PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

SINUSTAT FLU CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Paracetamol	300 mg
Ascorbic acid	75 mg
Phenylephrine hydrochloride	5 mg
Chlorphenamine maleate	2 mg
Caffeine anhydrous	30 mg

For the full list of excipients, see section 6.1.

Contains sugar: Lactose (32,0 mg).

3. PHARMACEUTICAL FORM

CAPSULES

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

SINUSTAT FLU CAPSULES are indicated for the relief of the symptoms associated with colds and influenza such as nasal congestion, sniffing, headache, minor aches and pains.

4.2. Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE

Adults: 2 capsules 3 times daily

Children (6 – 12 years): 1 capsule 3 times daily

Contraindicated in children under the age of 6 years.

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

Method of administration

Oral

4.3. Contraindications:

- hypersensitivity to paracetamol, ascorbic acid, caffeine, phenylephrine hydrochloride, chlorphenamine maleate any of the other ingredients (see section 6.1)
- prostatic enlargement, paralytic ileus or pyloric stenosis,
- closed angle glaucoma or with a narrow angle between the iris and the cornea,
- Sever coronary disease, severe hypertension, cardiovascular disease,
- hyperthyroidism,
- epilepsy,
- pregnancy,
- phaeochromocytoma,
- severe hepatic impairment (Child Pugh C)
- severe renal impairment,
- diabetes.
- patients being treated with monoamine oxidase inhibitors or within 10 days of stopping such treatment.
- Do not use in children under 6 years of age.

4.4. Special warnings and precautions for use

This product 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 with any other paracetamol-containing products.

The concomitant use with other medicines containing paracetamol may lead to an overdose.

Paracetamol overdose may cause liver failure, which may require liver transplant or lead to death. Underlying liver disease increases the risk of paracetamol-related liver damage.

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

Use with caution in conditions characterised by tachycardia such as thyrotoxicosis, cardiac insufficiency or failure, and in cardiac surgery.

Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index, are chronic heavy users of alcohol or have sepsis.

In patients with glutathione depleted states, the use of paracetamol may increase the risk of metabolic acidosis.

Caffeine should be given with care to patients with a history of peptic ulcer.

Chlorphenamine maleate, in common with other medicines having anticholinergic effects, should be used with caution in patients with bronchitis, bronchiectasis and asthma; hepatic impairment or renal impairment.

Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation of (eg. increased energy, restlessness, nervousness). Avoid use in elderly patients with confusion.

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

Paediatric population

Use in children under 6 years of age: Safety and efficacy have not been established (see section 4.2).

Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take SINUSTAT FLU CAPSULES.

Severe cutaneous adverse reactions (SCARs)

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-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 [TRADE NAME] must immediately be discontinued and appropriate treatment instituted.

SINUSTAT FLU CAPSULES should not be used with other antihistamine containing products, including antihistamine containing cough and cold medicines. (see section 4.5 Interactions with other medicines and other forms of interactions).

4.5. Interaction with other medicines and other forms of interaction

The rate of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Excretion may be affected, and plasma concentrations of paracetamol altered when given with probenecid.

Ascorbic acid may increase the absorption of iron in iron-deficiency states.

Omeprazole may affect the bioavailability of dietary vitamin C.

Caffeine undergoes extensive metabolism by hepatic microsomal cytochrome P450 isoenzyme CYP1A2, and is subject to many interactions with other medicines and substances that enhance or reduce its metabolic clearance.

The antihistamine chlorphenamine maleate may enhance the sedative effect of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers and may produce a soothing effect in certain individuals.

Chlorphenamine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

The effects of phenylephrine hydrochloride are enhanced by guanethidine and to a lesser extent by reserpine, methyldopa and tricyclic antidepressants.

Administer with caution to patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics.

If used concomitantly with ergot alkaloids (ergotamine and methylsergide) there is an increased risk of ergotism.

4.6. Fertility pregnancy and lactation:

Safety in pregnancy and lactation has not been established (see section 4.3).

Therefore, the use of SINUSTAT FLU CAPSULES ~~SYRUP~~ is contraindicated in pregnancy and lactation.

4.7. Effects on ability to drive and use machines:

SINUSTAT FLU CAPSULES may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8. Undesirable effects

Paracetamol:

Skin and subcutaneous disorders:

Less frequent: exfoliative dermatitis, rash, urticaria, photosensitivity

Immmune system disorders:

Less frequent: Anaphylaxis, cutaneous hypersensitivity reactions, including skin rashes, angioedema and Stevens Johnson syndrome, toxic epidermal necrolysis,

Blood and lymphatic system disorders:

Less frequent: Sensitivity reactions resulting in blood disorders including neutropenia, pancytopenia, thrombocytopenia, agranulocytosis and leucopenia.

Hepatobiliary disorders:

Less frequent Hepatic dysfunction

Renal and urinary disorders

Frequency unknown: Renal colic, nephropathy, renal failure and sterile pyuria

Gastrointestinal disorders

Frequency unknown: Pancreatitis

Respiratory, thoracic and mediastinal disorders

Less frequent: bronchospasm in patients sensitive to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs)

Phenylephrine hydrochloride:

Psychiatric disorders:

Frequency unknown: Fear, anxiety, insomnia, confusion, nervousness, irritability, psychotic states

Nervous system disorders:

Frequency unknown: Restlessness, tremor, weakness, headache, sweating, dizziness, insomnia

Gastrointestinal disorders:

Frequency unknown: Reduced appetite, nausea and vomiting, hypersalivation, diarrhoea

Vascular disorders:

Frequency unknown: Vasoconstriction, hypertension with headache, cerebral haemorrhage, hypotension with dizziness fainting, flushing, palpitations and vomiting

Cardiac disorders:

Frequency unknown: Tachycardia, palpitations

Eye disorders:

Frequency unknown: Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma.

Skin and subcutaneous disorders:

Frequency unknown: Allergic reactions (e.g. rash, urticaria, allergic dermatitis).

Renal and urinary disorders:

Frequency unknown: Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Chlorphenamine maleate:

Nervous system disorders:

Frequent: sedation, somnolence, incoordination, insomnia, tremors, convulsions, headache, disturbance in attention, abnormal coordination, dizziness

Eye disorders:

Frequent: Blurred vision

Gastrointestinal disorders:

Frequent: Nausea, dryness of mouth

Frequency unknown: vomiting, abdominal pain, diarrhoea, dyspepsia, constipation, colic and epigastric pain

Ear and labyrinth disorders:

Frequency unknown: Tinnitus

Psychiatric disorders:

Frequency unknown: Elation or depression, irritability, nightmares, confusion, excitation*

Renal and urinary disorders:

Frequency unknown: Difficulty in micturition

Respiratory, thoracic and mediastinal disorders:

Frequency unknown: Tightness of chest and heaviness, thickening of bronchial secretions

Immune system disorders:

Frequency unknown: Particularly in children, allergy and anaphylaxis may occasionally occur, angioedema

Blood and lymphatic system disorders:

Frequency unknown: Haemolytic anaemia, blood dyscrasias

Metabolism and nutritional disorders:

Frequency unknown: Anorexia

Cardiac disorders:

Frequency unknown: Palpitations, tachycardia, arrythmias

Vascular disorders:

Frequency unknown: Hypotension

Hepatobiliary disorders:

Frequency unknown: Hepatitis, including jaundice

Skin and subcutaneous disorders:

Frequency unknown: Exfoliative dermatitis, rash, urticaria, photosensitivity

Musculoskeletal and connective tissue disorders:

Frequency unknown: Muscle twitching, muscle weakness

General disorders and administration site conditions:

Frequent: Fatigue

Frequency unknown: Chest tightness

Caffeine anhydrous:

Nervous system disorders:

Frequency unknown: Headache, nervousness, anxiety, irritability, restlessness, excitability and dizziness.

Gastrointestinal disorders:

Frequency unknown: Nausea

Cardiac disorders:

Frequency unknown: Palpitations

Psychiatric disorders:

Frequency unknown: Insomnia

When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects such as insomnia, restlessness, anxiety, irritability, headaches, gastrointestinal disturbances and palpitations.

Post-Marketing Experience

Frequency unknown: Fixed drug eruptions (FDE), Drug-induced hypersensitivity syndrome (DIHS)

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 provders 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

Acino Pharma (Pty) Ltd: E-mail: drugsafety_za@acino.swiss Tel: 060 998 7896

By reporting side effects, you can help provide more information on the safety of SINUSTAT FLU CAPSULES.

4.9. Overdose

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 -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 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.

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.

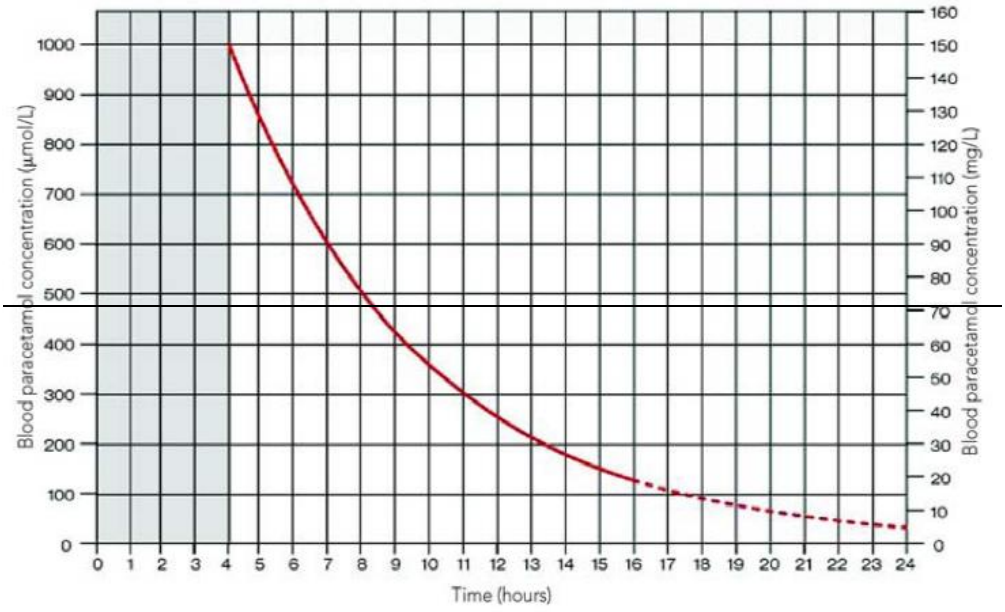
For overdose with an extended/modified release preparation the value of the nomogram is unknown. As there is no information on the plasma levels of paracetamol after an overdose of extended/modified release paracetamol preparations, all patients with suspected or known overdose with such preparations should receive N-acetylcysteine. Because of lack of data for

extended/modified release formulations, a level below the “treatment line” of the nomogram may not exclude the possibility of toxicity.

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

Nomogram for paracetamol plasma concentration

against time after ingestion



Ascorbic acid: Large doses are reported to cause diarrhoea and other gastrointestinal disturbances. It has also been stated that large doses may result in hyperoxaluria, and the formation of renal calcium oxalate calculi and ascorbic acid should therefore be given with care to patients with hyperoxaluria.

Chlorphenamine maleate overdosage may result in excitement, convulsions in susceptible persons and hypotension.

The estimated lethal dose of chlorphenamine is 25 – 50 mg/kg body

mass. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, convulsions, apnoea, anticholinergic effects, dystonic reactions and cardiovascular collapse including dysrhythmias.

Management should be as clinically indicated. Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions and fluid and electrolyte balance. If overdosage is by the oral route, treatment with activated charcoal should be considered, provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion). Treat hypotension and dysrhythmias

vigorously. CNS convulsions may be treated with IV diazepam. Haemoperfusion may be used in severe cases

Overdosage of phenylephrine hydrochloride may cause tachycardia.

Symptoms of overdosage of caffeine include restlessness, excitement, muscle tremor, tinnitus, scintillating scotoma, tachycardia and extrasystoles.

Symptoms of overdosage with phenylephrine hydrochloride – see UNDESIRABLE EFFECTS.

Symptoms of overdosage with caffeine anhydrous – see UNDESIRABLE EFFECTS.

5. PHARMACOLOGICAL PROPERTIES:

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

5.1. Pharmacodynamic properties

Paracetamol has analgesic and antipyretic actions. The mechanism of action is probably similar to that of aspirin and dependant on the inhibition of prostaglandin synthesis. This inhibition appears, however, to be on a selective basis.

Ascorbic acid is vitamin C.

Caffeine is a mild stimulant.

Phenylephrine hydrochloride is a sympathomimetic agent.

Chlorphenamine maleate is a potent antihistamine (H1-antagonist). Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H1- receptor sites on tissues. Chlorphenamine also has anticholinergic activity. Antihistamines act to revent the release of histamine, prostaglandins and leukotrienes and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenamine include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

5.2. Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. The concentration in plasma reaches a peak in 30 to 60 minutes and the plasma half-life is 1 – 4 hours after therapeutic doses. Paracetamol is relatively uniformly distributed throughout most body fluids.

Binding of paracetamol to plasma proteins is variable; 20 – 30 % may be bound at the concentrations encountered during acute intoxication. Following therapeutic doses 90 – 100 % of paracetamol may

be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation.

Ascorbic acid is readily absorbed from the gastrointestinal tract and is widely distributed in the body tissues. Body stores of ascorbic acid normally are about 1,5 g. The concentration is higher in leucocytes and platelets than in erythrocytes and plasma. Ascorbic acid additional to the body's needs, generally amounts above 200 mg daily, is rapidly eliminated. Unmetabolised ascorbic acid and its inactive metabolic products are primarily excreted in the urine. The amount of ascorbic acid excreted unchanged in the urine is dose-dependent and may be accompanied by mild diuresis.

Caffeine is absorbed readily after oral doses. Maximum plasma concentrations are achieved within one hour and the plasma half-life is about 3,5 hours. 65 – 80 % of administered caffeine is excreted in the urine as 1-methyluric acid and 1-methylxanthine.

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver. Orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

Chlorphenamine maleate is well absorbed from the gastrointestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours. Chlorphenamine is metabolised to the monodesmethyl and didesmethyl derivatives. About 22 % of an oral dose is excreted unchanged in the urine

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients:

Aerosol, lactose, purified talc.

6.2. Incompatibilities

None reported.

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

No. 0 capsule with an opaque light green cap and opaque white body.

Polypropylene securitainers with snap-on tamperproof closures of 24 capsules or aluminium/PVC/PVDC blister packs containing 20 capsules.

6.6. Special precautions for disposal and other handling

Any unused medicine should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Acino Pharma (Pty) Ltd.

106, 16th Road

Midrand, 1686

8. REGISTRATION NUMBER:

27/5.8/0449

9. DATE OF FIRST AUTHORISATION

23 February 1993

10. DATE OF REVISION OF THE TEXT

22 September 2025.

Namibia:
Reg. no.:
13/5.8/0236