1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1. NAME OF MEDICINE

ACUFLU P SYRUP/STROOP 15 mg/ 0,625 mg/ 125 mg per 5 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of ACUFLU P SYRUP/STROOP contains 15 mg of pseudoephedrine hydrochloride, 0,625 mg of triprolidine hydrochloride and 125 mg of paracetamol.

Preservatives:

Methyl hydroxybenzoate 0,12 % *m/v*

Propyl hydroxybenzoate 0,02 % *m/v*

Contains sugar: Sorbitol 1,01 g

Contains sweetener: Saccharin sodium 45 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup.

ACUFLU P SYRUP/STROOP is a pink, viscous syrup with a raspberry odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

ACUFLU P 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 three times daily

Children 2 to 6 years: Take 5 ml three times daily

Paediatric population

The safety and efficacy of ACUFLU P in children younger than two years of age has not been established (see section 4.3).

Method of administration

For oral administration.

4.3 Contraindications

ACUFLU P SYRUP/STROOP is contraindicated in:

- Patients with hypersensitivity to triprolidine HCl, pseudoephedrine HCl, paracetamol or to any of the excipients (see section 6.1).
- Severe cardiovascular disease (especially coronary insufficiency).
- Severe hypertension.
- Thyrotoxicosis.
- Prostatism.
- Bladder dysfunction.
- Closed angle glaucoma.

- Phaeochromocytoma.
- During an attack of acute asthma in asthmatic patients.
- In 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.
- Safety in pregnancy and lactation has not been established.
- Children under two years of age.
- 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

ACUFLU P 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.

Cardiovascular diseases

Great care is needed in patients with cardiovascular disease such as ischaemic heart disease, dysrhythmia or tachycardia, occlusive vascular disorders, including arteriosclerosis, hypertension or aneurysms (see section 4.3).

Paracetamol

ACUFLU 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.

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

Do not take concurrently with any other paracetamol- or sympathomimetic-containing medicines.

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, as contained in ACUFLU P SYRUP/STROOP. If a patient develops SCAR, treatment with ACUFLU P SYRUP/STROOP must immediately be discontinued and appropriate treatment instituted.

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 HCl

Pseudoephedrine should be given with caution to patients with organic heart disease, cardiac

decompensation or angina of effort and in patients receiving digitalis.

Special care should be taken in patients with hyperthyroidism, cardiovascular disease such as ischaemic heart disease, dysrhythmia or tachycardia, occlusive vascular disorders, including arteriosclerosis, hypertension and aneurysms, diabetes mellitus and closed-angle glaucoma (see section 4.3). Anginal pain may be precipitated in patients with angina pectoris (see section 4.8).
Symptoms of central nervous system excitation, may occur, including sleep disturbances and hallucinations. Difficulty with micturition may also be experienced. Dyspnoea; altered metabolism including disturbances of glucose metabolism, sweating and hypersalivation are possible (see section 4.8).

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. Pseudoephedrine should be discontinued, and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop (see section 4.8).

Ischaemic optic neuropathy

Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs (see section 4.8).

Acute Generalised Exanthematous Pustulosis (AGEP)

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported with pseudoephedrine-containing medicines, such as ACUFLU P 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.

Triprolidine HCl

ACUFLU P SYRUP/STROOP should not be given to premature infants or neonates (see section 4.2).

ACUFLU P SYRUP/STROOP should be used with care in the elderly who are more susceptible to many of the side effects, patients with closed angle glaucoma, urinary retention, prostatic hypertrophy or pyloroduodenal obstruction, epilepsy, severe cardiovascular disorders (see section 4.3).

Patients should avoid alcoholic drinks.

Allergic reactions and cross-sensitivity to related medicines are possible with systemic triprolidine administration.

Blood disorders including agranulocytosis, leukopenia and haemolytic anaemia have been reported (see section 4.8).

Elderly patients are more susceptible to the central nervous system depressant and hypotensive effects of antihistamines even at therapeutic doses.

It is possible that some sedating antihistamines, such as triprolidine, as contained in ACUFLU P SYRUP/STROOP could mask the warning signs of ototoxic damage caused by medicines, such as aminoglycoside antibiotics (see section 4.5).

Do not use this product without consulting a doctor or pharmacist if you are presently taking monoamine oxidase inhibitors or other medicines for depression, psychiatric or emotional conditions or hypertension (see section 4.3).

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.

Paediatric population

The safety and efficacy of ACUFLU P SYRUP/STROOP in children younger than two years of age has not been established (see section 4.2 and 4.3).

Excipients

ACUFLU P SYRUP/STROOP contains sorbitol and may have a laxative effect. Patients with the rare hereditary condition of sorbitol intolerance should not take ACUFLU P SYRUP/STROOP. The additive effect of concomitantly administered medicines containing sorbitol and dietary intake of sorbitol should be taken into account. The content of sorbitol in medicines for oral use may affect the bioavailability of other medicines for oral use administered concomitantly.

4.5 Interaction with other medicines and other forms of Interaction

Triprolidine HCl

Tricyclic antidepressants

The antimuscarinic effects of atropine and some antidepressants (both tricyclic antidepressants and monoamine oxidase inhibitors) may be enhanced by triprolidine.

Triprolidine, as contained in ACUFLU P SYRUP/STROOP may affect the metabolism of certain medicines in the liver.

Ototoxic medicines

Triprolidine could mask the warning signs of damage caused by ototoxic medicines such as aminoglycosides.

CNS depressants

The sedative effects of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics can be enhanced with triprolidine.

Laboratory tests

Triprolidine may suppress the positive results of allergen skin tests and therefore should be stopped several days before skin testing.

Pseudoephedrine HCl

Anaesthetics

Pseudoephedrine should be avoided or used with caution in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics, as they may induce ventricular fibrillation (see section 4.3).

Cardiac glycoside, quinidine and tricyclic antidepressants

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

Monoamine oxidase inhibitors

Interaction with monoamine oxidase inhibitors and should not be given to patients receiving such treatment or within 14 days of its termination (see section 4.3). Pseudoephedrine, as contained in ACUFLU P SYRUP/STROOP, may give rise to a hypertensive crisis in patients receiving monoamine oxidase inhibitors (MAOIs) including reversible inhibitors of monoamine oxidase A (RIMAs).

Antihypertensives

Pseudoephedrine increases blood pressure and therefore special care is advised in patients receiving antihypertensive therapy. Pseudoephedrine may partially reverse the hypotensive action of medicines which interfere with sympathetic activity including bretylium, bethanidine, debrisoquine, methyldopa and beta-adrenergic blocking medicines.

The effects of pseudoephedrine are diminished by guanethidine, reserpine and probably methyldopa and may be diminished or enhanced by antidepressants. Pseudoephedrine, as contained in ACU-FLU SYRUP/STROOP may also diminish the effects of guanethidine and may increase the possibility of dysrhythmias in digitalised patients.

Sympathomimetic medicines

Concomitant use of ACUFLU P SYRUP/STROOP with sympathomimetic medicines, such as

nasal decongestants, appetite suppressants and amphetamine-like psychostimulants, or with medicines that interfere with the catabolism of sympathomimetic medicines, may cause a rise in blood pressure largely because of interaction with pseudoephedrine.

Doxapram

Doxapram used concurrently with ACUFLU P SYRUP/STROOP may increase the pressor effects of either doxapram or sympathomimetic amines such as pseudoephedrine as contained in ACUFLU P SYRUP/STROOP.

Rauwolfia alkaloids

Concurrent use with rauwolfia alkaloids may inhibit the indirect-acting sympathomimetic action of pseudoephedrine.

Aluminium hydroxide-containing medicines

Aluminium hydroxide containing preparations may increase the absorption rate of pseudoephedrine hydrochloride.

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.

Metoclopromide and domperidone

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

Colestyramine

The speed of absorption of paracetamol may be reduced by colestyramine.

Anticoagulants

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.

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 contained in ACUFLU P 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.

4.6 Fertility, pregnancy and lactation

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

Pregnancy

Pseudoephedrine

Defective closure of the abdominal wall (gastroschisis) reported very rarely in newborns after first trimester exposure. The product should not be used in pregnancy unless considered essential by the physician.

Breastfeeding

Pseudoephedrine is excreted in breast milk in small amounts, but the effect of this on breast-fed infants is not known. It has been estimated that 0.5–0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast milk over 24 hours.

Fertility

No data available.

4.7 Driving and using machines

ACUFLU P SYRUP/STROOP has moderate influence on the ability to drive or operate machinery. ACUFLU SYRUP/STRROP 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 not drive, climb dangerous heights or operate machinery as impaired decision-making could lead to accidents. (see section 4.4 and 4.8).

4.8 Undesirable effects

a) Summary of the safety profile

Sedation or insomnia may occur.

b) Tabulated list of adverse reaction

Triprolidine hydrochloride

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Blood and the lymphatic system disorders		Blood dyscrasias, including agranulocytosis, leucopenia, haemolytic anaemia and thrombocytopenia.	
Immune system disorders			Allergy, anaphylaxis, and hypersensitivity reactions (including bronchospasm and angioedema).
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, euphoria, irritability, tremors, and rarely, nightmares, hallucinations tachycardia, muscle twitching, and convulsions.		Inability to concentrate, elation or depression and sleep disturbances.

Nervous system disorders	Headache and psychomotor impairment.		Paraesthesias. tremor, muscular weakness, confusion deepening coma, extrapyramidal effects, 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			In high doses, transient bradycardia followed by tachycardia with palpitations and dysrhythmias, hypotension, impaired circulation to the extremities
Respiratory, thoracic and mediastinal disorders	Thickened respiratory-tract secretions		Tightness of the chest
Gastrointestinal disorders	Dry mouth, a reduction in tone and motility of the gastrointestinal tract resulting in constipation and increased gastric reflux.		Other gastrointestinal disturbances include nausea, vomiting, diarrhoea and epigastric pain, colic and anorexia.

Skin and subcutaneous tissue disorder			Sweating dermatological reactions may occur, including photosensitisation of the skin and lichenoid skin eruption, hair loss.
Musculoskeletal and connective tissue disorders			Myalgia
Renal and urinary disorders	Urinary difficulty and retention.		
General disorders and administrative site conditions			Lassitude

Pseudoephedrine HCl

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Metabolism and nutrition disorders		Decreased appetite, hypokalaemia, altered metabolism including disturbances of glucose metabolism.	Thirst
Psychiatric disorders	Anxiety, restlessnes, insomnia, nervousness central effects include fear, confusion, irritability and psychotic	Hallucinations	Giddiness, agitation, Adverse mental effects (particularly in children) have been associated with combination preparations containing pseudoephedrine.

	states.		
Nervous system disorders	Dizziness, tremors and restlessness.	Headache, convulsions, weakness.	Fainting
Eye disorders			Miosis, Ischaemic optic neuropathy.
Cardiac disorders	Tachycardia	Reflex bradycardia, palpitations, pulmonary oedema, anginal pain, cardiac arrest, cardiac dysrhythmias.	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.
Respiratory, thoracic and mediastinal disorders		Dyspnoea or troubled breathing.	Pulmonary oedema
Gastrointestinal disorders		Nausea and vomiting may occur, 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 due to pseudoephedrine, taking the form of erythematous nummular patches, have been reported.

Musculoskeletal 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** (cannot be estimated from the available data)
Blood and the lymphatic system disorders			Thrombocytopenia, leukopenia, pancytopenia, neutropenia and agranulocytosis.
Immune system disorders		Sensitivity/allergic reactions resulting in skin rash, laryngeal oedema, angioedema and anaphylaxis.	

Skin and subcutaneous tissue disorders	Erythematous rash, urticarial rash.		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.
Gastrointestinal disorders		Pancreatitis occurs occasionally, mucosal lesions.	
General disorders and administration site conditions		Fever	

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** via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Triprolidine Hydrochloride

Symptoms

Overdosage may be fatal especially in infants and children. In infants and children, CNS excitement predominates with ataxia, excitement, tremors, psychoses, hallucinations and convulsions; hyperpyrexia may also occur. Deepening coma and respiratory collapse may follow.

In adults, CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure and possibly cardiovascular collapse.

Treatment

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

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

Pseudoephedrine hydrochloride

Symptoms

Convulsions and hyperpyrexia in children due to cerebral stimulation. In adults, symptoms of stimulation include insomnia, nervousness, tachycardia, tremors, muscle twitching and convulsions. Severe cardiovascular repercussions include hypertension, angina, arrhythmias, myocardial infarction and cerebral haemorrhage.

Treatment

To decrease absorption:

Because pseudoephedrine is rapidly absorbed from the gut, emetics and gastric lavage should be instituted within 4 hours of overdosage in order to be effective. Charcoal is useful only if administered within 1 hour.

To enhance elimination:

Forced diuresis will increase elimination of pseudoephedrine provided renal function is adequate; however, diuresis is not recommended for severe overdosage.

Specific treatment:

For delirium or convulsions, intravenous diazepam may be administered.

The cardiac state should be monitored and serum electrolytes measured. If there are signs of cardiac toxicity, intravenous propranolol may be indicated.

Hypokalaemia may be treated, if necessary, with a slow infusion of a dilute potassium chloride solution; serum potassium concentration should be monitored during and for several hours after administration of potassium chloride.

Paracetamol

Symptoms

Nausea, vomiting and anorexia. Liver damage, which may be fatal, may only appear after a few days. Acute intoxication may cause kidney failure.

Prompt treatment is essential. In the event of overdosage consult a doctor or take the patient to the nearest hospital immediately. 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 are pallor, nausea, vomiting, anorexia and 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

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

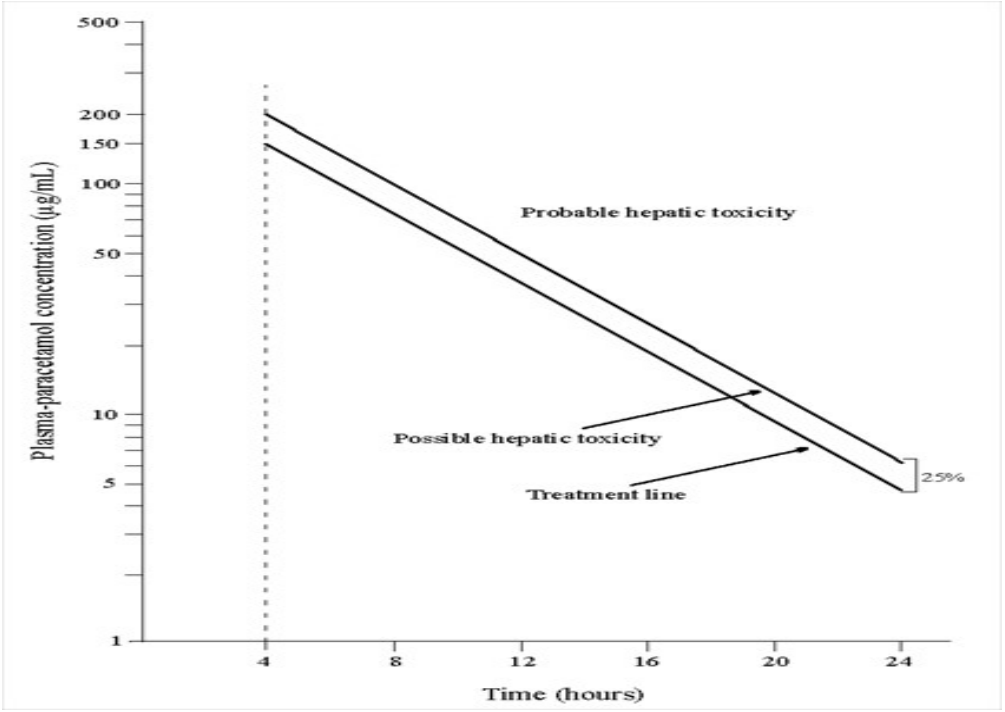
N-acetylcysteine should be administered as soon as possible, preferably within 8 hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

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 1000 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 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.

5. PHARMACOLOGICAL ACTION

5.1 Pharmacodynamic properties

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

Pharmacotherapeutic group: Sympathomimetics, pseudoephedrine, combinations.

ATC Code: R01BA52

Mechanism of action

ACUFLU P SYRUP/STROOP has decongestive, antipyretic, antihistamine and analgesic properties.

5.2 Pharmacokinetic properties

Absorption

Tripolidine Hydrochloride

After absorption from the gastrointestinal tract, triprolidine is metabolised.

Pseudoephedrine

Pseudoephedrine is readily absorbed from the gastrointestinal tract.

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.

Following oral administration of a single 30 mg tablet, a mean maximum plasma concentration of 104 ± 19 ng/mL is attained in 1,46 ± 0,55 hours. Following oral administration of a single 60 mg dose as tablets, mean maximum plasma concentrations of 180 ± 30 and 232 ± 30 ng/mL are attained at 1,94 ± 0,86 and 1,96 ± 0,62 hours, respectively.

Paracetamol

Oral paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract, primarily in the small intestine. Absorption occurs by passive transport. The rate of oral absorption depends mainly upon the rate of gastric emptying. The relative bioavailability ranges from 85 % to 99 %. Peak plasma concentrations are usually attained about 30 – 60 minutes after oral dosing.

For individual adults, maximum plasma concentrations occur within 1 hour following ingestion, and range from 14,8 to 17,6 µg/mL for a single 1 000 mg dose. Maximum plasma concentrations at steady state after 1 000 mg doses every 6 hours range from 17,6 to 18,2 µg/mL.

Distribution

Tripolidine Hydrochloride

Triprolidine is distributed into breast milk.

Pseudoephedrine

The apparent volume of distribution for pseudoephedrine ranges from 2,3 to 3,3 L/kg. Up to 0,7 % of a single 60 mg dose of pseudoephedrine may be distributed into breast milk over 24 hours. Pseudoephedrine concentrations in milk are from 2 to 3-fold higher than those in plasma. This milk/plasma drug concentration profile suggests low protein binding, although no protein plasma binding data in humans are available. Data from a study of lactating mothers taking 60 mg pseudoephedrine every 6 hours suggests that from 2,2 to 6,7 % of the maximum daily dose (240 mg) may be available to the infant from a breastfeeding mother.

Paracetamol

Paracetamol appears to be widely distributed throughout most body tissues except fat. Its apparent volume of distribution is 0,7 to 1 L/kg in children and adults. A relatively small proportion(10 % to 25 %) of paracetamol is bound to plasma protein.

Biotransformation

Pseudoephedrine

In adults, only a minor fraction of pseudoephedrine is metabolised in the liver. About 1 % to 6,2 % of a dose undergoes N-demethylation to the metabolite, norpseudoephedrine, which is excreted in the urine.

Paracetamol

Paracetamol is primarily metabolised in the liver and involves three main pathways: conjugation with glucuronide; conjugation with sulphate; and oxidation via cytochrome P450 enzyme pathway. The oxidative pathway forms a reactive intermediate, which is detoxified by conjugation with glutathione to form inert cysteine and mercapturic acid metabolites. The principal cytochrome P450 isoenzyme involved in vivo appears to be CYP2E1, although CYP1A2 and CYP3A4 were considered minor pathways based on in vitro microsomal data.

Subsequently, both CYP1A2 and CYP3A4 were found to have negligible contribution in vivo.

Elimination

Tripolidine Hydrochloride

A carboxylated derivative accounts for about half the dose excreted in the urine. Reported half- lives vary from 3 to 5 hours or more.

Pseudoephedrine

Pseudoephedrine is mainly eliminated by renal excretion as unchanged medicine. 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.

Paracetamol

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

24 months

6.4 Special Precautions for storage

Store at or below 25 °C. 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 and sealed with a white, polypropylene screw cap with expanded polyethylene liner. The bottle is placed in an outer cardboard carton.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

X/5.8/9

9. DATE OF FIRST AUTHORISATION

Date of registration: 17 May 1991

10. DATE OF REVISION OF TEXT

02 February 2024

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

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