients taking antihypertensives with NSAIDs may have an impaired antihypertensive response.

Careful consideration should also be exercised before initiating long term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.

Nurofen Cold and Flu with Decongestant tablets should be used with caution in patients with hypertension (See also section 4.3 Contraindications).

Hypertension

NSAIDs may lead to onset of new hypertension or worsening of pre-existing hypertension and patients taking antihypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

Hepatic

Patients with impaired liver function or a history of liver disease who are on long term ibuprofen therapy should have hepatic function monitored at regular intervals. Ibuprofen has been reported to have a minor and transient effect on liver enzymes.

As with other NSAIDs elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged or may resolve with continued therapy. Meaningful elevations (three times the upper limit of normal) of ALT or AST occurred in controlled clinical trials in less than 1% of patients.

Patients should be advised to remain alert for hepatotoxicity and be informed about the signs and/or symptoms of hepatotoxicity (e.g. nausea, fatigue, lethargy, pruritus, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms).

Gastrointestinal effects

Ibuprofen should be used with extreme caution, and at the lowest effective dose, in patients with a history of gastro-intestinal haemorrhage or ulcer since their condition may be exacerbated.

NSAIDs 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 Adverse effects).

Gastrointestinal 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 gastrointestinal 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 Contraindications) and in the elderly. These patients should commence treatment on the lowest dose available.

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.

All NSAIDs can cause gastrointestinal discomfort and serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation which may increase with dose or duration of

use, but can occur at any time without warning. Upper GI ulcers, gross bleeding or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, as well as patients requiring concomitant low dose aspirin, or for other drugs likely to increase gastrointestinal risk (see section 4.5).

The concomitant administration of ibuprofen and other NSAIDs, including cyclooxygenase-2 (Cox-

2) selective inhibitors, should be avoided due to the increased risk of ulceration or bleeding (see section 4.5).

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 Interactions with Other Medicines).

When GI bleeding or ulceration occurs in patients receiving Nurofen Cold and Flu with Decongestant, the treatment should be withdrawn.

Ischaemic colitis
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 symptoms of ischaemic colitis develop.

Respiratory

Use of ibuprofen may precipitate bronchospasm in patients suffering from or with a previous history of bronchial asthma or allergic disease.

SLE and mixed connective tissue disease

Use of ibuprofen in patients with systemic lupus erythematosus (SLE) and mixed connective tissue disease can increase the risk of aseptic meningitis.

Renal

Caution should be used when initiating treatment with ibuprofen in patients with considerable dehydration. There is a risk of renal impairment especially in dehydrated children and adolescents.

The two major metabolites of ibuprofen are excreted mainly in the urine and impairment of renal function may result in their accumulation. The significance of this is unknown. NSAIDs have been reported to cause nephrotoxicity in various forms; interstitial nephritis, nephrotic syndrome and renal failure. In patients with renal, cardiac or hepatic impairment, those taking diuretics and ACE Inhibitors, and the elderly, caution is required since the use of NSAIDs may result in deterioration of renal function.

For patients with renal, hepatic or cardiac impairment, use the lowest effective dose, for the shortest possible duration and monitor renal function especially in long term treated patients.

Risk of renal impairment as renal function may deteriorate, especially in dehydrated children and adolescents (see section 4.3 Contraindications and section 4.8 Adverse Effects).

Dermatological

Serious skin reactions, some of them fatal including exfoliative dermatitis, Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS) (see Drug Reaction with Eosinophilia with Systemic Symptoms (DRESS) syndrome), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported very rarely in association with the use of NSAIDs (see section 4.8 Adverse Effects). 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. Nurofen Cold and Flu with Decongestant should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome
DRESS syndrome has been reported in patients taking NSAIDs. Some of these events have been fatal or life-threatening. DRESS syndrome 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 syndrome 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 the NSAID and evaluate the patient immediately.

In exceptional cases, varicella can be at the origin of serious cutaneous and soft tissue 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.

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with ibuprofen-containing products. The 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 and Flu with decongestant should be discontinued and appropriate measures taken if needed.

Infections and infestations

Exacerbation of skin infection-related inflammations (e.g. development of necrotising fasciitis) coinciding with the use of NSAIDs has been described. If signs of an infection occur or get worse during use of ibuprofen the patient is therefore recommended to go to a doctor without delay.

Ophthalmological effects

Adverse ophthalmological effects have been observed with NSAIDs; accordingly, patients who develop visual disturbances during treatment with ibuprofen should have an ophthalmological examination.

Use in the elderly

Ibuprofen should not be taken by adults over the age of 65 without careful consideration of co-morbidities and co-medications because of an increased risk of adverse effects, in particular heart failure, gastro-intestinal ulceration and renal impairment (see also section 4.3 Contraindications).

Paediatric use

Nurofen Cold and Flu with Decongestant is not recommended for use in children under 12 years. Nurofen for Children suspension should be used for this age group.

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics

The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist, an anti-inflammatory drug (NSAID or COX-2 inhibitor) and thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre- existing renal impairment.

Aseptic meningitis

Aseptic meningitis has been reported only rarely, usually but not always in patients with systemic lupus erythematosus (SLE) or other connective tissue disorders.

Haematological monitoring

Blood dyscrasias have been rarely reported. Patients on long term therapy with ibuprofen should have regular haematological monitoring.

Coagulation defects

Like other NSAIDs, ibuprofen can inhibit platelet aggregation. Ibuprofen has been shown to prolong bleeding time (but within the normal range), in normal subjects. Because this prolonged bleeding effect may be exaggerated in patients with underlying haemostatic defects, ibuprofen should be used with caution in persons with intrinsic coagulation defects and those on anti-coagulation therapy.

Masking signs of infection

As with other drugs of this class, ibuprofen may mask the usual signs of infection.

Withdrawal of concomitant steroid therapy

In order to avoid exacerbation of disease or adrenal insufficiency, patients who have been on prolonged corticosteroid therapy should have their therapy tapered slowly rather than discontinued abruptly when ibuprofen is added to the treatment program.

Effects on laboratory tests

No data available

4.5 Interaction with other medicines and other forms of interaction

This product must not be used in combination with:

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 4.3 Contraindications).

Monoamine oxidase inhibitors: Pseudoephedrine should not be given to patients receiving MAOI therapy or within 14 days of ceasing such treatment.

This product should be avoided in combination with:

Acetylsalicylic acid (Aspirin: Unless low-dose acetylsalicylic acid (Aspirin) (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions (see also section 4.4 Precautions). Experimental data suggest that ibuprofen may inhibit the effect of low-dose acetylsalicylic acid (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 setting 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.

This product should be used with caution in combination with:

Anticoagulants: Concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal haemorrhage. The mechanism of this interaction is not known but may involve increased bleeding from NSAID-induced gastrointestinal ulceration or an additive effect of NSAID inhibition of platelet function with the anticoagulant effect of warfarin.
Nurofen Cold and Flu with Decongestant should only be used in patients taking warfarin if absolutely necessary. Patients taking this combination should be closely monitored.

Antihypertensives and diuretics: The combined use of the three classes of drugs, diuretics, an ACE inhibiting drug (ACE inhibitor or angiotensin receptor antagonist) and an anti-inflammatory drug (NSAID or cyclooxygenase-2 (COX-2) inhibitor) all at the same time increases the risk of renal impairment. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.
NSAIDS and pseudoephedrine may diminish the effect of these drugs. Diuretics can also increase the risk of nephrotoxicity of NSAIDs.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding when co-administered with ibuprofen,

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels. Sympathomimetics such as pseudoephedrine may increase risk of dysrhythmias.

Methotrexate: there is a potential for an increase in plasma levels of methotrexate when co-administered with ibuprofen.

Cyclosporin: Increased risk of nephrotoxicity when co-administered with ibuprofen.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding when co-administered with ibuprofen.

Lithium: Ibuprofen has been shown to decrease the renal clearance and increase plasma concentrations of lithium. Lithium plasma concentrations should be monitored in patients on concurrent ibuprofen therapy.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

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.

Ergot alkaloids (ergotamine and methysergide): Increased risk of ergotism with concomitant use of sympathomimetics.

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 positive haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Other sympathomimetics (including appetite suppressants and amphetamine-like psychostimulants): Risk of hypertension with concomitant use of sympathomimetics.

Oxytocin: Risk of hypertension with concomitant use of sympathomimetics.

Anticholinergics (including tricyclic antidepressants): Enhanced effects of anticholinergic drugs, thus increasing risk of hypertension.

Ibuprofen may also interact with salicylates, probenecid, anti-diabetic medications and phenytoin.

The effect of pseudoephedrine may be diminished by antihypertensive agents such as methyldopa and may be diminished or enhanced by tricyclic antidepressants. Pseudoephedrine may also increase the possibility of arrhythmias in digitalised patients or in those receiving quinidine or tricyclic antidepressants.

4.6 Fertility, pregnancy and lactation

Effects on 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 on withdrawal of treatment. If ibuprofen is used by a woman attempting to conceive, the dose should be kept as low and duration of treatment as short as possible.

Use in pregnancy – Pregnancy Category C

Category C: Inhibition of prostaglandin synthesis by ibuprofen may adversely affect pregnancy and/or the embyro/foetal development. During the first and second trimester of pregnancy, this product should not be given unless clearly necessary, and is contraindicated in the third trimester.

During the third trimester, all prostaglandin synthesis inhibitors may expose the foetus to cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension) and renal dysfunction, which may progress to renal failure with oligohydramnios. At the end of pregnancy, prostaglandin synthesis inhibitors may expose the mother and the neonate to possible prolongation of bleeding time and inhibition of uterine contractions, which may result in delayed or prolonged labour.

Data from epidemiological studies suggest an increased risk of miscarriage after the use of a prostaglandin synthesis inhibitor in early pregnancy.

There is a possible association between the development of foetal abnormalities and the first trimester exposure to pseudoephedrine and whilst no teratogenic effects have been demonstrated in animal studies, the use of Nurofen Cold and Flu with Decongestant should, if possible, be avoided during the first trimester of pregnancy.

Use in lactation

Although ibuprofen appears in breast milk in very low concentrations, significant amounts of pseudoephedrine are secreted into breast milk and therefore use of Nurofen Cold and Flu with Decongestant during lactation should be avoided.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Undesirable effects

Reporting suspected adverse effects

The list of the following adverse events relates to those experienced with ibuprofen at OTC doses (maximum 1200mg per day) and sympathomimetics including pseudoephedrine in short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse events may occur.

Adverse events which have been associated with ibuprofen and sympathomimetics including pseudoephedrine are given below, listed by system organ class and frequencies. Frequencies are defined as: Very common (≥1/10): Common (≥1/100, <1/10): Uncommon (≥1/1,000, <1/100); Rare (≥1/10,000, <1/1,000); Very Rare (<1/10,000); Not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse Event
Blood and Lymphatic System Disorders	Very rare	Haematopoietic disorders[1], reversible platelet aggregation, alveolitis, pulmonary eosinophilia, pancreatitis, neutropenia, aplastic anaemia, haemolytic anaemia, eosinophilia, reduction of haemoglobin and haematocrit.
Immune System Disorders	Uncommon	Hypersensitivity with urticaria and pruritus[2]
	Very rare	Severe hypersensitivity reactions including facial, tongue and throat swelling, dyspnoea, apnoea, tachycardia,

		hypotension (anaphylaxis, angioedema or severe shock)[2]
Psychiatric Disorders	Not known	Decrease in appetite, thirst, anorexia nervosa, insomnia, agitation, hallucination, anxiety, restlessness
Nervous System Disorders	Uncommon	Headache, tremor
	Very rare	Dizziness, nervousness, tinnitus, depression, drowsiness, irritability, difficulty in concentrating, emotional instability, convulsions, auditory and visual problems, aseptic meningitis[3]
Cardiac Disorders	Not known	Cardiac failure and oedema[4], tachycardia, arrhythmia, palpitations
Vascular Disorders	Not known	Hypertension[4], cerebrovascular accidents[4], hypotension, congestive cardiac insufficiency in patients with compromised cardiac function.
Respiratory, Thoracic and Mediastinal Disorders	Not known	Respiratory tract reactivity comprising asthma, bronchospasm or dyspnoea[2]
Gastrointestinal Disorders	Uncommon	Abdominal pain, nausea and dyspepsia[5]
	Rare	Diarrhoea, flatulence, constipation and vomiting
	Very Rare	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]
	Not known	Ischaemic colitis
Hepatobiliary Disorders	Very rare	Liver disorders, especially in long term treatment, including hepatotoxicity, hepatitis, jaundice alterations of hepatic function tests, pancreatitis, duodenitis, oesophagitis, hepato-renal syndrome, hepatic necrosis, hepatic insufficiency.
Skin and Subcutaneous Tissue Disorders	Not known	Hyperhidrosis
	Uncommon	Skin rashes[2]
	Rare	Skin peeling, alopecia, exfoliative dermatitis, photosensitive dermatitis, maculopapular rash.
	Very rare	Bullous reactions, including Stevens-Johnson Syndrome, erythema multiforme and toxic epidermal necrolysis[2]
Renal and Urinary Disorders	Very rare	Acute renal failure[8]
	Not known	Urinary retention. Cystitis, haematuria, interstitial nephritis, nephritic syndrome, oliguria, tubular necrosis, glomerulonephritis, alteration in renal function tests, polyuria.
General and Administration Site Conditions	Not known	Irritability, muscle weakness.

Investigations	Very rare	Haemoglobin decreased
Ocular	Very rare	Blurred vision, changes in visual colour perception, toxic amblyopia, episodes of ocular alteration with consequent visual disorders.
Other	Rare	Dryness of the eyes and mouth, gingival ulcers, rhinitis, hearing disturbances.

Description of Selected Adverse Reactions

[1]Examples include anaemia, leucopaenia, thrombocytopaenia, pancytopaenia and agranulocytosis. First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.
[2] Hypersensitivity reactions have been reported following treatment with ibuprofen. These may consist of (a) non-specific allergic reactions and anaphylaxis, (b) respiratory tract reactivity, including asthma, aggravated asthma, bronchospasm, and dyspnoea, or (c) various skin reactions, including pruritus, urticaria, purpura, angioedema and, more rarely, exfoliative and bullous dermatoses, including toxic epidermal necrolysis, Stevens-Johnson Syndrome and erythema multiforme. Severe shock syndrome may be characterised by abdominal pain, fever, shivering, nausea and vomiting. Hepatotoxicity and aseptic meningitis which occur less frequently may also be hypersensitivity reactions.
[3] The pathogenic mechanism of drug-induced aseptic meningitis is not fully understood. However, the available data on NSAID-related aseptic meningitis points to a hypersensitivity reaction (due to a temporal relationship with drug intake, and disappearance of symptoms after drug discontinuation). 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 2400 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke), (see Precautions).
[5] The adverse events observed most often are gastrointestinal in nature.
[6] Sometimes fatal, particularly in the elderly.
[7] See section 4.4 Precautions.
[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. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

In adults the dose response effect is less clear cut than in children where ingestion of more than 400 mg ibuprofen per kg bodyweight may cause symptoms. The half-life of ibuprofen in overdose is 1.5 to 3 hours.

Symptoms

Ibuprofen: Symptoms of overdosage include headache, nausea, vomiting, epigastric pain or more rarely diarrhoea, tinnitis, gastrointestinal bleeding. 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 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.
Pseudoephedrine: Symptoms of overdose may include symptoms of irritability, palpitations, hypertension, convulsions, tremor, hyperactivity, hyperpyrexia, dryness of the skin and mucous membranes.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Ibuprofen is a non-steroidal anti-inflammatory agent that possesses analgesic, anti-inflammatory and anti-pyretic activities. Ibuprofen acts through the inhibition of cyclooxygenase (COX) 1 and 2, preventing the conversion of arachidonic acid to prostaglandin H2, a critical intermediate in the biosynthesis of prostaglandins, thromboxanes and other mediators.

Pseudoephedrine hydrochloride is a sympathomimetic agent with direct and indirect effects on adrenergic receptors, producing vasoconstriction which in turn relieves nasal congestion.

Clinical trials

No data available

5.2 Pharmacokinetic properties

After administration of a single dose of two Nurofen Cold and Flu with Decongestant tablets to healthy, fasting volunteers, the following pharmacokinetic parameters were derived:

Tmax: ibuprofen 0.5-2.5 hours
pseudoephedrine 1-3 hours

Cmax: ibuprofen 25-65µg/mL
pseudoephedrine 150-369ng/mL

t1/2: ibuprofen 2 hours
pseudoephedrine 7 hours

Absorption
The rate and extent of absorption of ibuprofen and pseudoephedrine when Nurofen Cold and Flu with Decongestant is taken with food is not known.

Distribution
Ibuprofen. The apparent volume of distribution of ibuprofen is 0.14L/kg. Ibuprofen and its metabolites readily cross the placental barrier in pregnant rabbits and rats. Ibuprofen appears in very low concentrations in breast milk. It is not known if the drug enters the CSF. 99% of ibuprofen is plasma protein bound.

Pseudoephedrine. The apparent volume of distribution of pseudoephedrine is 2-3L/kg. It is excreted in breast milk at concentrations consistently higher than those in maternal placenta.

The fraction of the dose excreted in milk has been estimated at approximately 0.5% of a single oral dose over 24 hours. Pseudoephedrine is likely to cross the placenta. There is no specific information concerning its penetration into the CNS. The extent of plasma protein binding of pseudoephedrine is unknown.

Metabolism
90% of ibuprofen is metabolized in the liver to produce two major metabolites, a hydroxylated and carboxylated compound.

Less than 1% of pseudoephedrine is metabolized by hepatic metabolism.

Excretion
Both the inactive metabolites and a small amount of unchanged ibuprofen are excreted rapidly and completely by the kidney with 95% of the administered dose eliminated in the urine within 4 hours of ingestion.

Pseudoephedrine is excreted essentially unchanged in urine (<90% of the dose in 24 hours). Alkaline urinary pH may delay the excretion of pseudoephedrine.

5.3 Preclinical safety data

Genotoxicity

No data available

Carcinogenicity

No data available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

It also contains: cellulose microcrystalline, calcium phosphate, croscarmellose sodium, hypromellose, magnesium stearate, mastercoat yellow FA 0156 or opaspray Yellow MI-IF-6168, povidone, talc-purified and opacode monogramming ink S-1-277001 BLACK'

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C

6.5 Nature and contents of container

Container type:
Tablets are packed in aluminium blister packs in cartons

Pack sizes:
Packs of 24 tablets.

6.6 Special precautions for disposal

Not Applicable

7. MEDICINE SCHEDULE

Controlled Drug C3

8. SPONSOR

Reckitt Benckiser (New Zealand) Ltd
Level 1, 2 Fred Thomas Drive
Takapuna, Auckland 0622
New Zealand

9. DATE OF FIRST APPROVAL

12 April 2024

10. DATE OF REVISION OF THE TEXT

12 April 2024

SUMMARY TABLE OF CHANGES

Section Changed	**Summary of new information**
All	New Datasheet created for provisional consent.
Date of first approval and revision of text	Updated date to 12 April 2024