1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

SINUCLEAR 18 mg/325 mg capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each SINUCLEAR capsule contains 18 mg phenylpropanolamine hydrochloride and 325 mg paracetamol.

Sugar free

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule.

Standard yellow opaque and blue transparent hard gelatin capsule, imprinted in white “Sinuclear” on the cap and body. Each capsule contains a fine, white, free-flowing powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SINUCLEAR is indicated for the temporary symptomatic relief of nasal, sinus and Eustachian tube mucal congestion and associated pain and fever due to colds and influenza.

4.2 Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE.

Adults: Take one capsule every six hours. Do not exceed five capsules in 24 hours.

Paediatric population

SINUCLEAR is not to be used in children younger than 6 years (see section 4.3).

Method of administration

For oral administration.

4.3 Contraindications

SINUCLEAR is contraindicated in:

- Patients with hypersensitivity to phenylpropanolamine hydrochloride, paracetamol or to any excipients in SINUCLEAR (see section 6.1).
- Patients whose sensitivity to small doses of sympathomimetic substances is manifested by sleeplessness, dizziness, light-headedness, weakness, tremulousness or cardiac dysrhythmia.
- Concomitant use with any monoamine-oxidase inhibitors for depression (e.g. tranylcypromine), or within 14 days of stopping such a treatment.
- Cardiovascular disease.
- Hypertension.
- Hyperthyroidism.
- Hyperexcitability.
- Phaeochromocytoma.
- Closed-angle glaucoma.

- Safety in pregnancy and lactation has not been established (see section 4.6).
- Children younger than 6 years.

4.4 Special warnings and precautions for use

SINUCLEAR 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.

Do not use continuously for more than 7 days without consulting your doctor.

Dosages in excess of those recommended may cause severe liver or kidney damage.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Intracranial haemorrhage

Severe hypertensive episodes leading to intracranial haemorrhage have followed phenylpropanolamine ingestion. Patients should be informed of the dangers of exceeding the recommended dose; in particular the increased risk of serious adverse effects such as hypertensive crisis and haemorrhagic stroke. Patients with cardiovascular disease, hypertension or hyperthyroidism should not use SINUCLEAR (see section 4.3 and 4.8).

In addition, SINUCLEAR may aggravate conditions such as diabetes, glaucoma or prostatic enlargement. Patients on monoamine oxidase inhibitors (e.g. tranylcypromine) should not use SINUCLEAR (see section 4.3 and 4.4).

Prostatic enlargement

In patients with prostatic enlargement, difficulty in micturition may be experienced (see section 4.8).

Diabetes

SINUCLEAR should be used with caution in patients with diabetes.

Skin reactions

Patients should be advised that paracetamol, as contained in SINUCLEAR, may cause severe skin reactions, such as acute generalised exanthematous pustulosis (AGEP). If a skin reaction such as skin reddening, blisters, or rash occurs, they should stop use and seek medical assistance right away.

4.5 Interaction with other medicines and other forms of interaction

Monoamine-oxidase inhibitors

SINUCLEAR should not be given concomitantly with any monoamine-oxidase inhibitors for depression (e.g. tranylcypromine), or within 14 days of stopping such a treatment (see section 4.3).

Bromocriptine

Phenylpropanolamine, as contained in SINUCLEAR, and bromocriptine may lead to hypertension and life-threatening complications if used concomitantly.

Anaesthetics

Phenylpropanolamine hydrochloride, as contained in SINUCLEAR should be given with caution to patients receiving chloroform, cyclopropane, halothane or other halogenated anaesthetics.

Colestyramine

The speed of absorption of paracetamol as contained in SINUCLEAR is reduced by colestyramine. Therefore, the colestyramine should not be taken within one hour if maximal analgesia is required.

Metoclopramide and domperidone The absorption of SINUCLEAR is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

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

Chloramphenicol

SINUCLEAR may increase plasma concentration of chloramphenicol.

Amantadine

Severe psychosis has been reported in woman taking amantadine with phenylpropanolamine, as contained in SINUCLEAR.

Antivirals

Phenylpropanolamine, as contained in SINUCLEAR, may cause hypertensive crisis when taken together with a triple-medicine HIV prophylactic regimen,

NSAIDs (Non-steroidal anti-inflammatory drugs)

The inhibition of prostaglandin synthesis by indomethacin may cause enhancement of the sympathomimetic effect of phenylpropanolamine, as contained in SINUCLEAR.

The effects of phenylpropanolamine hydrochloride, as contained in SINUCLEAR, are diminished by guanethidine, reserpine, methyldopa and may be diminished or enhanced by tricyclic antidepressants. It may diminish the effect of guanethidine and may increase the possibility of dysrhythmias in digitalised patients.

4.6 Fertility, pregnancy and lactation

The use of SINUCLEAR is contraindicated in pregnancy and lactation (see section 4.3).

Pregnancy

Epidemiological studies on neurodevelopment in children exposed to paracetamol, as contained in SINUCLEAR, *in utero* show inconclusive results.

The use of paracetamol, as contained in SINUCLEAR, during the last trimester of pregnancy may lead to a risk of premature closure of the foetal ductus arteriosus.

Breastfeeding

Paracetamol, as contained in SINUCLEAR, is excreted in breast milk but not in a clinically significant amount.

Fertility

There is no data available.

4.7 Effects on ability to drive and use machines

SINUCLEAR has moderate influence on the ability to drive and operate machinery.

Since adverse reactions such as giddiness, headache, sweating, muscular weakness and tremors have been reported in patients receiving SINUCLEAR, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that SINUCLEAR does not adversely affect their ability to do so safely (see section 4.8).

4.8 Undesirable effects

a) Summary of the safety profile

Severe hypertensive episodes have followed phenylpropanolamine ingestion, as contained in SINUSTAT. As with other indirect-acting sympathomimetics, tolerance to the therapeutic effects of phenylpropanolamine has been reported with prolonged use.

Severe reactions included hypertensive crisis with hypertensive encephalopathy, seizures, dysrhythmias, psychosis, and acute tubular necrosis. High blood pressure or symptoms suggestive of this were the presenting feature.
An acute, persistent, severe headache was also noted in many cases.

b) Tabulated list of adverse reactions

System organ class	Frequency unknown (cannot be estimated from the available data)
Infections and infestations	Sweating[1], fever
Blood and the lymphatic system disorders	Neutropenia[2], pancytopenia[2], leukopenia[2],
	blood dyscrasias, thrombocytopenia, purpura, methaemoglobinaemia, agranulocytosis,
	intracranial haemorrhage[1]
Metabolism and nutrition disorders	Altered metabolism including disturbances of glucose metabolism, reduced appetite
Psychiatric disorders	Psychotic state, confusion,
	alteration of mental status[1]
Nervous system disorders	Insomnia[1], restlessness[1], anxiety[1], tremors[1], irritability, headache[1], giddiness[1],
	agitation[1]
Eye disorders	Blurred vision[1]
Cardiac disorders	Tachycardia[1], precordial pain[1], palpitations[1], ventricular dysrhythmias, haemorrhagic stroke
Vascular disorders	Vasoconstriction which results in hypertension[1], hypotension with dizziness, fainting and flushing may occur
Respiratory, thoracic and mediastinal disorders	Dyspnoea, rebound congestion[2]
Gastrointestinal disorders	Nausea[1], vomiting[1], hypersalivation
Skin and subcutaneous tissue disorders	Skin rashes[2], usually erythematous or urticarial, accompanied by medicine fever and mucosal lesions[2], other allergic reactions[2]
Musculoskeletal and connective tissue disorders	Muscular weakness[1]
Renal and urinary disorders	Urinary retention, difficulty in micturition[1]
General disorders and administrative site conditions	Thirst[1], weakness

[1] Phenylpropanolamine hydrochloride

[2] Paracetamol

c) Description of selected adverse reactions

Respiratory, thoracic and mediastinal disorders:

Prolonged use may lead to rebound congestion.

Vascular disorders

The rise in blood pressure may produce cerebral haemorrhage and pulmonary oedema. There may also be a reflex bradycardia, but stimulation of β-1 adrenergic receptors of the heart may produce tachycardia and cardiac dysrhythmias, anginal pain, palpitations and cardiac arrest

Skin and subcutaneous tissue disorders

The rash is usually erythematous or urticarial, but sometimes more serious and may be accompanied by medicine fever and mucosal lesions.

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. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/health-products-vigilance/

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Paracetamol:

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 the 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 medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms

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 of paracetamol, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentrations 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 dysrhythmias have been reported.

Treatment

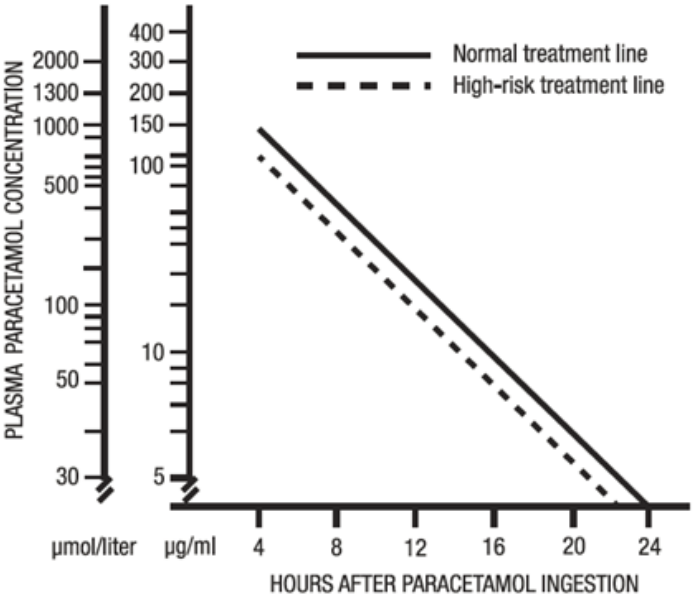
Although evidence is limited it is recommended that an adult who has ingested 5 to 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated 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 stuporous 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 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, 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 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the treatment nomogram below. The nomogram should be used in relation to a single acute ingestion only.



Reference: South African Medicines Formulary 11th Edition, 2014.

Notes for the use of the nomogram:

- Patients with plasma paracetamol concentrations on or above the Normal treatment line should be given N-acetylcysteine.
- For high risk patients (e.g. those taking enzyme inducing medicines, alcohol abusers or glutathione depleted patients) use the high risk treatment line.

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.

Phenylpropanolamine hydrochloride:

Symptoms

Symptoms of overdosage with phenylpropanolamine hydrochloride may include: rapid pulse and respiration, disorientation, elevated blood pressure, tachycardia, mydriasis, headache, excitation/stimulation of the central nervous system, nausea, vomiting and anorexia.

Treatment

Treatment is essentially symptomatic and supportive**.**

Immediate depletion of the stomach should be induced through emesis and gastric lavage. If marked excitation is present, one of the short-acting barbiturates or chloral hydrate may be used.

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: Nasal decongestants for systemic use

ATC code: R01BA53

Mechanism of action

SINUCLEAR has analgesic, antipyretic and decongestant properties.

Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent, through a peripheral action by blocking pain-impulse generation.

The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Paracetamol produces antipyresis by acting centrally on the hypothalamic heat-regulation centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action involves inhibition of prostaglandin synthesis in the hypothalamus.

Phenylpropanolamine is a mainly indirect-acting sympathomimetic.

5.2 Pharmacokinetic properties

Paracetamol

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion.

Distribution

Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life varies from about 1 to 4 hours.

Biotransformation

Paracetamol is metabolised in the liver.

Elimination

Paracetamol is excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5 % is excreted as unchanged paracetamol.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage.

Phenylpropanolamine

Absorption

Phenylpropanolamine is readily and completely absorbed from the gastrointestinal tract and peak plasma concentrations occur about 1 or 2 hours after oral doses.

Distribution

The half-life has been reported to be about 3 to 5 hours.

Biotransformation

Phenylpropanolamine undergoes some metabolism in the liver, to an active hydroxylated metabolite.

Elimination

Up to 80 % to 90 % of a dose is excreted unchanged in the urine within 24 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin capsule, magnesium stearate, sodium lauryl sulphate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the blister in the carton until required for use.

6.5 Nature and contents of container

Packs of 12 and 16 capsules in a clear polyvinyl chloride (PVC) blister strip sealed with aluminium foil. The strip is packed in an outer cardboard carton together with a leaflet.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8 REGISTRATION NUMBER

27/5.8/0101

Namibia: NS1 04/5.8/0391

9 DATE OF FIRST AUTHORISATION

Date of registration: 06 January 1993

Date of the most recent amendment to the professional information as approved by the Authority: 06 January 1993

10 DATE OF REVISION OF TEXT

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