1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINE FOR HUMAN USE

SCHEDULING STATUS

S2

PROPRIETARY NAME AND DOSAGE FORM

FLUSIN Sugar-coated Tablets

COMPOSITION

Each tablet contains:

Chlorphenamine maleate ……	2 mg
Ephedrine hydrochloride ……	6 mg
Paracetamol ……	200 mg
Caffeine ……..	20 mg

Excipients:

Tablet core: lactose, magnesium stearate, microcrystalline cellulose, povidine-K90, pregelatinized starch.

Sugar coating: gum acacia, maize starch, modified shellac as Opaglos NA 7150, Opalux AS-35014(red), sucrose (Sugar-H118), talc-purified titanium dioxide, wax-E.

CONTAINS LACTOSE and SUCROSE

PHARMACOLOGICAL CLASSIFICATION

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

PHARMACOLOGICAL ACTION

FLUSIN has analgesic, antipyretic, antihistaminic and decongestant properties.

INDICATIONS

FLUSIN is indicated for the symptomatic relief of colds and influenza associated with nasal and sinus congestion.

CONTRAINDICATIONS

FLUSIN is contraindicated in:

- Patients with hypersensitivity to the active ingredient or to any of the excipients in FLUSIN (see COMPOSITION).
- Coronary disease and cardiovascular disease such as ischaemic heart disease, dysrhythmia or tachycardia.
- Safety in pregnancy and lactation has not been established.
- Children under 8 years old.

Chlorphenamine maleate

- Patients sensitive to one histamine may be sensitive to others.

Ephedrine hydrochloride

- Patients receiving treatment with a monoamine oxidase inhibitors or a reversible inhibitor of monoamine oxidase type A, or within 14 days of stopping such treatment.
- Should be avoided in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics as they may induce ventricular fibrillation.

Paracetamol

- Severe liver function impairment.

WARNINGS AND SPECIAL PRECAUTIONS

May lead to drowsiness and impaired concentration, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressants e.g. sedatives and tranquilizers. Caution should be used when driving a motor vehicle or operating machinery or performing potentially dangerous tasks, where loss of concentration may lead to accidents.

Consult a doctor if no relief is obtained from the recommended dosage.

Do not use this product for more than 7 days without consulting a doctor.

Chlorphenamine maleate

Should be used with caution in patients with prostatic hypertrophy, narrow angle glaucoma, emphysema or chronic bronchitis, porphyria.

Paradoxical hyperexcitability, nervousness and insomnia may occur in children and in the elderly. Elderly patients are especially susceptible to dizziness, sedation, confusion, hypotension and anticholinergic effects such as dry mouth and urinary retention.

Should be used with care in patients with pyloroduodenal obstruction, epilepsy and severe cardiovascular disorders.

Ephedrine hydrochloride

If symptoms do not improve, or are accompanied by a fever, consult a doctor. Exceeding the

recommended dosage may result in nervousness, dizziness, sleeplessness, tremulousness or cardiac dysrhythmia. This may also occur in sensitive individuals at small doses. Should be used with caution in patients with hypertension, hyperthyroidism, diabetes mellitus, closed-angle glaucoma, prostatic hypertrophy, phaeochromocytoma, occlusive vascular disease including arteriosclerosis, aneurysms.

Paracetamol

Consult your doctor if pain or fever persists or gets worse, if new symptoms occur or if redness and swelling is present, as these could be signs of a serious condition.
In the event of overdosage or suspected overdosage, prompt medical attention is critical for adults as well as children, even if there is no obvious signs or symptoms. The nearest doctor, hospital or poisons control centre must be contacted immediately (see KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT).

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

Consult a doctor if no relief is obtained from the recommended dosage.

Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take paracetamol.

Use with caution in renal disease.

Caffeine

Should be given with caution to patients with peptic ulceration, hyperthyroidism, hypertension or cardiac dysrhythmias as these conditions may be exacerbated.

INTERACTIONS

Chlorphenamine maleate

All sedatives, including alcohol, will potentiate depressant effects on the central nervous system if taken with antihistamines.

May enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics.

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

Medications tending to cause extra pyramidal reactions and those with anticholinergic effects may be potentiated. These include tricyclic antidepressants, maprotiline and monoamine oxidase inhibitors.

Ephedrine hydrochloride

Reversal of the action of antihypertensive agents may occur and therefore special care is advisable in patients receiving antihypertensive therapy. Interactions with alpha-and beta-blockers may be complex and can produce hypertensive crisis.

May cause a hypertensive crisis in patients receiving a monoamine oxidase inhibitor (including reversible inhibitors of monoamine oxidase type A).

Interactions are possible with tricyclic antidepressants, guanethidine, reserpine, alpha-methyldopa and digoxin.

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

An increased risk of dysrhythmias may occur when given to patients receiving cardiac glycosides, quinidine or tricyclic depressants and there is an increased risk of vasoconstrictor effects in patients receiving alkaloids or oxytocin.

DOSAGE AND DIRECTIONS FOR USE

Adults and children over 12 years of age: Take two tablets every 4 hours.

Children 8 to 12 years: Take one tablet every 4 hours.

SIDE EFFECTS

Chlorphenamine maleate:

Central nervous system reactions include sedation, drowsiness, confusion, hallucinations, convulsions, headache, dizziness, tinnitus, lassitude, incoordination, fatigue, nervousness, insomnia and tremors. Extra pyramidal effects with muscle spasms and dystonia.
Gastrointestinal disturbances such as nausea, vomiting, epigastric pain and diarrhoea have occurred. Anticholinergic effects with ataxia, flushing, blurred vision, dryness of the mouth, throat and respiratory passages, thickening of mucus, urinary retention or frequency, dysuria, reduction in tone and motility of the gastrointestinal tract, resulting in constipation and gastric reflux.
Palpitation and dysrhythmias, hypertension, hypotension, tachycardia, headache, tightness of the chest, tingling, heaviness, and weakness of the hands.

Photosensitivity and skin rash, allergic dermatitis and drug fever.
Blood dyscrasia, including agranulocytosis, leucopenia, haemolytic anaemia and thrombocytopenia have been reported.

May cause rashes and hypersensitivity reactions (including bronchospasm, angioedema and

anaphylaxis).

Sweating, myalgia, paraesthesias, sleep disturbances, depression, hair loss.

Ephedrine hydrochloride

Fear, anxiety, restlessness, tremor, insomnia, confusion, irritability, dry mouth, impaired circulation to the extremities, weakness and psychotic states. Appetite may be reduced and nausea and vomiting may occur.

Vasoconstriction with resultant hypertension. The rise in blood pressure may produce cerebral haemorrhage and pulmonary oedema. There may also be reflex bradycardia, but stimulation of B_1-adrenergic receptors of the heart may produce tachycardia and cardiac dysrhythmias, anginal pain, palpitations and cardiac arrest. Hypotension with dizziness and fainting and flushing may occur.

Difficulty in micturition and urinary retention, dyspnoea, altered metabolism, including disturbances of glucose metabolism, sweating and hypersalivation.
Headache is also common.

Paracetamol

Pancreatitis, skin rashes and other allergic reactions may occur. The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesions.

The use of paracetamol has been associated with the occurrence of agranulocytosis, thrombocytopenia, neutropenia, pancytopenia, leucopenia, anaemia, dermatitis, hepatitis,

renal colic, renal failure and sterile pyuria.

Caffeine

Nausea, vomiting, abdominal pain and gastrointestinal irritation and gastrointestinal bleeding. Stimulation of the central nervous system with insomnia, headache, anxiety, restlessness, vertigo and palpitations can occur.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Chlorphenamine maleate

Symptoms

Central excitatory effects constitute the greatest danger in overdose. Symptoms include drowsiness or paradoxical excitement, hallucinations, ataxia, incoordination, athetosis and convulsions. Fixed dilated pupils with a flushed face, sinus tachycardia, dyspnoea, urinary retention, dry mouth and fever. Terminally deepening coma and cardiorespiratory collapse.

Children and the elderly are more likely to exhibit anticholinergic and central nervous system stimulant effects. The elderly are prone to hypotension.

Treatment

The stomach should be emptied by emesis or lavage. There is no specific antidote and treatment is symptomatic and supportive. It may be necessary to treat extrapyramidal reactions with barbiturates or diphenhydramine.

The patient must be taken to a doctor or hospital immediately as specialised treatment may be necessary.

Ephedrine hydrochloride

Ephedrine overdosage may result in paranoid psychosis, delusions, hallucinations, convulsions and hypertension in susceptible patients. Overdosage may also cause tachycardia, dysrhythmias and anginal pain and respiratory depression.

Paracetamol

Symptoms

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 to10 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 of paracetamol overdosage in the first 24 hours are 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 dysrhythmias have been reported.

Treatment

Prompt treatment is essential in the management of paracetamol overdosage. Any adult person who has ingested about 7,5 g or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding 4 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.

IV: An initial dose of 150 mg/kg N-acetylcysteine in 200 ml glucose injection given intravenously over 15 minutes, followed by an intravenous infusion of 50 mg/kg in 500 ml of glucose injection over the next 4 hours, and then 100 mg/kg in 1000 ml glucose injection over the next 16 hours. The volume of intravenous fluids should be modified for children.
Orally (not the treatment of choice): 140 mg/kg as a 5 % solution initially, followed by a 70 mg/kg solution every 4 hours for 17 doses. N-acetylcysteine is more likely to be effective if administratered within 8 hours of overdosage.

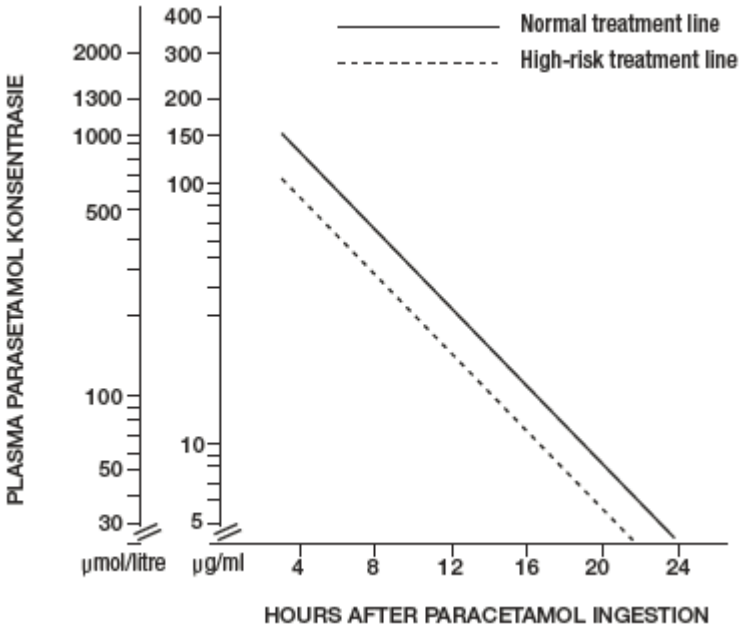
A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours, unless high, may be misleading. Patients at risk of liver damage, and hence requiring continued treatment of N-acetylcysteine, can be identified according to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

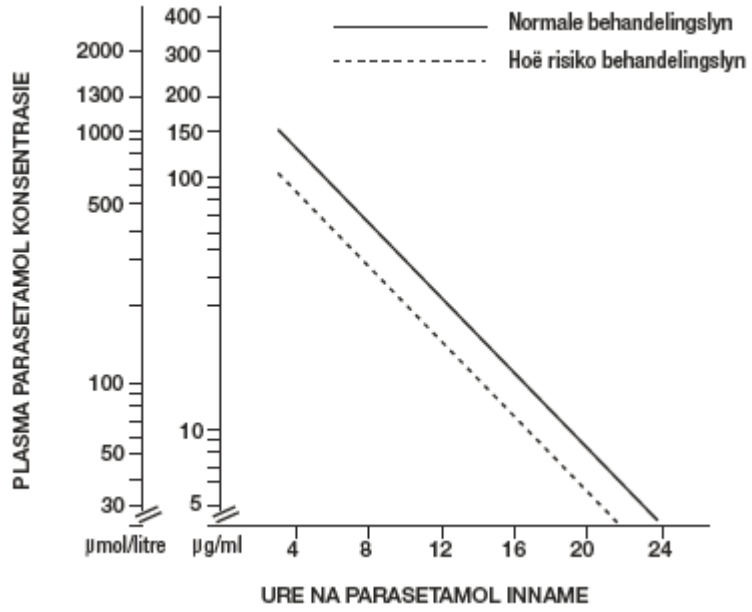
Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the “high risk treatment line”. Prothrombin index correlates best with survival.

If N-acetylcysteine is not available, methionine 2,5 g may be given immediately, followed by 2,5 g every four hours for three doses. Patients should however preferably be transferred to a facility where N-acetylcysteine can be given.

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

Paracetamol Nomogram





Notes for the use of the nomogram:

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

- The nomogram should be used in relation to a single acute ingestion only.

Caffeine

Symptoms

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

Treatment

Treatment is symptomatic and supportive.

The patient must be taken to a doctor or hospital immediately as specialised treatment may be necessary.

IDENTIFICATION

A biconvex sugar-coated orange tablet.

PRESENTATION

Available in packs of 24's.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store in a dry place at or below 25°C.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER

C562 (Act 101/1965)

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PACKAGE INSERT

8 September 1970

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