Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nurofen Sinus and Pain Film-Coated Tablets
Ibuprofen 200mg
Pseudoephedrine Hydrochloride 30mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredients	Quantity
Ibuprofen	200mg
Pseudoephedrine Hydrochloride	30mg

Excipients: Sunset Yellow (E110), up to 16.8 micrograms per tablets.
Sodium 6mg (0.26 mmol) per tablet. Total maximum daily dose (MDD) is 36mg (1.56mmol).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated 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 two tablets every four hours. Do not exceed six tablets in any 24 hour period.

Paediatric population:
Children over 12 years of age: As above

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

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 to any of the excipients listed in section 6.1.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, bronchospasm, 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.

Severe heart failure (NYHA Class IV), renal failure or hepatic failure (see section 4.4).

History of gastrointestinal bleeding or perforation related to previous NSAIDs therapy. Active, or 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 previous history of, bronchial asthma or allergic disease.

Other NSAIDs: The use of Nurofen Sinus and Pain Tablets with concomitant NSAIDs including cyclo-oxygenase-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 the use of ibuprofen, particularly at high doses (2400mg/ 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. ≤1200mg 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, 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.

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).

Impaired female fertility: There is some 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 – undesirable 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 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 acetylsalicylic acid (aspirin) (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Nurofen Sinus and Pain, 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: Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see 4.8). 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 Sinus and Pain should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Serious skin reactions such as acute generalised exanthematous pustulosis (AGEP) may occur with ibuprofen and pseudoephedrine- containing products. This acute pustular eruption may occur within 2 days of treatment, with fever, and

numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localised 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 Sinus and Pain should be discontinued and appropriate measures taken if needed.

Masking of symptoms of underlying infections:

Nurofen Sinus and Pain 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 Sinus and Pain Film Coated Tablets are administered for fever or pain relieve 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 combination with antihypertensives 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.

4.5 Interaction with other medicinal products and other forms of interactions

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 cyclooxygenase-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 antagonists 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 cyclooxygenase 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 cardiac 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.

Ciclosporin: 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 (including tricyclic antidepressants): Enhances the effects of anticholinergic drugs, 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.

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

No adverse effects known.

4.8 Undesirable effects

The list of the following adverse effects relates to those experienced with the product 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 effects 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.

Table of Adverse events

System Organ Class	Frequency	Adverse Event
Blood and Lymphatic System Disorders	Very Rare	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis)[a]. First signs are fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, nose and skin bleeding and bruising.
Immune System Disorders	Common	Hypersensitivity reactions consisting of[a,b,1]: Including cross sensitivity reaction with other sympathomimetics
	Uncommon	Urticaria[a] and pruritus[a]
	Very Rare	Severe hypersensitivity reactions[a]. Symptoms could be facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock)[1].
	Not Known	Respiratory tract reactivity[a] comprising asthma, aggravated asthma, bronchospasm or dyspnoea.
Metabolism and nutrition disorders	Not Known	Decreased appetite[b]
Psychiatric disorders	Not known	Restlessness[a,b], insomnia[a,b], anxiety[a,b]delusion[b] , excitability[b] , hallucination[a,b] (particularly in children), agitation[b]
Nervous System Disorders	Uncommon	Headache[a,] , tremor[a]
	Very Rare	Aseptic meningitis[a,2]
	Not known	Dizziness[a], muscular weakness[a]
Ear and labyrinth disorders	Not known	Hearing impaired[a]
Cardiac Disorders	Not Known	Cardiac failure and oedema[a,3], tachycardia, arrhythmia[b], palpitations[a]
Vascular Disorders	Not Known	Hypertension[a,b,3]
Gastrointestinal Disorders	Uncommon	Abdominal pain[a], nausea[a,b] and dyspepsia[a,4]
	Rare	Diarrhoea[a], flatulence[a], constipation[a] and vomiting[a,b]
	Very Rare	Peptic ulcers[a], gastrointestinal perforation[a] or gastrointestinal haemorrhage[a], melaena[a], haematemesis[a,5], sometimes fatal, particularly in the elderly.Mouth ulceration[a], gastritis[a]
	Not Known	Exacerbation of colitis and Crohn's disease (section 4.4) [a,6], nausea[b], dry mouth[b] Ischaemic colitis
Hepatobiliary Disorders	Very Rare	Liver disorders[a]
Skin and Subcutaneous Tissue Disorders	Uncommon	Various skin rashes[a,1]
	Very Rare	Severe forms of skin reactions such as bullous reactions including Stevens-Johnson syndrome,

		erythema multiforme and toxic epidermal necrolysis can occur[a,1].
	Not known	Hyperhidrosis[a], Severe skin reactions, including acute generalised exanthematous pustulosis (AGEP). Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).
Renal and Urinary Disorders	Very Rare	Acute renal failure[a,7], papillary necrosis[a] especially in long-term use associated with increased serum urea and oedema.
	Not known	Urinary retention[b], dysuria[a]
General disorders and administration site conditions	Not known	Chest pain[a], thirst[a], irritability[b]
Investigations	Very Rare	Haemoglobin decreased[a]
Infections and infestations	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

[a]Ibuprofen
[b]Pseudoephedrine

[1] 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.

[2] 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).

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

[4] 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 1200mg.

[5] Sometime fatal.

[6] See Section 4.4.

[7] 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL –Dublin 2; Tel: + 353 1 6764971; Fax: + 353 1 6762517. Website: www.hpra.ie, e-mail: medsafety@hpra.ie.

4.9 Overdose

In children ingestion of more than 400mg/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: dizziness, thirst, anxiety, fever, sinus tachycardia and sweating. 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 time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

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, sinus 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 administrated to promote the excretion of the 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.

Pseudoephredine 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 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 Mastercote Yellow FA 0156 containing:
Titanium dioxide
Sunset yellow (E110)
Quinoline yellow (E104)

Printing ink
Iron oxide black (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 250 µm PVC/40 gsm PVDC laminate heat-sealed to lacquered 20 µm aluminium foil containing 12 tablets. One or two trays packed in a cardboard carton (12 or 24 tablets).

Not all pack sizes may be marketed.

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

PA0979/065/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20th June 2014
Date of last renewal: 19th June 2019

10 DATE OF REVISION OF THE TEXT

September 2021