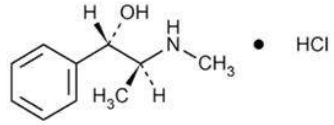
PRODUCT INFORMATION

SUDAFED® Sinus + Anti-inflammatory Pain Relief Caplets

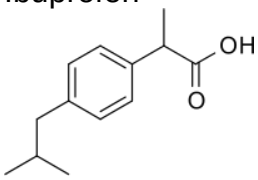
NAME OF THE MEDICINE

Pseudoephedrine Hydrochloride



CAS[2] Registry Number: 345-78-8

Ibuprofen



CAS[2] Registry Number: 15687-27-1

DESCRIPTION

SUDAFED® Sinus + Anti-inflammatory Pain Relief caplets contain pseudoephedrine hydrochloride 30 mg and ibuprofen 200 mg.

SUDAFED® Sinus + Anti-inflammatory Pain Relief caplets also contain: candelilla wax, microcrystalline cellulose, croscarmellose sodium, sodium lauryl sulfate, stearic acid, methyl hydroxybenzoate, propyl hydroxybenzoate, Opadry Aqueous Film Coating YS-1-7034 Clear UK, Opadry Aqueous Film Coating YS-1-7717 White UK.

PHARMACOLOGY

Pharmacokinetics
Pseudoephedrine is readily absorbed from the gastrointestinal tract. It is largely excreted unchanged in the urine together with small amounts of its hepatic metabolite. It has a half-life of about 5-8 hours; elimination is enhanced and half-life reduced accordingly in acid urine.

Ibuprofen is well absorbed from the gastrointestinal tract. It is highly bound (90-99%) to plasma proteins and is extensively metabolised to inactive compounds in the liver, mainly by glucuronidation. 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 four hours of ingestion. The elimination half-life of ibuprofen is in the range of 1.9 to 2.2 hours.

Pharmacodynamics/Mechanism of action
Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective decongestant in the upper respiratory tract. It is a stereoisomer of ephedrine and has a similar action, but has been found to have less pressor activity and fewer central nervous system (CNS) effects.

Sympathomimetic agents are used as nasal decongestants to provide symptomatic relief. They act by causing vasoconstriction resulting in redistribution of local blood flow to reduce oedema of the nasal mucosa, thus improving ventilation, drainage and nasal stuffiness.

Ibuprofen possesses analgesic, antipyretic and anti-inflammatory properties, similar to other non-steroidal anti-inflammatory drugs (NSAIDs). Its mechanism of action is unknown, but is thought to be through peripheral inhibition of cyclooxygenases and subsequent prostaglandin synthetase inhibition.

INDICATIONS

SUDAFED® Sinus + Anti-inflammatory Pain Relief provides relief of symptoms of sinus pain with sinus congestion occurring as a result of cold and flu, allergic rhinitis or sinusitis.

CONTRAINDICATIONS

SUDAFED® Sinus + Anti-inflammatory Pain Relief is contraindicated for use in patients:

- with known hypersensitivity or idiosyncratic reaction to pseudoephedrine or ibuprofen (or any of the other ingredients in the product)
- with severe hypertension or coronary artery disease
- taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days.
- known hypersensitivity to aspirin and other NSAIDS
- asthma that is aspirin or NSAID sensitive
- active gastrointestinal bleeding or peptic ulceration
- renal impairment
- heart failure
- severe liver impairment
- undergoing treatment of perioperative pain in setting of coronary artery bypass surgery (CABG)

Use of ibuprofen is contraindicated during the third trimester of pregnancy.

Use of ibuprofen is contraindicated right before or after heart surgery.

SUDAFED® Sinus + Anti-inflammatory Pain Relief should not be taken with other products containing ibuprofen or with other anti-inflammatory medicines.

Refer to ‘Interactions with other drugs’ for additional information.

PRECAUTIONS

SUDAFED® Sinus + Anti-inflammatory Pain Relief should be used with caution in patients with:

- hypertension
- hyperthyroidism or thyroid disease
- diabetes mellitus
- coronary heart disease
- ischaemic heart disease
- glaucoma
- prostatic hypertrophy
- severe hepatic or renal dysfunction.
- previous history of gastrointestinal haemorrhage or ulcers
- asthma who have not previously taken an NSAID
- hepatic or renal impairment.
- cardiac impairment or heart disease
- fluid retention
- alcohol dependence
- pregnancy (see 'Use in pregnancy').

Due to the ibuprofen component, this medicine should be taken with caution when using other products containing aspirin and salicylates.

Ibuprofen may cause a severe allergic reaction, especially in patients allergic to aspirin. Symptoms include hives, facial swelling, asthma (wheezing), shock, skin reddening, rash or blisters. If any of these symptoms occur, patients should stop use and seek medical help right away.

Refer to 'Interactions with other drugs' for additional information.

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.

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

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.

SUDAFED® Sinus + Anti-inflammatory Pain Relief should be used with caution in patients with hypertension (see Contraindications – heart failure).

Hepatic:
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, pruritis, jaundice, abdominal tenderness in the right upper quadrant and "flu-like" symptoms).

Use in pregnancy: Category C
Pseudoephedrine has been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals are inadequate or may be lacking, but available data shows no evidence of an increased occurrence of foetal damage.

Ibuprofen inhibits prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the foetal ductus arteriosus, foetal renal impairment, inhibition of platelet aggregation and may delay labour and birth. Use of ibuprofen is thus contraindicated during the third trimester of pregnancy, including the last few days before expected birth.

Further, there is insufficient experience about the safety of use of ibuprofen in humans during pregnancy. Sudafed® Sinus + Anti-inflammatory Pain Relief should therefore not be used during the first six months of pregnancy unless the potential benefits to the patient outweigh the possible risk to the foetus.

Use in lactation
Pseudoephedrine is secreted in breast milk in small amounts. It has been estimated that 0.5% to 0.7% of a single dose of pseudoephedrine ingested by the mother will be excreted in the breast milk over 24 hours. Therefore, it is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Ibuprofen appears in breast milk in very low concentrations and is unlikely to affect the breast fed infant adversely.

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 Contraindications).

INTERACTIONS WITH OTHER MEDICINES

The following interactions with pseudoephedrine have been noted:

- antidepressant medication eg tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) – may cause a serious increase in blood pressure or hypertensive crisis
- other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants – may cause an increase in blood pressure and additive effects
- methyldopa and β-blockers – may cause an increase in blood pressure
- urinary acidifiers enhance elimination of pseudoephedrine
- urinary alkalinisers decrease elimination of pseudoephedrine.

The following interactions with ibuprofen have been noted:
- Anticoagulants, including warfarin – ibuprofen interferes with the stability of INR and may increase risk of severe bleeding and sometimes fatal haemorrhage, especially from the gastrointestinal tract. Ibuprofen should only be used in patients taking warfarin if absolutely necessary and they must be closely monitored.
- Ibuprofen may decrease the cardioprotective and antiplatelet activity of aspirin.
- Ibuprofen may decrease renal clearance and increase plasma concentration of lithium
- Ibuprofen may reduce the antihypertensive effect of ACE inhibitors, beta-blockers and diuretics and may cause natriuresis and hyperkalemia in patients under these treatments
- Ibuprofen reduces methotrexate clearance
- Ibuprofen may increase plasma levels of cardiac glycoside
- Ibuprofen may increase the risk of gastrointestinal bleeding especially if taken with corticosteroids or with alcohol use.
- Ibuprofen may prolong bleeding time in patients treated with zidovudine.

Ibuprofen may also interact with probenecid, antidiabetic medicines and phenytoin.

ADVERSE EFFECTS

Children and the elderly are more likely to experience adverse effects than other age groups.

Clinical Trial Data
The safety of the combination of ibuprofen and pseudoephedrine from clinical trial data is based on data from 4 double-blind placebo-controlled single dose randomized studies in the treatment of sinus headache.
The following table includes adverse events that occurred where greater than one event was reported, and the incidence was greater than placebo and in 1% of patients or more.

AEs Reported by >1% of Subjects Treated with Ibuprofen and Pseudoephedrine combination in 4 Randomized Placebo-Controlled Clinical Trials

System Organ Class	400 mg ibu/60 mg	200 mg ibu/30 mg PSE x 1 dose	Placebo (N=241)

Preferred Term	**PSE x 1 dose (N=244) % (frequency)**	**(N=238) % (frequency)**	**% (frequency)**
General Disorders and Administration Site Conditions			
Thirst	0.4 (Uncommon)	1.3 (Common)	0.4 (Uncommon)
Gastrointestinal Disorders			
Abdominal pain upper	- 1.6 (Common)	-	-
Nervous System Disorders			
Dizziness	4.9 (Common)	6.3 (Common)	5.8
Tremor	-	1.7 (Common)	-
Psychiatric Disorders			
Anxiety	1.6 (Common)	0.4 (UnCommon)	-
Nervousness	6.1 (Common)	2.5 (Common)	1.7 (Common)
Eye Disorders			
Eye Disorder	1.2 (Common)	-	-
Ear and Labyrinth Disorders			
Tinnitus	0.4 (Uncommon)	1.7 (Common)	0.4 (Uncommon)

Adverse drug reactions identified during post-marketing experience with ibuprofen, pseudoephedrine and the combination of ibuprofen/ pseudoephedrine appear in the following table. The frequency category was estimated from spontaneous reporting rates.

Frequency category	Adverse Event Preferred term
Infections and Infestations	
Very Rare	*Meningitis aseptic*
Blood and Lymphatic Disorders	
Very rare	*Bone Marrow Suppression*
Very rare	*Eosinophilia*
Very rare	*Thrombocytopenia*
Very rare	*Anaemia*
Immune Disorders	
Very Rare	*Hypersensitivity reactions*
Very Rare	*Angioedema*
Very Rare	*Anaphylactic reaction*
Psychiatric Disorders	

Very Rare	*Anxiety*
Very Rare	*Insomnia*
Very Rare	*Nervousness*
Very Rare	*Euphoric Mood*
Rare	*Hallucination*
Common	*Restlessness*
Nervous System Disorders	
Very Rare	*Headache*
Very Rare	*Dizziness*
Very Rare	*Psychomotor hyperactivity*
Very Rare	*Stroke*
Very Rare	*Somnolence*
Common	*Tremor*
Rare	*Fatigue*
Eye Disorders	
Very rare	*Vision Blurred*
Very rare	*Visual Impairment*
Cardiac Disorders	
Very rare	*Palpitations*
Very rare	*Arrhythmia*
Very rare	*Tachycardia*
Very rare	*Cardiac Failure*
Very rare	*Myocardial Infarction*
Rare	*Fluid retention*
Rare	*Oedema*
Vascular Disorders	
Very Rare	*Bleeding*
Very Rare	*Hypertension*
Respiratory, Thoracic and Mediastinal Disorders	
Very Rare	*Asthmatic Conditions*
Very Rare	*Bronchospasm*
Rare	*Breathing difficulties*
Gastrointestinal Disorders	
Very Rare	*Dry Mouth*
Very Rare	*Nausea*
Very Rare	*Constipation*
Very Rare	*Diarrhoea*
Very Rare	*Gastrointestinal Inflammation*
Very Rare	*Gastrointestinal Haemorrhage*
Very Rare	*Gastrointestinal Ulcer perforation*

Very Rare	*Gastrointestinal Ulceration*
Very Rare	*Gastrointestinal Ulcer haemorrhage*
Very Rare	*Dyspepsia*
Very Rare	*Abdominal pain*
Very Rare	*Oral discomfort (local burning sensation, irritation*
Very Rare	*Pancreatitis*
Very Rare	*Vomiting*
Rare	*Heartburn*
Hepatobiliary Disorders	
Very Rare	*Hepatotoxicity (Hepatic function abnormal, Hepatitis, Transaminases increased)*
Skin and Subcutaneous Tissue Disorders	
Very Rare	*Acute generalised exanthematous pustulosis*
Very Rare	*Angioedema*
Very Rare	*Rash*
Very Rare	*Pruritus*
Very Rare	*Erythema*
Very Rare	*Erythema Multiforme*
Very Rare	*Stevens-Johnson Syndrome*
Very Rare	*Toxic Epidermal Necrolysis*
Very Rare	*Urticaria*
Rare	*Photosensitivity*
Renal and Urinary Disorders	
Very Rare	*Dysuria*
Very Rare	*Urinary Retention*
Very Rare	*Nephritis*
Very Rare	*Nephrotic Syndrome*
Very Rare	*Renal Failure*
Very Rare	*Renal Impairment*
Very Rare	*Renal Papillary Necrosis*
General Disorders and Administrative Site Conditions	
Very Rare	*Feeling Jittery*
Very Rare	*Asthenia*
Very Rare	*Hypothermia*
Metabolism and nutrition disorders	
Rare	*Loss of appetite*

DOSAGE AND ADMINISTRATION

The recommended dosage of **SUDAFED®** Sinus + Anti-inflammatory Pain Relief for adults and children over 12 years is 1 or 2 caplets with fluid every four to six hours when necessary. Do not exceed 6 caplets in 24 hours.

SUDAFED® Sinus + Anti-inflammatory Pain Relief should not be used for children under 12 years of age.

SUDAFED® Sinus + Anti-inflammatory Pain Relief should not be used for more than a few 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. Excessive use can increase the risk of heart attack, stroke or liver damage.

OVERDOSAGE

In case of overdose, immediately contact the Poisons Information Centre (in Australia, call 13 11 26; in New Zealand call 0800 764 766) for advice.

PRESENTATION

SUDAFED® Sinus + Anti-inflammatory Pain Relief caplets are white, capsule-shaped, film-coated tablets.
SUDAFED® Sinus + Anti-inflammatory Pain Relief caplets are available in blister packs of the following sizes:

- 4 caplets (S3) Pharmacist Only Medicine
- 12 caplets (S3) Pharmacist Only Medicine
- 24 caplets[#] (S3) Pharmacist Only Medicine

[#] marketed

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Storage

Store below 30°C. Keep in a dry dark place.

SPONSOR

Johnson & Johnson Pacific Pty Ltd
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Ultimo NSW 2007
Australia

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Poison schedule of the medicine

Schedule 3

TGA approved: 4 October 2006
Date of most recent amendment: 28 February 2017