

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Nurofen Cold & Flu Film-coated Tablets Ibuprofen 200mg Pseudoephedrine hydrochloride 30mg

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

<u>Active Ingredients</u>	<u>Quantity</u>
Ibuprofen	200 mg
Pseudoephedrine Hydrochloride	30 mg

Excipients with known effect: Sunset yellow (E110), up to 16.8 micrograms per tablet.

For a full list of excipients see section 6.1

## 3 PHARMACEUTICAL FORM

Film coated tablet (Short term: tablet)

Yellow, circular, biconvex, tablets printed in black with an identifying motif.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

For the symptomatic relief of head colds and influenza, including nasal congestion and to ease the pain of sore throats.

### 4.2 Posology and method of administration

For short-term use only.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms (see section 4.4).

The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 3 days.

#### Posology

**Adults:** Initial dose two tablets, then if necessary 1 – 2 tablets every four hours. Do not exceed six tablets in any 24 hour period.

#### Paediatric population:

**Children over 12 years of age:** As above for adults.

**Children under 12 years of age:** Ibuprofen + pseudoephedrine combination solid dose strength products are contraindicated in children aged less than 12 years.

**Elderly population:** There is no indication that dosage needs to be modified in the elderly. However, it may be advisable to monitor renal and hepatic function and, if there is serious impairment, caution should be exercised.

**Hepatic Impairment:** It may be advisable to monitor hepatic function. The product should not be used in severe hepatic failure (see section 4.3 and 4.4).

**Renal Impairment:** It may be advisable to monitor renal function. The product should not be used in severe renal failure (see section 4.3 and 4.4).

#### Method of administration

For oral administration.

### 4.3 Contraindications

Hypersensitivity to ibuprofen, pseudoephedrine or any of the excipients in section 6.1.

Patients who have previously shown hypersensitivity reactions (e.g. bronchospasm, asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, acetylsalicylic acid (aspirin) or other non-steroidal anti-inflammatory drugs (NSAIDs).

Severe coronary heart disease and cardiovascular disorders.

Severe hypertension or uncontrolled hypertension.

Severe heart failure (NYHA Class IV) (see section 4.4).

Severe acute or chronic kidney disease/renal failure (see section 4.4)

History of gastrointestinal bleeding or perforation, related to previous NSAID therapy. Active, or a history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding) or other gastrointestinal disorders.

Pregnancy. (See Section 4.6)

Use in children under 12 years.

Diabetes mellitus

Phaeochromocytoma

Hyperthyroidism

Closed angle glaucoma

Sympathomimetic drugs

Tricyclic antidepressants

Prostatic enlargement

Concomitant use of the product with Monoamine oxidase inhibitors (MAOIs, or within 14 days of stopping treatment, see section 4.5)

Beta blockers (see section 4.5).

### 4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to relieve symptoms.

**Elderly:** The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2). Prolonged use of NSAIDs in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

#### **Respiratory**

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

**Other NSAIDs:** The use of ibuprofen 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:** To be used with caution in patients with heart disease due to adverse cardiovascular effects with sympathomimetics such as pseudoephedrine (see section 4.8).

Caution (discussion with doctor or pharmacist) 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.

Clinical studies suggest that use of ibuprofen, particularly at high doses (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 (e.g.  $\leq 1200$ mg daily) is associated with an increased risk of arterial thrombotic events.

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.

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.

Cases of Kounis syndrome have been reported in patients treated with Nurofen. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

**Renal:** Caution in moderate to severe renal impairment. Risk of renal impairment as renal function may deteriorate (see section 4.3 and 4.8). There is a risk of renal impairment in dehydrated children and adolescents (see section 4.3 and 4.8).

**Hepatic:** Hepatic dysfunction (see section 4.3 and 4.8).

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)

Cases of PRES and RCVS have been reported with the use of pseudoephedrine containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3).

Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

**Impaired female 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.

**Gastrointestinal effects:** 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).

Gastrointestinal bleeding, ulceration or perforation which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without any warning symptoms or a previous history of serious GI 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), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton

pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and 4.5).

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

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).

When GI bleeding or ulceration occurs in patients receiving ibuprofen, 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.

#### **Dermatological effects: Severe cutaneous adverse reactions (SCARs)**

Severe cutaneous adverse reactions (SCARs) including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month. If signs and symptoms suggestive of these reactions appear, ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate).

Masking of symptoms of underlying infections:

Nurofen Cold and Flu Film Coated Tablets 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 Nurofen Cold and Flu Film Coated Tablets are 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.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. It is advisable to avoid use of ibuprofen in cases of varicella.

To be used with caution in patients with hyperexcitability or elevated intraocular pressure.

Use with caution in occlusive vascular disease.

Although pseudoephedrine has virtually no pressor effects in patients with normal blood pressure, this product should be used with caution in patients taking antihypertensive agents including adrenergic neurone blockers & Beta blockers (see section 4.5), other sympathomimetic agents, such as decongestants, appetite suppressants, and amphetamine-like psycho-stimulants (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.

If hallucinations, restlessness, or sleep disturbances are experienced whilst taking the product, use of the product should be discontinued.

#### Ischaemic optic neuropathy

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.

### **4.5 Interaction with other medicinal products and other forms of interaction**

**The product should be avoided in combination with:**

**Acetylsalicylic acid (Aspirin):** Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid (aspirin) on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

**Other NSAIDs including cyclo-oxygenase-2 selective inhibitors:** Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

**Monoamine oxidase inhibitors (MAOIs) and/or Reversible inhibitors of monoamine oxidase A (RIMAs):** should not be given to patients treated with MAOIs or within 14 days of ceasing such treatment: increased risk of hypertensive crisis.

**The product should be used with caution in combination with:**

**Anti-coagulants:** NSAIDs may enhance the effects of anti-coagulants, such as warfarin or heparin (see section 4.4).

**Antihypertensives (including adrenergic neurone blockers & betablockers, ACE inhibitors and Angiotensin II Antagonists) and diuretics:** NSAIDs may diminish the effects of these drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible.

These interactions should be considered in patients taking a cyclo-oxygenase inhibitor concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Pseudoephedrine may block the hypotensive effects. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

**Corticosteroids:** Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

**Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):**

Increased risk of gastrointestinal bleeding (see section 4.4).

**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 levels of methotrexate.

**Cyclosporin:** increased risk of nephrotoxicity with NSAIDs.

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

**Other sympathomimetics (including appetite suppressants and amphetamine like psychostimulants):** Risk of hypertension.

**Aminoglycosides:** reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations.

**Probenecid:** reduction in metabolism and elimination of NSAID and metabolites.

**Oral hypoglycaemic agents:** inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

**Moclobemide:** risk of hypertensive crisis.

**Ergot alkaloids (erotamine & methysergide):** increased risk of ergotism. Sympathomimetic agents, such as decongestants and appetite suppressants and amphetamine-like psychostimulants: as it may potentiate their effects. Risk of hypertension.

**Oxytocin:** risk of hypertension.

**Anticholinergics:** Enhances effects of anticholinergic drugs (such as TCAs) thus increasing the risk of hypertension.

The effect of pseudoephedrine may be diminished by guanethidine, reserpine and methyldopa.

Pseudoephedrine may diminish the effects of guanethidine and may increase the possibility of arrhythmias in digitalised patients, or in those receiving quinidine or tricyclic antidepressants.

**Linezolid:** Pseudoephedrine may cause elevated blood pressure in patients taking linezolid.

This medicinal product contains 6mg (0.26mmol) of sodium per tablet. To be taken into consideration by patients on a controlled sodium diet.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

The product is contraindicated throughout pregnancy.

#### **Ibuprofen:**

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest 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%. The risk is believed to increase with dose and duration of therapy. 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. During the third trimester of pregnancy, all 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-hydroamniosis; the mother and the neonate, at the end of the pregnancy, 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.

#### **Pseudoephedrine:**

Defective closure of the abdominal wall (gastroschisis) reported very rarely in newborns after first trimester exposure. The product should not be used in pregnancy unless considered essential by the physician.

### Lactation and breast feeding

The product should be avoided during lactation and breast feeding as ibuprofen and pseudoephedrine are excreted in breast milk. However the effects on breast fed infants are unlikely.

#### **Ibuprofen:**

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect the breast-fed infant adversely.

#### **Pseudoephedrine:**

Pseudoephedrine is excreted in breast milk in small amounts, but the effect of this on breast fed infants is not known. It has been estimated that 0.5 to 0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast milk over 24 hours.

### **Fertility**

#### **Ibuprofen:**

There is some evidence that medicinal products which inhibit cyclooxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment. See section 4.4 regarding female fertility.

#### **Pseudoephedrine:**

Unknown

### **4.7 Effects on ability to drive and use machines**

#### **Ibuprofen:**

No adverse effects known.

#### **Pseudoephedrine:**

None known.

### **4.8 Undesirable 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 frequency. Frequencies are defined as: very common (1/10), common (1/100 and <1/10), uncommon (1/1000 and <1/100), rare (1/10,000 and <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

#### **Adverse events:**

<b>System Organ Class</b>	<b>Frequency</b>	<b>Adverse Event</b>
<b>Blood and Lymphatic System Disorders</b>	Very Rare	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis) <sup>a</sup> .  First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, nose and skin bleeding and bruising.
<b>Immune System Disorders</b>	Common	Hypersensitivity reactions consisting of <sup>a, b1</sup> : - including cross-sensitivity reaction with other sympathomimetics <sup>b</sup>

	Uncommon	Urticaria <sup>a</sup> and pruritus <sup>a</sup>
	Very Rare	Severe hypersensitivity reactions <sup>a</sup> . Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock) <sup>1</sup> .
	Not Known	Respiratory tract reactivity <sup>a</sup> comprising asthma, aggravated asthma, bronchospasm or dyspnoea.
<b>Metabolism and nutrition disorders</b>	Not known	Decreased appetite <sup>b</sup>
<b>Psychiatric disorders</b>	Not known	Restlessness <sup>a,b</sup> , insomnia <sup>a,b</sup> , anxiety <sup>a,b</sup> , delusion <sup>b</sup> , excitability <sup>b</sup> , hallucination <sup>a,b</sup> (particularly in children), agitation <sup>b</sup>
<b>Nervous System Disorders</b>	Uncommon	Headache <sup>a</sup> , tremor <sup>a</sup>
	Very Rare	Aseptic meningitis <sup>a,2</sup>
	Not known	Dizziness <sup>a</sup> , muscular weakness <sup>a</sup> ,
	Not Known	Posterior reversible encephalopathy syndrome (PRES) (see section 4.4)
	Not Known	Reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4)
<b>Eye Disorders</b>	Unknown	Ischaemic optic neuropathy
<b>Ear and labyrinth disorders</b>	Not known	Hearing impaired <sup>a</sup>
<b>Cardiac Disorders</b>	Not Known	Cardiac failure and oedema <sup>a,3</sup> , tachycardia, arrhythmia <sup>b</sup> , palpitations <sup>a</sup>
	Not known	Kounis syndrome
<b>Vascular Disorders</b>	Not Known	Hypertension <sup>a,b,3</sup>
<b>Gastrointestinal Disorders</b>	Uncommon	Abdominal pain <sup>a</sup> , nausea <sup>a,b</sup> and dyspepsia <sup>a,4</sup>
	Rare	Diarrhoea <sup>a</sup> , flatulence <sup>a</sup> , constipation <sup>a</sup> and vomiting <sup>a,b</sup>
	Very Rare	Peptic ulcers <sup>a</sup> , gastrointestinal perforation <sup>a</sup> or gastrointestinal haemorrhage <sup>a</sup> , melaena <sup>a</sup> , haematemesis <sup>a,5</sup> , sometimes fatal, particularly in the elderly. Mouth ulceration <sup>a</sup> , gastritis <sup>a</sup>
	Not Known	Exacerbation of colitis and Crohn's disease (section 4.4) <sup>a,6</sup> , nausea <sup>b</sup> , dry mouth <sup>b</sup>
	Not known	Ischaemic colitis
<b>Hepatobiliary Disorders</b>	Very Rare	Liver disorders <sup>a</sup>
	Not known	Ischaemic colitis
<b>Skin and Subcutaneous Tissue Disorders</b>	Uncommon	Various skin rashes <sup>a,1</sup>
	Very Rare	Severe cutaneous adverse reactions (SCARs) (including erythema multiforme, exfoliate dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis) <sup>a,1</sup> .
	Not known	Hyperhidrosis <sup>a</sup> , Acute generalised exanthematous pustulosis (AGEP). Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome). Photosensitivity reactions
<b>Renal and Urinary Disorders</b>	Very Rare	Acute renal failure <sup>a,7</sup> , papillary necrosis <sup>a</sup> especially in long-term use associated with increased serum urea and oedema.



	Not known	Urinary retention <sup>b</sup> , dysuria <sup>a</sup>
<b>General disorders and administration site conditions</b>	Not known	Chest pain <sup>a</sup> , thirst <sup>a</sup> , irritability <sup>b</sup>
<b>Investigations</b>	Very Rare	Haemoglobin decreased <sup>a</sup>
<b>Infections and infestations</b>	Very Rare	Exacerbation of infections related inflammation (e.g. development of necrotizing fasciitis), in exceptional cases, severe skin infections and soft-tissue complications may occur during a varicella infection.

### Description of Selected Adverse Reactions

<sup>a</sup>Ibuprofen

<sup>b</sup>Pseudoephedrine

<sup>1</sup>Hypersensitivity reactions: 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.

<sup>2</sup> 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).

<sup>3</sup>Clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg/day), may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke), (see section 4.4).

<sup>4</sup>The adverse events observed most often are gastrointestinal in nature. Adverse events are mostly dose-dependent, in particular the risk of occurrence of gastrointestinal bleeding which is dependent on the dosage range and duration of treatment. The undesirable effects are less frequent when the maximum daily dose is 1200 mg.

<sup>5</sup>Sometimes fatal.

<sup>6</sup>See section 4.4.

<sup>7</sup>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 medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to:

HPRa Pharmacovigilance, Earlsfort Terrace, IRL- Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

### 4.9 Overdose

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

**Symptoms:** Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Other symptoms include sweating, insomnia, dilated pupils, blurred vision, delusions and hallucinations, muscular weakness, drowsiness, thirst, and

anxiety. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as vertigo, drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning hyperkalaemia and metabolic acidosis may occur and the prothrombin to interference with the actions of circulating clotting factors. Acute renal failure, liver damage, hypotension, respiratory depression and cyanosis may occur. Exacerbation of asthma is possible in asthmatics.

Prolonged use at higher than recommended doses or overdose may result in renal tubular acidosis and hypokalaemia.

As with other sympathomimetics, pseudoephedrine overdose may cause symptoms of central nervous system and cardiovascular stimulation, including irritability, restlessness, tremor, palpitations, convulsions, urinary retention, hypertension, difficulty in micturition, nausea, vomiting, tachycardia and cardiac arrhythmias.

**Management:** Management should be symptomatic and supportive and should include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If ibuprofen has already been absorbed, alkaline substances may be administered to promote the excretion of acid ibuprofen in the urine. If frequent or prolonged, convulsions should be treated with an anticonvulsant (e.g. intravenous diazepam or lorazepam). Time/INR may be prolonged, probably due to interference with the aforementioned clotting factors. Give bronchodilators for asthma. Chlorpromazine may be used to control marked excitement and hallucinations.

Elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis. Hypertensive effects may be treated with an IV alpha-receptor blocking agent such as phentolamine. Cardiac effects may require the use of a beta-adrenergic blocking agent after alpha-adrenergic blockade.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

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

#### **Ibuprofen:**

Ibuprofen is a propionic acid derivative, having analgesic, anti-inflammatory and antipyretic activity. The therapeutic effects of ibuprofen as a NSAID are thought to result from its inhibitory activity on the enzyme prostaglandin synthetase. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelets aggregation when they are dosed concomitantly. Some pharmacodynamics studies show that when a single dose of ibuprofen 400mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.

#### **Pseudoephedrine:**

The sympathomimetic effect of pseudoephedrine produces vasoconstriction which in turn relieves nasal and bronchial congestion and reduces oedema.

It is a stereoisomer of ephedrine and has a similar action. Pseudoephedrine is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. It has alpha and beta stimulant adrenergic activity and some stimulant effect on the central nervous system. It has a more prolonged, though less potent action than adrenaline. However, pseudoephedrine has been stated to have less pressor activity and central nervous system effects than ephedrine.

### 5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1 to 2 hours after administration.

Ibuprofen is extensively bound to plasma proteins.

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. The elimination half-life is approximately 2 hours. Excretion by the kidney is both rapid and complete.

No significant differences in pharmacokinetic profile are observed in the elderly.

In limited studies, ibuprofen appears in the breast milk in very low concentrations.

**Pseudoephedrine:**

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 half-life of about 5 to 8 hours; elimination; is enhanced and half-life accordingly shorter in acid urine. Small amounts are distributed into breast milk.

**5.3 Preclinical safety data**

No data is available which is of relevance to the consumer.

**6 PHARMACEUTICAL PARTICULARS****6.1 List of excipients**

Core:

Calcium Phosphate

Microcrystalline Cellulose

Povidone

Croscarmellose Sodium

Magnesium stearate

Film Coating:

Hypromellose

Talc

Opaspray yellow M-1F-6168 or

Mastercoat Yellow FA 0156 containing:

Titanium dioxide

Sunset yellow (E110)

Quinoline yellow

Black printing Ink:

Black iron oxide (E172)

Propylene glycol

Shellac

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years.

**6.4 Special precautions for storage**

Do not store above 25°C.

Store in the original package in order to protect from moisture.

**6.5 Nature and contents of container**

A strip pack consisting of a blister tray of white pigmented 250µm PVC/40 gsm PVDC laminate heat-sealed to lacquered 20µm aluminium foil containing 12 tablets. One or two trays packed in a cardboard carton (12 or 24 tablets).

#### **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements.

#### **7 MARKETING AUTHORISATION HOLDER**

Reckitt Benckiser Ireland Ltd  
7 Riverwalk  
Citywest Business Campus  
Dublin 24  
Ireland

#### **8 MARKETING AUTHORISATION NUMBER**

PA0979/033/001

#### **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 18 April 1994

Date of last renewal: 18 April 2009

#### **10 DATE OF REVISION OF THE TEXT**

April 2025