1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

SINUCLEAR PAEDIATRIC SYRUP/STROOP 0,625 mg/15 mg/125 mg per 5 ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of SINUCLEAR PAEDIATRIC SYRUP/STROOP contains:

Pseudoephedrine hydrochloride	15 mg
Triprolidine hydrochloride	0,625 mg
Paracetamol	125 mg
Preservatives:	
Methyl hydroxybenzoate	0,12 % *m/v*
Propyl hydroxybenzoate	0,02 % *m/v*

Contains sugar: Sorbitol 1,018 g

Contains sweetener: Saccharin sodium 45 mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Syrup.

SINUCLEAR PAEDIATRIC SYRUP/STROOP is a pink, viscous syrup with a raspberry odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SINUCLEAR PAEDIATRIC SYRUP/STROOP is indicated for the relief of symptoms such as nasal congestion, sniffing and headache associated with the common cold and influenza.

4.2 Posology and method of administration

Posology

Children 6 to 12 years: Take 5 ml to 10 ml (one to two medicine measures) three times daily

Children 2 to 6 years: Take 5 ml (one medicine measure) three times daily

SINUCLEAR PAEDIATRIC SYRUP/STROOP is contraindicated in children under 2 years of age (see section 4.3).

DO NOT EXCEED THE RECOMMENDED DOSE.

Not to be used continuously for longer than 10 days without consulting a doctor.

Method of administration

For oral administration.

4.3 Contraindications

SINUCLEAR PAEDIATRIC SYRUP/STROOP is contraindicated in:

- Patients with hypersensitivity to triprolidine hydrochloride, pseudoephedrine hydrochloride, paracetamol or to any of the excipients in SINUCLEAR PAEDIATRIC SYRUP/STROOP (see section 6.1).
- Severe liver function impairment.

- Severe acute or chronic kidney disease/renal failure.
- Patients using other sympathomimetic decongestants or beta-blockers.
- Patients suffering from cardiovascular disease including ischaemic heart disease, occlusive vascular disease and hypertension.
- Thyrotoxicosis.
- Diabetes.
- Prostatism.
- Bladder dysfunction.
- Closed angle glaucoma.
- Phaeochromocytoma.
- During an attack of asthma in asthmatic patients.
- Patients being treated with monoamine oxidase inhibitors and within two weeks of stopping such treatment as a hypertensive response may result.
- Avoid during cyclopropane and halothane anaesthesia (or any other halogenated anaesthetic) (see section 4.5).
- Premature infants or neonates.
- Children under two years of age.
- Safety in pregnancy and lactation has not been established.
- Treatment with ephedrine and other sympathomimetic agents, as a hypertensive response may result (see section 4.5).
- Patients at risk of developing respiratory failure.

4.4 Special warnings and precautions for use

SINUCLEAR PAEDIATRIC SYRUP/STROOP may lead to drowsiness and impaired concentration, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressant medicines. Patients should be warned not to drive a motor

vehicle, climb dangerous heights or operate dangerous machinery, as impaired mental alertness could lead to accidents.

Consult your doctor if no relief is obtained with the recommended dosage.

Do not use continuously for longer than 10 days without consulting your doctor.

Paracetamol

SINUCLEAR PAEDIATRIC SYRUP/STROOP 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.

Paracetamol should not be taken concomitantly with any other paracetamol containing medicine.

Persisting or worsening pain or fever at the recommended dosage, new symptoms or redness and swelling, and could be signs of a more serious condition.

Kidney or liver impairment

SINUCLEAR PAEDIATRIC SYRUP/STROOP should be given with care to patients with impaired kidney and liver function, and patients taking other medications that affect the liver. SINUCLEAR PAEDIATRIC SYRUP/STROOP contains paracetamol. Dosages of SINUCLEAR PAEDIATRIC SYRUP/STROOP in excess of those recommended, may cause severe liver damage.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), Drug reaction with eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with SINUCLEAR PAEDIATRIC SYRUP/STROOP must immediately be discontinued and appropriate treatment instituted.

These reactions can occur with first-time use or at any time while the medicine is being taken.

Flucloxacillin

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Pseudoephedrine

SINUCLEAR PAEDIATRIC SYRUP/STROOP should be used with caution in mild to moderate renal impairment.

Special care should be taken in patients with hyperthyroidism.

SINUCLEAR PAEDIATRIC SYRUP/STROOP SHOULD be used with caution in patients with severe hepatic impairment, or with mild to moderate renal impairment.

Symptoms of central nervous system excitation, may occur, including restlessness, sleep disturbances and hallucinations. If any of these symptoms occur, SINUCLEAR PAEDIATRIC SYRUP/STROOP should be stopped.

Difficulty with micturition may also be experienced. Dyspnoea, altered metabolism including disturbances of glucose metabolism, sweating and hypersalivation are possible (see section 4.8).

Cardiac disorders

Pseudoephedrine should be given with caution to patients with organic heart disease, cardiac decompensation or angina of effort and in patients receiving digitalis.

Fixed drug eruption

Fixed drug eruption to pseudoephedrine, taking the form of erythematous nummular patches and lichenoid skin eruption due to triprolidine have been reported. Paradoxical central nervous system stimulation may occur particularly in children, with insomnia, nervousness, tachycardia, tremors and convulsion (see section 4.8).

Seizures

Epileptiform seizures may be precipitated in patients with focal lesions of the cerebral cortex.

Ischaemic colitis

Some cases of ischaemic colitis have been reported with pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP. Pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Ischaemic optic neuropathy

Cases of ischaemic optic neuropathy have been reported with pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP. Pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

Acute Generalised Exanthematous Pustulosis (AGEP)

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported with pseudoephedrine-containing medicines, such as SINUCLEAR PAEDIATRIC SYRUP/STROOP. 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.

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 medicines (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). SINUCLEAR PAEDIATRIC SYRUP/STROOP 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.

Triprolidine

Do not use this product without consulting a doctor or pharmacist if you are presently taking medicines for depression, psychiatric or emotional conditions or hypertension (see sections 4.3 and 4.5).

Patients should avoid alcoholic drinks.

Elderly

SINUCLEAR PAEDIATRIC SYRUP/STROOP should be used with care in the elderly, who are more susceptible to many of the side effects, urinary retention, prostatic hypertrophy or pyloroduodenal obstruction, epilepsy, hepatic and renal impairment.
Elderly patients are more susceptible to the central nervous system depressant and hypotensive effects of antihistamines even at therapeutic doses.

Paediatric population

SINUCLEAR PAEDIATRIC SYRUP/STROOP should not be given to premature infants, neonates, or children under two years of age (see section 4.3).

Excipients

SINUCLEAR PAEDIATRIC SYRUP/STROOP contains:

- sorbitol, which may cause gastrointestinal discomfort and mild laxative effect. Patients with the rare hereditary conditions of sorbitol intolerance or hereditary fructose intolerance (HFI) should not take SINUCLEAR PAEDIATRIC SYRUP/STROOP.
- glycerol, which may cause headache, stomach upset and diarrhoea.
- the excipients methyl hydroxybenzoate, propyl hydroxybenzoate and erythrosine may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicines and other forms of interaction

Triprolidine

Anticholinergics

SINUCLEAR PAEDIATRIC SYRUP/STROOP has an additive antimuscarinic action with other antimuscarinic medicines, such as atropine and some antidepressants (both tricyclics and MAOIs).

Aminoglycoside antibacterials

Some sedating antihistamines such as triprolidine as contained in SINUCLEAR PAEDIATRIC SYRUP/STROOP, could mask the warning signs of damage caused by ototoxic medicines such as aminoglycoside antibacterials.

Central nervous system depressants

SINUCLEAR PAEDIATRIC SYRUP/STROOP may enhance the sedative effects of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics.

Allergen tests

Antihistamines such as triprolidine as contained in SINUCLEAR PAEDIATRIC SYRUP/STROOP, may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing.

Pseudoephedrine

Anaesthetics

Pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, should be avoided in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics, as they may induce ventricular fibrillation.

Cardiac glycosides, quinidine or tricyclic antidepressants

An increased risk of dysrhythmias also occurs if given with cardiac glycosides, quinidine or tricyclic antidepressants.

Monoamine oxidase inhibitors (MAOI's)

Hypertensive crisis may occur if pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, is co-administered with MAOIs. Concomitant use of pseudoephedrine should be avoided with MAOIs or within 14 days of its termination (see section 4.3).

Antihypertensives

Pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, may antagonise the effects of antihypertensive medications, such as adrenergic neuron blockers, including bretylium, bethanidine, guanethidine, debrisoquine and methyldopa, and severe hypertension may occur in patients receiving beta-blockers.

Sympathomimetic medicines

Caution should be exercised with patients receiving other sympathomimetic medications (e.g. avoid use with apraclonidine), nasal decongestants, appetite suppressants or other amphetamine -like psychostimulants, as there is a risk of hypertension.

Doxapram, oxytocin, aluminium hydroxide

The effects of pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, may be increased by doxapram and oxytocin (as there is a risk of hypertension) and its absorption may be increased by aluminium hydroxide.

Ergot alkaloids

Pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, also increases the risk of ergotism if used with ergot alkaloids, ergotamine and methysergide.

Antipsychotics, kaolin

The effects of pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, may be antagonised by antipsychotics and its absorption rate may be reduced by kaolin.

Aluminium hydroxide-containing medicines

Aluminium hydroxide containing preparations may increase the absorption rate of pseudoephedrine hydrochloride, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP.

Paracetamol

Hepatic enzyme inducers

Medicines which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after overdosage.

Metoclopramide, domperidone and cholestyramine

The rate of absorption of paracetamol, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

Warfarin and other coumarins

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, with increased risk of bleeding; occasional doses have no significant effect.

Flucloxacillin

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4).

Non-steroidal anti-inflammatory drugs (NSAIDs)

Prolonged concurrent use of paracetamol, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, with other NSAIDs may also increase the risk of adverse renal effects.

Zidovudine

Paracetamol may competitively inhibit the hepatic glucuronidation and decrease the clearance of zidovudine; zidovudine may also inhibit the hepatic glucuronidation of paracetamol.

Paracetamol

Paracetamol, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, should not be taken concomitantly with any other paracetamol containing medicine.

Alcohol

Alcohol reduces liver capacity to deal with paracetamol, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP.

Chloramphenicol

The use of SINUCLEAR PAEDIATRIC SYRUP/STROOP may cause an increased plasma concentration of chloramphenicol.

4.6 Fertility, pregnancy and lactation

The safety of SINUCLEAR PAEDIATRIC SYRUP/STROOP in pregnancy and lactation has not been established (see section 4.3).

Pregnancy

Pseudoephedrine

There are limited data from the use of pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, in pregnant women. It is advised that pseudoephedrine should be avoided during pregnancy, particularly during the first trimester, as defective closure of the abdominal wall (gastroschisis) has been reported very rarely in new-borns after first trimester exposure (see section 4.3).

Lactation

Pseudoephedrine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, has been detected in human milk with a small percentage of the total maternal dose potentially administered to the suckling infant. The use of pseudoephedrine should be avoided during breastfeeding as lactation may be suppressed, and irritability and disturbed sleep have been reported in breast fed infants (see section 4.3).

Triprolidine, as in SINUCLEAR PAEDIATRIC SYRUP/STROOP, is distributed into breast milk.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

SINUCLEAR PAEDIATRIC SYRUP/STROOP has moderate influence on the ability to drive or operate machinery.

Since adverse reactions such as drowsiness, dizziness, sedation and blurred vision have been reported in patients receiving SINUCLEAR PAEDIATRIC SYRUP/STROOP, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that SINUCLEAR PAEDIATRIC SYRUP/STROOP does not adversely affect their ability to do so (see section 4.8).

4.8 Undesirable effects

a. Summary of the safety profile

The following adverse reactions have been reported and is listed according to system organ class and frequency (frequent, less frequent and frequency unknown).

b. Tabulated summary of adverse reactions

Triprolidine

System organ class	Frequent	Less frequent	Frequency unknown
Blood and the lymphatic system disorders		Blood disorders, including agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia	

System organ class	Frequent	Less frequent	Frequency unknown
Immune system disorders			Allergy, anaphylaxis, and hypersensitivity reactions (including bronchospasm and angioedema), cross-sensitivity to related medications
Psychiatric disorders	Sedation varying from slight drowsiness to deep sleep, and including lassitude, dizziness, and incoordination, although paradoxical stimulation may occasionally occur, especially at high doses and in children or the elderly. Symptoms of cerebral stimulation in adults include insomnia, nervousness,		Confusion, sleep disturbances, depression, inability to concentrate

System organ class	Frequent	Less frequent	Frequency unknown
	euphoria, irritability, tremors, and rarely, nightmares, hallucinations tachycardia, muscle twitching, and convulsions		
Nervous system disorders	Headache and psychomotor impairment		Extrapyramidal effects, paraesthesias, muscular weakness, deepening coma, as well as tingling, heaviness, and weakness of the hands. Large doses may precipitate fits in epileptics
Eye disorders	Blurred vision		
Ear and labyrinth disorders			Tinnitus
Cardiac disorders		Palpitations, dysrhythmias	In high doses, transient

System organ class	Frequent	Less frequent	Frequency unknown
			bradycardia followed by tachycardia, hypotension, impaired circulation to the extremities
Respiratory, thoracic and mediastinal disorders	Thickened respiratory-tract secretions		Tightness of the chest
Gastro-intestinal disorders	Dry mouth, a reduction in tone and motility of the gastrointestinal tract resulting in constipation, increased gastric reflux	Nausea, vomiting, diarrhoea, epigastric pain	Anorexia, other gastrointestinal disturbances including colic
Skin and subcutaneous tissue disorders			Rash, sweating, hair loss, photosensitisation of the skin, lichenoid skin eruption

System organ class	Frequent	Less frequent	Frequency unknown
Musculo-skeletal and connective tissue disorders			Myalgia
Renal and urinary disorders	Urinary difficulty, urinary retention		
General disorders and administrative site conditions			Lassitude

Pseudoephedrine

System organ class	Frequent	Less frequent	Frequency unknown
Immune system disorders			Hypersensitivity reactions – cross-sensitivity may occur with other sympathomimetics
Metabolism and nutrition disorders		Decreased appetite, hypokalaemia, altered metabolism including disturbances of glucose metabolism	Thirst

System organ class	Frequent	Less frequent	Frequency unknown
Psychiatric disorders	Anxiety, insomnia, nervousness, central effects include fear, confusion, irritability and psychotic states	Psychotic disorders due to misuse, hallucinations	Sleep disturbances, excitability, giddiness, agitation. Adverse mental effects (particularly in children), have been associated with combination preparations containing pseudoephedrine
Nervous system disorders	Dizziness, tremors and restlessness	Headache, convulsions, weakness	Fainting, Posterior reversible encephalopathy syndrome (PRES)/ reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4).
Eye disorders			Angle-closure glaucoma, miosis, ischaemic optic neuropathy.

System organ class	Frequent	Less frequent	Frequency unknown
Cardiac disorders	Tachycardia	Reflex bradycardia, palpitations, cardiac dysrhythmia, anginal pain, cardiac arrest	Vasoconstriction which may result in hypertension and cerebral haemorrhage, impaired circulation to the extremities, precordial pain
Vascular disorders			Hypotension with dizziness and fainting, and flushing may also occur. Hypertension which may produce cerebral haemorrhage and pulmonary oedema and reflex bradycardia, hypotension with dizziness and fainting, and flushing, impaired

System organ class	Frequent	Less frequent	Frequency unknown
			circulation to the extremities
Respiratory, thoracic and mediastinal disorders		Dyspnoea or troubled breathing	Pulmonary oedema
Gastro-intestinal disorders		Nausea, vomiting, hypersalivation	Loss of appetite, dry mouth, ischaemic colitis has been reported after acute or chronic use of pseudoephedrine in combination cold and allergy preparations
Skin and subcutaneous tissue disorders		Sweating, skin rashes	Fixed drug eruption (FDE) due to pseudoephedrine, in the form of erythematous nummular patches, have been reported

System organ class	Frequent	Less frequent	Frequency unknown
Musculo-skeletal and connective tissue disorders			Muscular weakness
Renal and urinary disorders		Difficulty in micturition and urinary retention especially in patients with prostatic enlargement, or painful urination	
General disorders and administrative site conditions	Weakness, tolerance with dependence	Pallor	

Paracetamol

System organ class	Frequent	Less frequent	Frequency unknown
Blood and the lymphatic system disorders			Blood dyscrasias including thrombocytopenia, agranulocytosis, leukopenia,

System organ class	Frequent	Less frequent	Frequency unknown
			pancytopenia, neutropenia
Immune system disorders		Sensitivity/allergic reactions resulting in skin rash, laryngeal oedema, angioedema and anaphylaxis	
Gastrointestinal disorders		Pancreatitis occurs occasionally, mucosal lesions	
Skin and subcutaneous tissue disorders	Erythematous rash, urticarial rash	Hypersensitivity including skin rash may occur	Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven- Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-

System organ class	Frequent	Less frequent	Frequency unknown
			induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol-containing medicines
General disorders and administration site conditions		Fever	

Post marketing data

System organ class	Frequent	Less frequent	Frequency unknown
Blood and the lymphatic system disorders			Thrombocytopenia and agranulocytosis
Immune system disorders			Anaphylaxis, cutaneous

System organ class	Frequent	Less frequent	Frequency unknown
			hypersensitivity reactions including rashes, angioedema and Stevens Johnson syndrome/ toxic epidermal necrolysis
Respiratory, thoracic and mediastinal disorders			Bronchospasm*
Hepato-biliary disorders			Hepatic dysfunction
Skin and subcutaneous tissue disorders		Serious skin reactions	

**There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs*

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/ +27 11 239-6200

4.9 Overdose

Triprolidine

Symptoms

Overdosage with sedating antihistamines as contained in SINUCLEAR PAEDIATRIC SYRUP/STROOP is associated with antimuscarinic, extrapyramidal, and CNS effects. Overdosage may be fatal, especially in children where the main symptoms are central nervous system stimulation and antimuscarinic effects. Deepening coma, cardiorespiratory collapse and death may occur. When CNS stimulation predominates over CNS depression, which is more likely in children or the elderly, it causes ataxia, excitement, tremors, psychoses, hallucinations, and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma, and convulsions, progressing to respiratory failure and cardiovascular collapse.

Treatment

The stomach should be emptied. Emetics may be tried if the patient is alert and there is no symptoms of toxicity.

Other treatment should be symptomatic and supportive and may include artificial respiration, external cooling and IV fluids.

Paracetamol

Prompt treatment is essential.

In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. 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 to 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of drugs that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms

Symptoms of paracetamol overdosage, as ~~contained~~ in SINUCLEAR PAEDIATRIC SYRUP, 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 may develop even in the absence of severe liver damage. Cardiac dysrhythmias have been reported.

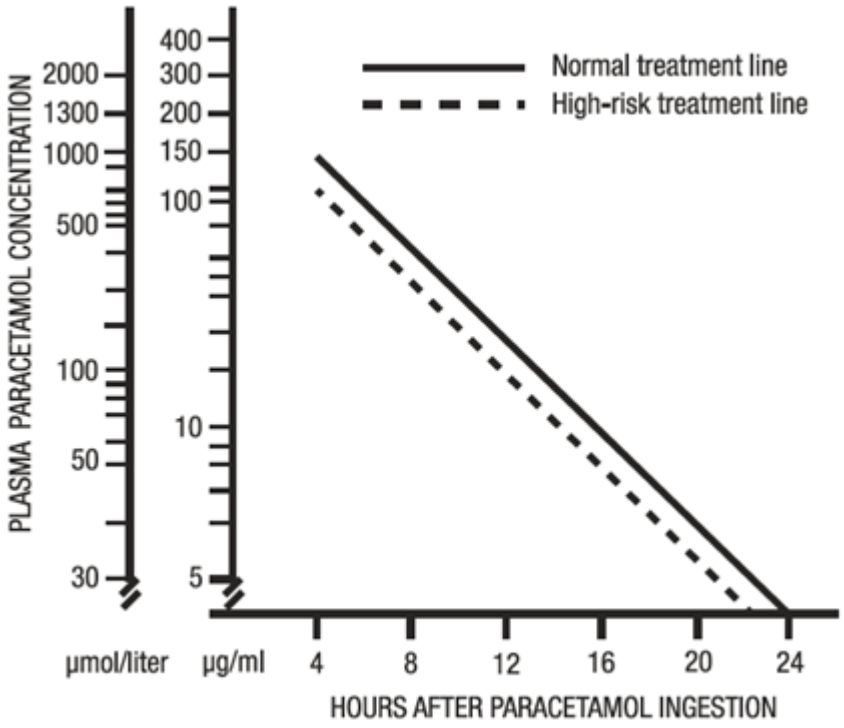
Treatment

Although evidence is limited it is recommended that any adult person who has ingested 5 to 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg), as contained in SINUCLEAR PAEDIATRIC SYRUP, within the preceding four hours, should have a single dose of 50 g activated charcoal given. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning.

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 1 000 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 may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below. The nomogram should be used only in relation to a single acute ingestion.

Figure 1: A semi-logarithmic plot of plasma-paracetamol concentration against hours after ingestion.



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

Symptoms

The symptoms of overdose include irritability, nervousness, tremor, cardiac dysrhythmias, palpitations, tachycardia, convulsions, urinary retention and hypertension, restlessness, dry mouth, anxiety, insomnia, nausea, vomiting and possible tolerance to pseudoephedrine. Severe cardiovascular repercussions include hypertension, angina, dysrhythmias, myocardial infarction and cerebral haemorrhage. Convulsions and hyperpyrexia in children due to cerebral stimulation.

Treatment

Overdose should be treated by general supportive measures. Respiratory and circulatory function should be maintained by supportive measures. Catheterisation of the bladder may be required. The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose: 50 g for adults; 1g/kg for children). Optimal effects are within 1 hour of ingestion of more than a toxic dose. Alternatively consider gastric lavage in adults within 1 hour of a potentially life-threatening overdose. Monitor pulse, blood pressure and cardiac rhythm. Treat any hypertension or convulsions as necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 5.8 Preparations for the common cold including decongestants

Pharmacotherapeutic group: Sympathomimetics, pseudoephedrine, combinations.

ATC code: R01BA52

Mechanism of action

SINUCLEAR PAEDIATRIC SYRUP/STROOP has decongestive, antipyretic, antihistamine and analgesic properties.

Paracetamol

Paracetamol is the active metabolite of phenacetin. Paracetamol has analgesic and antipyretic effects. However, it has weak anti-inflammatory effects, and has been thought to have a generally poor ability to inhibit cyclooxygenase (COX) in the presence of high concentrations of peroxides, as are found at sites of inflammation. COX inhibition might be disproportionately pronounced in the brain, explaining its antipyretic efficacy.

Pseudoephedrine

Pseudoephedrine is a direct and indirect acting sympathomimetic. It is a stereoisomer of ephedrine and has a similar action, but has been stated to have less pressor activity and fewer CNS effects. Pseudoephedrine is given for the symptomatic relief of nasal congestion.

Triprolidine

Triprolidine hydrochloride, an alkylamine derivative, is a sedating antihistamine with antimuscarinic and mild sedative effects.

Antihistamines have potential anti-inflammatory properties because histamine releases inflammatory cytokines and eicosanoids. The anticholinergic effects may lead to lessen rhinorrhoea.

5.2 Pharmacokinetic properties

Paracetamol

Absorption

Paracetamol has excellent bioavailability. Peak plasma concentrations occur within 30 to 60 minutes, and the $t_{1/2}$ in plasma is ~ 2 hours after therapeutic doses.

Distribution

Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of paracetamol to plasma proteins is variable.

Metabolism

Paracetamol primarily undergoes hepatic conjugation with glucuronic acid (~ 60 %), sulphuric acid (~ 35 %) or cysteine (~ 3 %). Small amounts of the hydroxylated and deacetylated metabolites have also been detected. A small proportion of paracetamol undergoes CYP-mediated N – hydroxylation to form NAPQI, a highly reactive intermediate. This metabolite normally reacts with

sulphydryl groups in glutathione (GSH) and thereby is rendered harmless. However, after ingestion of large doses of paracetamol, the metabolite is formed in amounts sufficient to deplete hepatic GSH and contributes significantly to the toxic effects of overdose.

Elimination

Some 90 to 100 % of paracetamol may be recovered in the urine within the first day of therapeutic dosing. 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

Absorption

Pseudoephedrine is readily absorbed from the gastrointestinal tract. At high urinary pH (> 7,0) pseudoephedrine is extensively reabsorbed. 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.

Elimination

It is excreted largely unchanged in the urine with small amounts of its hepatic metabolite. 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.

Triprolidine

After absorption from the gastrointestinal tract, triprolidine is metabolised to a carboxylated derivative which accounts for about half the dose excreted in the urine. Reported half-lives vary from 3 to 5 hours or more.

Special Populations

Triprolidine

Paediatric patients

H_1 antagonists are eliminated more rapidly by children than by adults.

Hepatic impairment

H_1 antagonists are eliminated more slowly in those with severe liver disease.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colour erythrosine (C.1. 45430), flavour raspberry special, glycerol, Kollidon 25, methyl hydroxybenzoate, propyl hydroxybenzoate, potassium acid phosphate (for pH adjustment), propylene glycol, purified water, saccharin sodium, sodium hydroxide (for pH adjustment), sorbitol.

Contains sugar: Sorbitol 1,018 g

Contains sweetener: Saccharin sodium 45 mg

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 ºC.

Protect from light.

Keep in original packaging until required for use.

6.5 Nature and contents of container

100 ml is packed into a round, amber glass bottle sealed with a white polypropylene screw cap, with an expanded polyethylene liner.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Hotline: 0800 122 912

8 REGISTRATION NUMBER

30/5.8/0053

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

09 September 2026

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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