Shanur Healthcare (Pty) Ltd, G979 (Act 101 of 1965), Sinucon Tablets, Paracetamol 200 mg, Ephedrine hydrochloride 6 mg, Caffeine 20 mg, Chlorpheniramine maleate 2 mg

Approved Professional Information for Medicines for Human Use

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

SINUCON 200 mg/6 mg/ 20 mg/2 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains paracetamol 200 mg, ephedrine hydrochloride 6 mg, caffeine 20 mg and chlorpheniramine maleate 2 mg.

Contains sugar: lactose 148,00 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

Round, biconvex, red and blue mottled tablets, plain on both sides, 11,10 mm in diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of colds, influenza, hay fever and sinus mucosal congestion.

4.2 Posology and method of administration

Shanur Healthcare (Pty) Ltd, G979 (Act 101 of 1965), Sinucon Tablets, Paracetamol 200 mg, Ephedrine hydrochloride 6 mg, Caffeine 20 mg, Chlorpheniramine maleate 2 mg

Posology

Adults: Two tablets every four hours.

DO NOT EXCEED THE RECOMMENDED DOSE.

Do not use continuously for longer than 10 days without medical supervision.

Paediatric population

Not recommended for children under 12 years.

Method of administration

SINUCON is for oral administration.

4.3 Contraindications

- Hypersensitivity to paracetamol, ephedrine hydrochloride, caffeine or chlorpheniramine maleate or to any of the excipients listed in section 6.1.
- Severe liver function impairment.
- Patients receiving monoamine oxidase inhibitor treatment, or within 14 days of stopping such treatment.
- Hyper-excitability and phaeochromocytoma.
- During an attack of asthma.

4.4 Special warnings and precautions for use

In the event of overdosage or suspected overdosage and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

Paracetamol

Dosages of paracetamol, as contained in SINUCON, in excess of those recommended may cause severe liver damage.

Prolonged or frequent use is discouraged. Patients should be advised not to take other paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver, medical assistance should be sought immediately. Prolonged use except under medical supervision may be harmful.

Caution is advised in the administration of paracetamol, such as in SINUCON to patients with moderate and severe renal insufficiency, mild to moderate hepatic insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (Child-Pugh > 9), acute hepatitis, concomitant treatment with medicines affecting hepatic functions, glutathione depleted states, glucose-6-phosphate dehydrogenase deficiency, haemolytic anaemia, alcohol abuse, dehydration, urinary retention, occlusive vascular disease (e.g. Reynaud’s Syndrome) and chronic malnutrition.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2 grams in such cases. Alcohol should not be used during treatment with SINUCON.

Hepatotoxicity at therapeutic doses of paracetamol

Cases of paracetamol induced hepatotoxicity, including fatal cases, have been reported in patients taking paracetamol at doses within the therapeutic range. These cases were reported in patients with one or more risk factors for hepatotoxicity including low body weight (< 50 kg), renal and hepatic impairment, chronic alcoholism, concomitant intake of hepatotoxic medicines and in acute and chronic malnutrition (low reserves of hepatic glutathione). Paracetamol should be administered with caution to patients with these risk factors. Caution is also advised in patients on concomitant treatment with medicines that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency.

Prolonged excessive use may cause irreversible kidney damage.

Sensitivity reactions resulting in reversible skin rash or blood dyscrasia may occur following paracetamol intake, as contained in SINUCON (see section 4.8).

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.

Caution is advised in asthmatic patients sensitive to aspirin because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5 % of patients tested.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised 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 SINUCON must immediately be discontinued and appropriate treatment instituted.

Chlorpheniramine maleate

Patients receiving monoamine oxidase inhibitor therapy should not take SINUCON. The anticholinergic properties of chlorpheniramine maleate, as contained in SINUCON, are intensified by monoamine oxidase inhibitors (MAOIs) (see section 4.3 and 4.5).

Children and the elderly are more likely to experience the neurological anticholinergic effects such as sedation and hypotension; and paradoxical excitation (e.g. increased energy, restlessness, nervousness). Avoid use in elderly patients with confusion.

Chlorpheniramine maleate should be used with care in patients suffering from conditions such as closed-angle glaucoma, urinary retention, prostatic hypertrophy, pyloroduodenal obstruction, severe hypertension or cardiovascular disease, bronchitis, bronchiectasis and asthma; hepatic impairment; renal impairment.

The anticholinergic properties of chlorphenamine may cause drowsiness, dizziness, blurred vision and psychomotor impairment in some patients which may seriously affect ability to drive and use machinery, see section 4.7.

Caution should be taken in patients with epilepsy or severe cardiovascular disorders. Chlorphenamine maleate may produce epileptiform seizures in patients with focal lesions of the cerebral cortex.

Allergic reactions and cross-sensitivity to related medicines may be produced.

The sedative effect of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers may be enhanced.

Should not be used with other antihistamine containing products, including antihistamine containing cough and cold medicines.

Chlorpheniramine maleate may mask the warning signs of damage caused by ototoxic medicines such as aminoglycoside antibiotics.

Ephedrine hydrochloride

Ephedrine hydrochloride, as contained in SINUCON, should be used with caution in patients with: hyperthyroidism; cardiovascular disease such as ischemic heart disease, arrhythmia or tachycardia; occlusive vascular disorders, including arteriosclerosis; hypertension or aneurysms; diabetes mellitus; closed-angle glaucoma, renal impairment.

Ephedrine has potentially life-threatening effects in its acute cardiovascular and central stimulant effects.

Anginal pains may be precipitated in patients with angina pectoris.

Ephedrine hydrochloride should be avoided or used with caution in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics as they induce ventricular fibrillation.

In patients with prostatic enlargement it may increase difficulty in micturition.

Ephedrine hydrochloride may cause an increased risk of dysrhythmias in patients receiving cardiac glycosides, quinidine or tricyclic antidepressants.

Caffeine

Caffeine, as contained in SINUCON, should be administered with caution to patients with a history of peptic ulceration or hyperacidity, hyperthyroidism, hypertension, cardiac arrhythmias or other cardiovascular diseases or uncontrolled seizure disorders as these conditions may be exacerbated.

With prolonged use, some degree of tolerance and psychic dependence may occur.

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Excessive intake of caffeine (e.g., coffee, tea, and some canned drinks) should be avoided while taking SINUCON.

Excipient lactose

This medicine contains lactose.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Paracetamol

Hepatic enzyme inducers

Paracetamol should be given with care to patients taking other medicines that affect the liver. 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 colestyramine

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

Warfarin and other coumarins

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

Salicylates

Prolonged concurrent use of paracetamol with salicylates increases the risk of adverse renal effects. Salicylamide may prolong the elimination half-life of paracetamol.

Isoniazid

Chronic use of isoniazid may increase the risk of liver damage when combined with paracetamol, even at recommended doses.

Probenecid

Excretion may be affected, and plasma concentrations altered when administered with probenecid.

Chloramphenicol

There is limited evidence suggesting that paracetamol may affect chloramphenicol pharmacokinetics.

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 risk factors (see section 4.4).

Rifampicin and some antiepileptics

Rifampicin and some antiepileptics such as carbamazepine, phenytoin, phenobarbital and primidone may interact with paracetamol.

Lamotrigine

Decrease in the bioavailability of lamotrigine, with possible reduction of its effect, due to possible induction of its metabolism in the liver.

Interference with other tests

Interference with laboratory tests: Paracetamol may affect uric acid tests by wolframatop phosphoric acid, and blood sugar tests by glucose-oxydase-peroxydase.

Chlorpheniramine maleate

Central nervous system depressants

Chlorpheniramine maleate may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquilisers.

Monoamine oxidase inhibitors

Monoamine oxidase inhibitors will potentiate both the drowsiness effect and the anticholinergic effect if taken with SINUCON. Concurrent use is not recommended (see section 4.4)

Other antimuscarinics

Chlorpheniramine maleate may have an additive action with other antimuscarinics such as atropine and tricyclic antidepressants.

Phenytoin

Chlorphenamine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

Interference with other tests

Chlorpheniramine maleate may suppress positive skin test results and should be stopped several days before the test.

Ephedrine hydrochloride

Other adrenoceptor stimulants:

Concurrent use of ephedrine with theophylline may result in increased nausea, nervousness, and insomnia.

Anaesthetics:

There may be an increased risk of arrhythmias when used with volatile liquid anaesthetics.

Antidepressants:

Ephedrine should not be given to patients who are being treated with monoamine oxidase inhibitors as they may cause hypertensive crisis with marked headache, severe hypertension and subarachnoid haemorrhage. Noradrenaline is displaced by ephedrine with the release of large amounts of catecholamine. The interaction may occur up to two weeks after stopping MAOI therapy. There may be an increased risk of arrhythmias when ephedrine is used with tricyclic antidepressants.

Antihypertensives

Loss of blood pressure control has been detected in hypertensive patients undergoing concurrent therapy with ephedrine and adrenergic neurone blocking medicines and may also occur with other antihypertensives such as guanethidine, reserpine, and alpha-methyldopa.. Special care is advisable in patients receiving antihypertensive therapy.

Antimigraine medicines

Enhanced vasoconstriction and pressor effects with ergotamine or methysergide; concurrent use of ergotamine not recommended (risk of gangrene).

Cardiac glycosides and quinidine

Increased risk of arrhythmias in patients receiving ephedrine and cardiac glycosides (e.g. digoxin) or quinidine.

Corticosteroids

Ephedrine has been shown to increase the clearance and prolong the half-life of dexamethasone in asthmatic patients.

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Oxytocin

Increased risk of vasoconstrictor or pressor effects in patients receiving oxytocin and ephedrine.

Urinary acidifiers/ alkalinisers

Effects of ephedrine may be reduced by acidification and increased by alkalinization of the urine.

Alpha and beta blocking medicines

Interactions with alpha and beta blocking medicines may be complex.

Caffeine

Caffeine, a CNS stimulant, has an antagonistic effect towards the action of sedative and tranquilizers.

Caffeine may enhance the tachycardia effect of some decongestants.

Lithium

Caffeine may increase clearance of lithium. Concomitant use is therefore not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of **SINUCON** tablets in pregnancy has not been established.

Breastfeeding

The safety of **SINUCON** tablets in lactation has not been established.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

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This medicine may lead to drowsiness and impaired concentration which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be warned not to drive a motor vehicle, operate dangerous machinery or climb dangerous heights, as impaired decisions could lead to accidents.

4.8 Undesirable effects

a) Tabulated list of adverse reactions

Paracetamol

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Blood and lymphatic system disorders		Haematological reactions e.g. thrombocytopenia, neutropenia, pancytopenia, leukopenia, anaemia, platelet disorders, stem cell disorders, agranulocytosis, haemolytic anaemia	
Immune system disorders		Allergies, hypersensitivity reaction (requiring discontinuation of treatment)	

Metabolism and nutrition disorders		Hypoglycaemia	
Psychiatric disorders		Depression, confusion, hallucinations	
Nervous system disorders		Tremor, headache	
Eye disorders		Abnormal vision	
Cardiac disorders		Oedema	
Gastrointestinal disorders		Pancreatitis, haemorrhage, abdominal pain, diarrhoea, nausea, vomiting	
Respiratory, thoracic and mediastinal disorders		Bronchospasm	
Hepatobiliary disorders		Hepatitis, hepatic function abnormal, hepatic failure, hepatic necrosis, jaundice, hepatotoxicity	

Skin and subcutaneous tissue disorders		Skin eruptions, rash, erythematous or urticarial, pruritus, sweating, purpura, urticarial angioedema	
Renal and urinary disorders		Renal colic, nephropathy, renal failure, and sterile pyuria	
General disorders and administration site conditions		Dizziness (excluding vertigo) malaise, pyrexia, sedation, drug interaction	
Injury, poisoning and procedural complications		Overdose and poisoning	

Post marketing data

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Blood and lymphatic system disorders		Agranulocytosis, thrombocytopenia	

Immune system disorders		Anaphylaxis, cutaneous hypersensitivity reactions including, among others, skin rashes and angioedema, serious skin reactions.	
Hepatobiliary disorders		Hepatic dysfunction	
Skin and subcutaneous tissue disorders			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)

Chlorpheniramine maleate

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Blood and lymphatic system disorders			Haemolytic anaemia, blood dyscrasias, agranulocytosis, leucopenia, thrombocytopenia
Immune system disorders			Allergic reaction, angioedema, anaphylactic reactions, cross sensitivity to related medicines

Metabolism and nutrition disorders			Anorexia
Psychiatric disorders			Confusion, excitation, irritability, nightmares, depression
Nervous system disorders	Sedation, somnolence, disturbance in attention, abnormal coordination, dizziness, headache, lassitude		Tremors, convulsions
Eye disorders	Blurred vision		
Ear and labyrinth disorders			Tinnitus
Cardiac disorders			Palpitations, tachycardia, arrythmias
Vascular disorders			Hypotension

Respiratory, thoracic and mediastinal disorders			Thickening of bronchial secretions
Gastrointestinal disorders	Nausea, dry mouth		Vomiting, abdominal pain, diarrhoea, constipation, dyspepsia (epigastric pain), increased appetite, increased gastric reflux
Hepatobiliary disorders			Hepatitis, including jaundice
Skin and subcutaneous tissue disorders			Exfoliative dermatitis, rash, urticaria, photosensitivity
Musculoskeletal and connective tissue disorders			Muscle twitching, muscle weakness
Renal and urinary disorders			Urinary retention, difficulty in micturition and dysuria

General disorders and administration site conditions	Fatigue		Chest tightness, paraesthesia

Ephedrine hydrochloride

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Metabolism and nutrition disorders			Altered metabolism including disturbances of glucose metabolism
Psychiatric disorders		Psychotic states	Tolerance with dependence (prolonged administration)
Nervous system disorders	Anxiety, restlessness, insomnia, headache	Tremor, fear	Confusion, irritability, weakness
Eye disorders			Miosis
Cardiac disorders	Tachycardia, palpitations	Reflex bradycardia, cardiac dysrhythmias,	Pulmonary oedema

		angina pain, cardiac arrest, myocardial infarction	
Vascular disorders		Vasoconstriction with resultant hypertension, hypotension with dizziness and fainting	Cerebral haemorrhage.
Respiratory, thoracic and mediastinal disorders		Chest discomfort or pain	Dyspnoea
Gastrointestinal disorders	Nausea	Decrease in appetite, vomiting	Hypersalivation, dry mouth
Skin and subcutaneous tissue disorders			Sweating
Musculoskeletal and connective tissue disorders		Muscle cramps	
Renal and urinary disorders			Difficulty in micturition, urinary retention

General disorders and administration site conditions		Flushing	Thirst

Caffeine

Post marketing data

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Psychiatric disorders			Restlessness, excitement, anxiety, irritability, nervousness
Nervous system disorders			Headache, insomnia, dizziness
Eye disorders			Scintillating scotoma
Ear and labyrinth disorders			Tinnitus
Cardiac disorders			Tachycardia, extrasystoles, palpitations

Gastrointestinal disorders			Nausea, gastro-intestinal irritation, increased gastric secretion which may cause gastric ulceration
Musculoskeletal and connective tissue disorders			Muscle tremor

b) Description of selected adverse reactions

Paracetamol

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

Skin eruptions have occurred. Sensitivity reactions including skin rash may occur. This is usually erythematous or urticarial but sometimes may be more serious and may be accompanied by drug fever and mucosal lesions. See also section 4.4 (SCARs).

Interstitial nephritis has been reported incidentally after prolonged use of high doses. Some cases of oedema of the larynx, anaphylactic shock, anaemia, liver alteration and hepatitis, renal alteration (severe renal impairment, nephrite interstitial, haematuria, anuresis) gastrointestinal effects and vertigo have been reported.

Chlorpheniramine maleate

Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation. Symptoms of cerebral stimulation include increased energy, insomnia, restlessness, nervousness, euphoria, irritability, tremors and rarely nightmares, hallucinations and convulsions.

If sedative effects occur, they may diminish after a few days of treatment.

Ephedrine hydrochloride

Ephedrine hydrochloride, as contained in SINUCON, may act as stimulant in children with nocturnal enuresis and cause sleeplessness. It may have sedative effects in some children.

The elderly are more sensitive to the cardiovascular effects of ephedrine hydrochloride.

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 professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8 Suspected adverse reactions can also be reported directly to the HCR via medsafety@austell.co.za

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 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.

Chlorpheniramine maleate

Overdosage of antihistamines may be fatal especially in children. Overdosage with chlorpheniramine maleate is associated with antimuscarinic, extrapyramidal, gastro-intestinal and CNS effects. In children CNS stimulation predominates. In adults CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure or possible cardiovascular collapse.

Ephedrine hydrochloride

Symptoms of ephedrine hydrochloride overdosage include nausea, vomiting, fever, palpitations, tachycardia, hypertension, respiratory depression, convulsions, coma, paranoid psychosis, delusions and hallucinations - also see section 4.8.

Caffeine

Severe overdosage of caffeine or idiosyncrasy may lead to manic behaviour, diuresis and repeated vomiting with extreme thirst, tremor, delirium, hyperthermia, tachycardia, tachypnoea, electrolyte disturbances, convulsions and death. See also section 4.8.

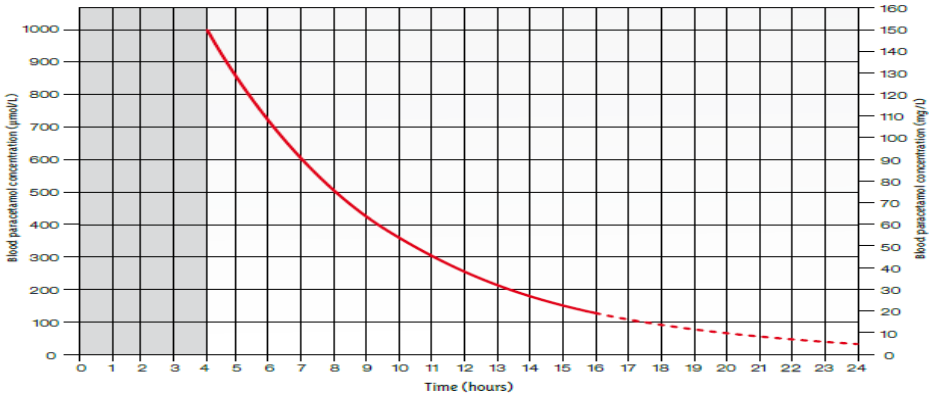
Treatment of overdosage

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 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:



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.

In severe overdosage with antihistamines or caffeine the stomach should be emptied. Activated charcoal has been given, as have saline laxatives. Convulsions may be controlled with diazepam although it has been suggested that CNS depressants should be avoided with overdosage of antihistamines. Cerebral stimulants may increase the risk of convulsions and should be avoided.

Other treatment is symptomatic and supportive.

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: Cough and cold preparations; other cold preparations.

ATC code: R05X

Shanur Healthcare (Pty) Ltd, G979 (Act 101 of 1965), Sinucon Tablets, Paracetamol 200 mg, Ephedrine hydrochloride 6 mg, Caffeine 20 mg, Chlorpheniramine maleate 2 mg

SINUCON tablets have analgesic, antipyretic, sympathomimetic and antihistaminic properties.

5.2 Pharmacokinetic properties

Absorption

Paracetamol

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.

Chlorpheniramine maleate

Chlorpheniramine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours.

Ephedrine hydrochloride

Ephedrine is rapidly and completely absorbed from the gastrointestinal tract.

Caffeine

Caffeine is absorbed readily after oral administration. Maximal plasma concentrations are achieved within one hour and the plasma half-life is about 3,5 hours.

Distribution

Paracetamol

Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of paracetamol to plasma proteins is variable; 20 to 30 % may be bound at the concentrations encountered during acute intoxication.

Chlorpheniramine maleate

The plasma half-life has been estimated to be 12 to 15 hours.

Ephedrine hydrochloride

Ephedrine is extensively distributed throughout the body with accumulation in the liver, lungs, kidneys, spleen and brain.

Biotransformation

Paracetamol

Practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation.

Chlorpheniramine maleate

Chlorpheniramine is metabolised to the monodesmethyl and didesmethyl derivatives.

Ephedrine hydrochloride

Small amounts of metabolites are produced by hepatic metabolism.

Elimination

Paracetamol

Following therapeutic doses 90 – 100 % of paracetamol may be recovered in the urine within the first day.

Chlorpheniramine maleate

About 22 % of an oral dose is excreted unchanged in the urine.

Ephedrine hydrochloride

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Ephedrine has been variously reported to have a plasma half-life ranging from 3 to 6 hours depending on urinary pH; elimination is enhanced and half-life accordingly shorter in acid urine. It is excreted largely unchanged in the urine with up to 95 % being excreted in the urine.

Caffeine

65 – 80 % of administered caffeine is excreted in the urine as 1-methyluric acid and 1-methylxanthine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch

Lactose

Gelatin

Carmoisine Red (CI 14720)

Green S (CI 44090)

Magnesium stearate

Talc

Sodium starch glycollate.

6.2 Incompatibilities

None.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 ºC. Protect from light and moisture.

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6.5 Nature and contents of container

Containers of 20 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Shanur Healthcare (Pty) Ltd

Loch House Unit 003

3A Eton Road, Parktown

Johannesburg, 2193

8. REGISTRATION NUMBER

G979 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

4 October 1974

10. DATE OF REVISION OF THE TEXT

31 October 2024