Professional information for SUDAFED® SINUS PAIN

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

SUDAFED® SINUS PAIN tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Pseudoephedrine hydrochloride	60 mg
Paracetamol	500 mg

Sugar free.

3. PHARMACEUTICAL FORM

Tablets.

A white, elongated tablet with flat-bevelled edges, having a score on the one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SUDAFED® SINUS PAIN is indicated for the symptomatic relief of nasal, sinus and Eustachian tube mucosal congestion associated with pain and pyrexia due to the common cold and influenza.

4.2 Posology and method of administration

Adults and children over 12 years: One tablet orally three times daily.

Children under 12 years: Not recommended.

Do not exceed the stated dose, if symptoms persist, consult a doctor.

DO NOT EXCEED THE RECOMMENDED DOSE.

4.3 Contraindications

- Hypersensitivity to pseudoephedrine, paracetamol or to any of the ingredients (see section 4.8).
- SUDAFED® SINUS PAIN is contraindicated in patients who are taking or have taken monoamine oxidase inhibitors within the preceding two weeks as this may cause a rise in blood pressure. The antibacterial agent furazolidone is known to cause a dose-related inhibition of monoamine oxidase. SUDAFED® SINUS PAIN and furazolidone should not be taken together.
- Due to its paracetamol content, SUDAFED® SINUS PAIN should not be used in cases of severe liver impairment.
- The safety of SUDAFED® SINUS PAIN in pregnancy has not been established.

4.4 Special warnings and precautions for use

SUDAFED® SINUS PAIN contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or poison centre must be contacted immediately.

Dosages of SUDAFED® SINUS PAIN in excess of those recommended, may cause severe liver damage.

Patients suffering from liver or kidney disease should take paracetamol under medical

supervision.

Consult your doctor if no relief is obtained from the recommended dosage. Do not use continuously for more than 10 days without consulting a doctor.

Do not use with any other product containing paracetamol.

Chronic alcohol users should ask their doctor whether they should take paracetamol or other pain relievers or fever reducers.

Serious skin reactions such as acute generalised exanthematous pustulosis (AGEP), Stevens Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported very rarely in patients receiving paracetamol.

Patients should be informed about the signs of serious skin reactions and use of SUDAFED® SINUS PAIN should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Great care is needed in patients with cardiovascular disease such as coronary heart disease, arrhythmia or tachycardia, occlusive vascular disorders including arteriosclerosis, hypertension or aneurysms. Care is required when pseudoephedrine is given to patients with, hyperthyroidism, diabetes, closed-angle glaucoma, decreased kidney function, difficulty in urination and/or enlargement of the prostate.

There have been reports of ischaemic colitis with pseudoephedrine. SUDAFED® SINUS PAIN should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop (see section 4.8).

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported with pseudoephedrine-containing medicines, such as SUDAFED® SINUS PAIN. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly

localised on the skin folds, body, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as formation of small pustules occur, with or without pyrexia or erythema, then treatment with pseudoephedrine should be discontinued and a doctor should be consulted.

If symptoms persist or get worse, or if new symptoms occur, patients should stop use and consult a doctor.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of SUDAFED® SINUS PAIN with sympathomimetic agents such as decongestants, tricyclic antidepressants, appetite suppressants and amphetamine-like psychostimulants, antihypertensive agents or with monoamine oxidase inhibitors, which interfere with the catabolism of sympathomimetic amines, may cause a rise in blood pressure. Pseudoephedrine may partially reverse the hypotensive action of medicines, which interfere with sympathetic activity including bretylium, bethanidine, guanethidine, debrisoquine and methyldopa. Pseudoephedrine should be avoided or used with caution in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics as they may induce ventricular fibrillation. An increased risk of arrhythmias may also occur if pseudoephedrine is given to patients receiving cardiac glycosides, quinidine or tricyclic antidepressants. Chronic ingestion of anticonvulsants and oral steroid contraceptives induces liver enzymes and may prevent attainment of therapeutic paracetamol levels by increasing first pass metabolism and clearance.

Warfarin-like compounds

For most patients, occasional use of paracetamol generally has little or no effect on the International Normalised Ratio (INR) in patients on chronic warfarin therapy; however, there has

been controversy regarding the possibility of paracetamol potentiating the anticoagulant effects of warfarin and other coumarin derivatives. Patients should consult a doctor or pharmacist before use if they are taking warfarin or other coumarin derivatives.

4.6 Fertility, pregnancy and lactation

There are no adequate and well-controlled clinical studies in pregnant or breastfeeding women for the combination of paracetamol and pseudoephedrine.

SUDAFED® SINUS PAIN is not recommended during pregnancy or lactation.

Pregnancy

The safety of pseudoephedrine in pregnancy has not been established.

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breastfeeding

Pseudoephedrine is excreted in breast milk in small amounts but the effect of this on breastfed infants is not known. It has been estimated that approximately 0,4 to 0,7 % of a single 60 mg dose of pseudoephedrine ingested by a nursing mother will be excreted in the breast milk over 24 hours. Data from a study of lactating mothers taking 60 mg pseudoephedrine every 6 hours suggests that from 2,2 to 6,7 % of the maximum daily dose (240 mg) may be available to the

infant from a breastfeeding mother.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding. A pharmacokinetic study of paracetamol in 12 nursing mothers revealed that less than 1 % of a 650 mg oral dose of paracetamol appeared in the breast milk. Similar findings have been reported in other studies, therefore maternal ingestion of therapeutic doses of paracetamol does not appear to present a risk to the infant.

Fertility

No studies have been conducted in animals to determine whether pseudoephedrine has the potential to impair fertility. There is no information on the effect of SUDAFED® SINUS PAIN on fertility.

4.7 Effects on ability to drive and use machines

It is not known if SUDAFED® SINUS PAIN has an effect on the ability to drive or operate machinery.

4.8 Undesirable effects

Central effects of pseudoephedrine include fear, anxiety, restlessness, tremor, insomnia, confusion, irritability, weakness and psychotic states. Appetite may be reduced and nausea and vomiting may occur. Symptoms of nervous system excitation may occur, including sleep disturbances and rarely hallucinations

Pseudoephedrine causes vasoconstriction which may lead to a resultant rise in blood pressure and possibly to cerebral haemorrhage or pulmonary oedema. Pseudoephedrine may also produce tachycardia, cardiac arrhythmias, anginal pain, palpitations, cardiac arrest, hypotension

with dizziness, fainting and flushing. Urinary retention has been reported occasionally in men receiving pseudoephedrine. Difficulty with micturition may also be experienced. Dyspnoea, altered metabolism including disturbances of glucose metabolism, sweating and hypersalivation are possible. Headaches are also common.

Angina may be precipitated in patients with angina pectoris. Fixed drug eruption to pseudoephedrine, taking the form of erythematous nummular patches has been reported. Skin rashes and other allergic reactions may occur due to paracetamol. The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by fever and mucosal lesions. The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia and leukopenia. Thrombocytopenic purpura, haemolytic anaemia and agranulocytosis have been recorded after paracetamol administration. Papillary necrosis has been reported after prolonged administration. Alcohol may increase the hepatotoxicity of paracetamol and may contribute to acute pancreatitis.

Pseudoephedrine/Paracetamol combination

Psychiatric disorders:

Frequent:

Nervousness

Post-marketing experience:

The following adverse drug reactions were identified during post-marketing experience with paracetamol, pseudoephedrine by frequency category estimated from clinical trials or epidemiology studies:

Immune system disorders:

Frequency unknown: Anaphylactic reaction, hypersensitivity.

Psychiatric disorders:

Frequency unknown: Anxiety, euphoric mood, hallucination, visual hallucination, restlessness.

Nervous system disorders:

Frequency unknown: Cerebrovascular accident, headache, paraesthesia, psychomotor hyperactivity, tremor.

Cardiac disorders:

Frequency unknown: Arrhythmia, myocardial infarction, palpitations, tachycardia.

Gastrointestinal disorders:

Frequency unknown: Abdominal pain, colitis ischaemic, diarrhoea, vomiting.

Skin and subcutaneous tissue disorders:

Frequency unknown: Acute generalised exanthematous pustulosis, angioedema, fixed eruption, pruritus, rash, pruritic rash, urticaria.

Renal and urinary disorders:

Frequency unknown: Dysuria, urinary retention.

Investigations:

Frequency unknown: Increased blood pressure, increased transaminases.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of SUDAFED® SINUS PAIN is important. It allows continued monitoring of the benefit/risk balance of SUDAFED® SINUS PAIN. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

See sections 4.4 and 4.8.

Paracetamol:

Nausea, vomiting and anorexia. Liver damage, which may be fatal, may only appear after a few days. Acute intoxication may cause kidney failure.

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person to a hospital directly. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5-10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning, do not reflect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.

Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage:

Although evidence is limited it is recommended that any adult person who has ingested 5 – 10

grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients who are stuperose or comatose endotracheal intubation should precede gastric lavage in order to avoid aspiration.

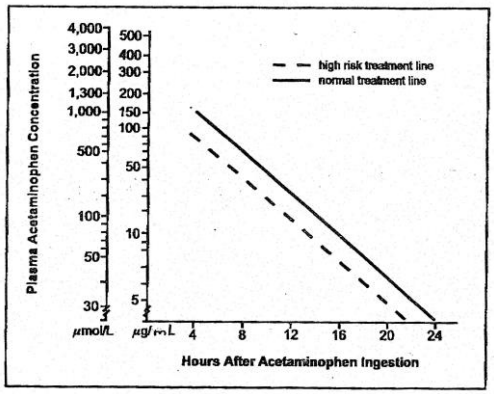
N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible, preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given intravenously over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1000 ml dextrose injection over the next sixteen hours. The volume of intravenous fluid should be modified for children.

Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours, unless high, may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their plasma paracetamol level.

The plasma paracetamol level can be plotted against time since ingestion in the nomogram below



Adapted from Smilkstein et al. Ann Emerg Med 1991;20:1059

Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery.

Patients with increased susceptibility to liver damage as identified above should continue treatment if concentrations are above the ‘high risk treatment line’. Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety-six hours.

Pseudoephedrine

The effect of acute toxicity from overdosage with pseudoephedrine may include irritability, convulsions, hypertension, restlessness, tremor and difficulty with micturition. Necessary measures should be taken to maintain and support respiration and circulation. Gastric lavage should be performed if indicated. Specialised treatment is essential as soon as possible.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Pharmacotherapeutic group: Other analgesics and antipyretics: paracetamol, combinations excl.

psycholeptics

ATC code: N02BE51

SUDAFED® SINUS PAIN has decongestive, analgesic and antipyretic actions.

5.2 Pharmacokinetic properties

Absorption:

Paracetamol

Oral paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract, primarily in the small intestine. Absorption occurs by passive transport. The rate of oral absorption depends mainly upon the rate of gastric emptying.

The relative bioavailability ranges from 85 % to 99 %. Peak plasma concentrations are usually attained about 30 – 60 minutes after oral dosing.

For individual adults, maximum plasma concentrations occur within 1 hour following ingestion, and range from 14,8 to 17,6 µg/mL for a single 1 000 mg dose. Maximum plasma concentrations at steady state after 1 000 mg doses every 6 hours range from 17,6 to 18,2 µg/mL.

Pseudoephedrine

Pseudoephedrine is rapidly absorbed from the gastrointestinal tract. The oral bioavailability of pseudoephedrine is high, as determined by urine collections greater than 96 % of administered doses. When pseudoephedrine is taken after a high-fat meal, the absorption rate is decreased, resulting in about an hour delay in attaining maximum concentrations.

Following oral administration of a single 30 mg tablet, a mean maximum plasma concentration of 104 ± 19 ng/mL is attained in 1,46 ± 0,55 hours. Following oral administration of a single 60 mg dose as tablets, mean maximum plasma concentrations of 180 ± 30 and 232 ± 30 ng/mL are attained at 1,94 ± 0,86 and 1,96 ± 0,62 hours, respectively.

Distribution:

Paracetamol

Paracetamol appears to be widely distributed throughout most body tissues except fat. Its apparent volume of distribution is 0,7 to 1 L/kg in children and adults. A relatively small proportion (10 % to 25 %) of paracetamol is bound to plasma protein.

Pseudoephedrine

The apparent volume of distribution for pseudoephedrine ranges from 2,3 to 3,3 L/kg. Up to 0,7 % of a single 60 mg dose of pseudoephedrine may be distributed into breast milk over 24 hours. Pseudoephedrine concentrations in milk are from 2 to 3-fold higher than those in plasma. This milk/plasma drug concentration profile suggests low protein binding, although no protein plasma binding data in humans are available. Data from a study of lactating mothers taking 60 mg pseudoephedrine every 6 hours suggests that from 2,2 to 6,7 % of the maximum daily dose (240 mg) may be available to the infant from a breastfeeding mother.

Biotransformation:

Paracetamol

Paracetamol is primarily metabolised in the liver and involves three main pathways: conjugation with glucuronide; conjugation with sulphate; and oxidation via cytochrome P450 enzyme pathway. The oxidative pathway forms a reactive intermediate, which is detoxified by conjugation with glutathione to form inert cysteine and mercapturic acid metabolites. The principal cytochrome P450 isoenzyme involved *in vivo* appears to be CYP2E1, although CYP1A2 and CYP3A4 were considered minor pathways based on *in vitro* microsomal data. Subsequently, both CYP1A2 and CYP3A4 were found to have negligible contribution *in vivo*.

Pseudoephedrine

In adults, only a minor fraction of pseudoephedrine is metabolised in the liver. About 1 % to 6,2 % of a dose undergoes N-demethylation to the metabolite, norpseudoephedrine, which is excreted in the urine.

Elimination:

Paracetamol

The elimination half-life of paracetamol is about 1 to 3,5 hours. It is approximately one hour longer in neonates and in cirrhotic patients. Paracetamol is eliminated from the body as glucuronide (45 – 60 %) and sulphate (25 – 35 %) conjugates, thiols (5 – 10 %) as cysteine and mercapturate metabolites, and catechols (3 – 6 %) that are excreted in the urine. Renal clearance of unchanged paracetamol is about 3,5 % of the dose.

Pseudoephedrine

Pseudoephedrine is mainly eliminated by renal excretion as unchanged medicine. Most of an oral dose (43 % to 96 %) is excreted unchanged in the urine within 24 hours. In adults, the elimination half-life (t½) for both immediate- and extended-release pseudoephedrine ranges from 5,5 to 7,0 hours. Oral clearance of pseudoephedrine is approximately 7,3 to 7,6 mL/min/kg.
Urinary pH affects the elimination t½ and clearance of pseudoephedrine due to extensive reabsorption in the renal tubules at alkaline pH; renal reabsorption is negligible at acidic pH. In a study in which participants received sodium bicarbonate to adjust their urine to an alkaline range and ammonium chloride tablets to adjust their urine to an acidic range, an alkaline urinary pH of 8,0 prolonged the t½ (range, 9,2 to 16,0 hours) and an acidic urinary pH of 5,0 reduced the t½ of pseudoephedrine (range, 3,0 to 6,4 hours). In a study which monitored but did not adjust urinary

pH, the t½ of pseudoephedrine in urine ranged from 1,9 hours at pH 5,66 to 21 hours at pH 7,80.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate

Microcrystalline cellulose

Povidone

Sodium starch glycollate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light and moisture.

6.5 Nature and contents of container

PVC/PVDC / aluminium blister packs of 10 tablets.

6.6 Special precautions for disposal and other handling

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Johnson & Johnson (Pty) Ltd.

241 Main Road

Retreat

7945

SOUTH AFRICA

8. REGISTRATION NUMBER

T/5.8/196

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 June 1992

10. DATE OF REVISION OF THE TEXT

6 August 2022

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EXPORT REGISTRATION DETAILS

Botswana: B9317145

Sign: