PACKAGE INSERT

SCHEDULING STATUS

Schedule 2

PROPRIETARY NAME AND DOSAGE FORM

SINUMAX®PED syrup

COMPOSITION

Each 5 ml contains paracetamol 160 mg and pseudoephedrine hydrochloride 15 mg.

Preservatives: Benzoic acid 0,05 % m/v and sodium benzoate 0,15 % m/v.

Inactive ingredients: Glycerin, malic acid (stabilizer), polyethylene glycol 1450, propylene glycol, sorbitol solution, sucrose.

Contains sugar.

PHARMACOLOGICAL CLASSIFICATION

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

PHARMACOLOGICAL ACTION

SINUMAX PED has antipyretic, analgesic and sympathomimetic properties.

Pharmacodynamic Properties

Paracetamol

Paracetamol is a centrally acting, non-opiate, non-salicylate analgesic. Paracetamol is a clinically proven analgesic/antipyretic, and it is thought to produce analgesia by elevation of the pain threshold and antipyresis through action on the hypothalamic heat-regulating center. Single-dose studies (12,5 mg/kg) of paracetamol in febrile children showed an onset of fever reduction within 15 to 30 minutes.

Pseudoephedrine

Pseudoephedrine is a sympathomimetic substance that has weak direct agonist activity at α- and β-adrenergic receptors. Its principal mechanism is indirect action on the adrenergic receptor system in which pseudoephedrine displaces norepinephrine from storage vesicles in presynaptic neurons. The displaced norepinephrine is released into the neuronal synapse where it is free to activate the postsynaptic α-adrenergic receptors. Stimulation of α1-adrenergic receptors located on capacitance blood vessels of the nasal mucosa (postcapillary venules) results in vasoconstriction, decreased blood volume and a decrease in the volume of the nasal mucosa (nasal decongestion). Constricted blood vessels allow less fluid to enter the nose, throat, and sinus linings, which result in decreased inflammation of nasal membranes as well as decreased mucous production. Thus, by constriction of blood vessels, mainly those located in the nasal congestion.

Pharmacokinetic Properties

ABSORPTION

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 1000 mg dose. Maximum plasma concentrations at steady state after 1000 mg doses every 6 hours range from 17,6 to 18,2 µg/mL. Pooled pharmacokinetic data from five company-sponsored studies for 59 febrile children, ages 6 months to 11 years, found that a mean maximum concentration of 12,08 ± 3,92 µg/mL was attained at 51 ± 39 min (median, 35 min) following a 12,5 mg/kg dose.

Food Effects

Although maximum concentrations of paracetamol are delayed when administered with food, the extent of absorption is not affected. Paracetamol can be taken independently of meal times.

Pseudoephedrine

Pseudoephedrine is rapidly 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. Food does not affect the rate or extent of pseudoephedrine absorption from various extended-release formulations.

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. For a single 60 mg dose as syrup, the mean maximum concentration of 179 ± 24 ng/mL is attained at 1,53 ± 0.91 hours. Repeat oral dosing of 60 mg pseudoephedrine every 6 hours as a syrup results in mean maximum concentrations at steady state of 403 ± 21 and 515 ± 98 ng/mL after the final doses over 12 hours.

DISTRIBUTION

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.

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 medicine 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.

METABOLISM

Paracetamol

Paracetamol is primarily metabolised in the liver and involves three main pathways: conjugation with glucuronide; conjugation with sulfate; 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.

In adults, the majority of paracetamol is conjugated with glucuronic acid and, to a lesser extent, with sulfate. The glucuronide-, sulfate-, and glutathione-derived metabolites lack biologic activity. In premature infants, newborns, and young infants, the sulfate conjugate predominates. In adults with liver impairment of differing severity and etiology, several metabolism studies have demonstrated that the biotransformation of paracetamol is similar to that in healthy adults, but somewhat slower. Importantly, consecutive daily dosing at 4000 mg per day induces glucuronidation (a nontoxic pathway) in healthy and liver-impaired adults, resulting in increased total clearance of paracetamol over time and limited plasma accumulation.

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, nor pseudoephedrine, which is excreted in the urine.

ELIMINATION

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 sulfate (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.

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.

SPECIAL POPULATIONS

PAEDIATRICS

Pseudoephedrine

In children ages 6 to 12 years who receive a single dose of 30 or 60 mg pseudoephedrine syrup, mean maximum plasma concentrations of 244 ± 21 and 492 ± 72 ng/mL, respectively, are achieved. The times to maximum concentrations are 2,1 ± 0,3 hours and 2,4 ± 0.2 hours after administration of the 30- and 60-mg doses, respectively. With repeat doses of 1.125 mg/kg pseudoephedrine every 6 hours (approximately 33 mg per dose), the mean steady-state maximum concentration is 295 ± 60 ng/mL at 1.39 ± 0.38 hours in children ages 4 to 11 years.

The apparent volume of distribution of pseudoephedrine reported in pharmacokinetic studies that enrolled children ages 4 through 12 years ranges from 2.4 to 3.3 L/kg, and is similar to the range reported in adults.

Pseudoephedrine is mainly eliminated intact by renal excretion in children, where most of an oral dose (66%) is excreted unchanged in the urine within 24 hours. The elimination t½ of pseudoephedrine is shorter compared with adults and depends on urine pH. It is 3,1 hours and oral clearance ranges from 9,2 to 10,3 mL/min/kg in children ages 6 through 12 years who had urinary pH of 6,5. In children ages 4 through 11 years who had a urinary pH of 5,3, the elimination t½ is 2,5 ± 0,7 hours and oral clearance is 12,3 ± 2,2 mL/min/kg.

RENALLY IMPAIRED

Pseudoephedrine

There are no pseudoephedrine pharmacokinetic data available in patients with kidney disease. However, a decrease in renal function may decrease oral clearance because pseudoephedrine is mainly excreted unchanged in urine.

HEPATIC IMPAIRED

Pseudoephedrine

There are no pseudoephedrine pharmacokinetic data available in patients with liver disease.

INDICATIONS

For the symptomatic relief of nasal, sinus and Eustachian tube mucal congestion and associated pain and fever due to colds and influenza.

CONTRAINDICATIONS

SINUMAX PED should not be used by persons with a hypersensitivity to paracetamol, pseudoephedrine or to any of the ingredients.

It is contraindicated in persons under treatment with monoamine oxidase inhibitors (MAOIs), or within two weeks of stopping treatment. The concomitant use of pseuoephedrine and MAOIs may cause a rise in blood pressure or hypertensive crisis.

Paracetamol should not be used in patients with severe liver disease.

Contraindicated in most types of cardiovascular disease, hypertension, hyperthyroidism, hyper-excitability, phaeochromocytoma and closed-angle glaucoma.

Pregnancy and lactation.

Pseudoephedrine should be avoided in patients receiving chloroform, cyclopropane, halothane or other halogenated anaesthetics.

WARNINGS and SPECIAL PRECAUTIONS

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.

Overdose warning: Taking more than the recommended dose (overdose) may result in liver damage. In case of overdose, get medical help immediately. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

Serious skin reactions such as acute generalised exanthematous pustulosis (AGEP), Stevens - Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported very rarely in

patients receiving paracetamol. Patients should be informed about the signs of serious skin reactions and use of the medicine should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Do not use with any other product containing paracetamol.

This product should be used under the direction of medical practitioner in patients with pre-existing cardiovascular disease in particular those with coronary heart disease and hypertension.

Patients with thyroid disease, diabetes, decreased kidney function (see PHARMACOKINETIC PROPERTIES – Special Populations) or adults with difficulty in urination due to enlargement of the prostate should not take pseudoephedrine unless directed by a physician.

Patients with hepatic disease should consult a physician before use (see PHARMACOKINETIC PROPERTIES – Metabolism).

There have been reports of ischaemic colitis with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischæmic colitis develop (see SIDE EFFECTS).

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported very rarely with pseudoephedrine-containing products. 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, trunk, 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 physician should be consulted (see SIDE EFFECTS).

If symptoms persist or get worse, or if new symptoms occur, patients should stop use and consult a physician.

Haemolysis may occur in patients with glucose-6-phosphate dehydrogenase deficiency.

Prolonged administration has no cumulative effect, but tolerance with dependence may occur.

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

Contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption of sucrase-isomaltase insufficiency should not take SINUMAX PED.

Contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

INTERACTIONS

Monoamine Oxidase Inhibitors (MAOIs)

Pseudoephedrine exerts its vasoconstricting properties by stimulating adrenergic receptors and displacing norepinephrine from neuronal storage sites. Since MAOIs impede the metabolism of sympathomimetic amines and increase the store of releasable norepinephrine in adrenergic nervous tissue, MAOIs may potentiate the pressor effect of pseudoephedrine. Acute hypertensive crises have been reported in the medical literature with the concomitant use of MAOIs and sympathomimetic amines.

Warfarin-Like Compounds

For most patients, occasional use of paracetamol generally has little or no effect on the international normalised ratio (INR) in patients on chronic warfarin therapy; however, there has been controversy regarding the possibility of paracetamol potentiating the anticoagulant effects of warfarin and other coumarin derivatives. Consumers should be instructed to ask a physician or pharmacist before use if they are taking the blood thinning medicine warfarin or other coumarin derivatives

Alcohol and medicines that induce liver enzymes can increase the hepatotoxicity of paracetamol.

The effects of pseudoephedrine hydrochloride are diminished by guanethidine, reserpine, methyldopa and may be diminished or enhanced by tricyclic antidepressants. It may diminish the effects of guanethidine and may increase the possibility of dy**s**rhythmias in digitalised patients.

HUMAN REPRODUCTION

Do not take this product during pregnancy or whilst breastfeeding.

There are no adequate and well-controlled clinical studies in pregnant or breast-feeding women for the combination of paracetamol and pseudoephedrine.

Effects on Ability to Drive or Use Machines

It is not known if the combination of paracetamol and pseudoephedrine has an effect on the ability to drive or operate machinery. (see SIDE EFFECTS)

DOSAGE AND DIRECTIONS FOR USE

Do not exceed the recommended dosage.

The following doses may be repeated every 4 - 6 hours as needed. Do not exceed 4 doses in 24 hours.

Always follow the chart below for proper dosing. If you have any questions, consult your doctor or pharmacist.		
AGE	**DOSAGE**	
	(ml)	**(Medicine measure)**
2 - 5 years	5,0 ml	1
6 - 12 years	10,0 ml	2
12 years and over	20,0 ml	4

Not recommended for children under 2 years of age.

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

SIDE EFFECTS

Paracetamol may cause pancreatitis, skin rashes and other allergic reaction.

The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by fever and mucosal lesions. The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia, leucopenia, thrombocytopenia and agranulocytosis.

Pseudoephedrine hydrochloride may cause giddiness, headache, nausea, vomiting, sweating, thirst, tachycardia, precordial pain, palpitations, difficulty in micturition, and urinary retention, dyspnoea, altered metabolism including disturbances in glucose metabolism, hypersalivation, muscular weakness and tremors. Other effects include central nervous system (CNS) stimulation such as: anxiety, restlessness and insomnia. Hypertension and ventricular dysrhythmias may occur. Appetite may be reduced.

Post Marketing Data

Adverse reactions identified during post-marketing experience with the combination of paracetamol, pseudoephedrine are included in the table below. Frequencies are provided according to the following convention:

Very common ≥ 1/10

Common ≥ 1/100 and < 1/10

Uncommon ≥ 1/1,000 and < 1/100

Rare ≥ 1/10,000 and < 1/1,000

Very rare < 1/10,000

Not known (cannot be estimated from the available data)

Adverse Reactions Identified During Post-Marketing Experience with Paracetamol, Pseudoephedrine by Frequency Category Estimated from Spontaneous Reporting Rates:

System Organ Class ***Frequency Category***	**Adverse Event Preferred** **Term**
Immune System Disorders	
Very rare	Anaphylactic reaction,
Very rare	Hypersensitivity.
Investigations	
Very rare	Increased Blood pressure,
Very rare	Increased Transaminases[++].
Psychiatric Disorders	
Very rare	Anxiety,
Very rare	Euphoric mood,
Very rare	Hallucination,
Very rare	Visual hallucination,
Very rare	Restlessness.
Nervous System Disorders	
Very rare	Cerebrovascular accident[+],
Very rare	Headache,
Very rare	Paraesthesia,
Very rare	Psychomotor hyperactivity,
Very rare	Tremor.
Cardiac Disorders	
Very rare	Dysrhythmia,
Very rare	Myocardial infarction[+],
Very rare	Palpitations,
Very rare	Tachycardia.

Gastrointestinal Disorders	
Very rare	Abdominal pain,
Very rare	Ischaemic colitis,
Very rare	Diarrhoea,
Very rare	Vomiting.
Skin and Subcutaneous Tissue Disorders	
Very rare	Acute generalised exanthematous pustulosis,
Very rare	Angioedema,
Very rare	Fixed eruption,
Very rare	Pruritus,
Very rare	Rash,
Very rare	Rash pruritic,
Very rare	Urticaria.
Renal and Urinary Disorders	
Very rare	Dysuria,
Very rare	Urinary retention.

[+]These events have been reported very rarely in post-marketing safety. A recent postauthorisation safety study (PASS) did not provide any evidence of increased risk of myocardial infarction or cerebrovascular accident associated with the use of vasoconstrictors for nasal decongestion, including pseudoephedrine.

++Low level transaminase elevations may occur in some patients taking labeled doses of paracetamol; these elevations are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of paracetamol.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Paracetamol

Prompt treatment is essential. In the event of paracetamol overdosage, consult your 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 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 dysrhythmias have been reported.

Hepatobiliary Disorders

In adults and adolescents (≥ 12 years of age), hepatic toxicity may occur following ingestion of greater than 7,5 to 10 grams over a period of 8 hours or less. Fatalities are infrequent (less than 3-4 % of untreated cases) and have rarely been reported with overdoses of less than 15 grams. In children (< 12 years of age), an acute overdosage of less than 150 mg/kg has not been associated

with hepatic toxicity. Early symptoms following a potentially hepatotoxic overdose may include: anorexia, nausea, vomiting, diaphoresis, pallor and general malaise.
Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Serious toxicity or fatalities have been extremely infrequent following an acute paracetamol overdose in young children, possibly because of differences in the way they metabolise paracetamol.

The following are clinical events associated with paracetamol overdose that if seen with overdose are considered expected, including fatal events due to fulminant hepatic failure or its sequelae.

Adverse Reactions Identified with Overdose of Paracetamol	
System Organ Class	**Preferred Term**
Metabolism and Nutrition Disorders	Decreased appetite
Gastrointestinal Disorders	Abdominal discomfort
	Nausea
	Vomiting
Hepatobiliary Disorders	Acute hepatic failure
	Hepatic necrosis
	Hepatomegaly
	Jaundice
	Liver tenderness
General Disorders and Administration Site Conditions	Hyperhidrosis
	Malaise
	Pallor
Investigations	Increased blood bilirubin
	Increased blood lactic acid
	Increased blood phosphorus
	Increased hepatic enzymes
	Increased international normalised ratio
	Prolonged prothrombin time

Blood and Lymphatic Disorders

Haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase [G6PD] deficiency): Haemolysis has been reported in patients with G6PD deficiency, with use of paracetamol in overdose.

Treatment of paracetamol overdosage:

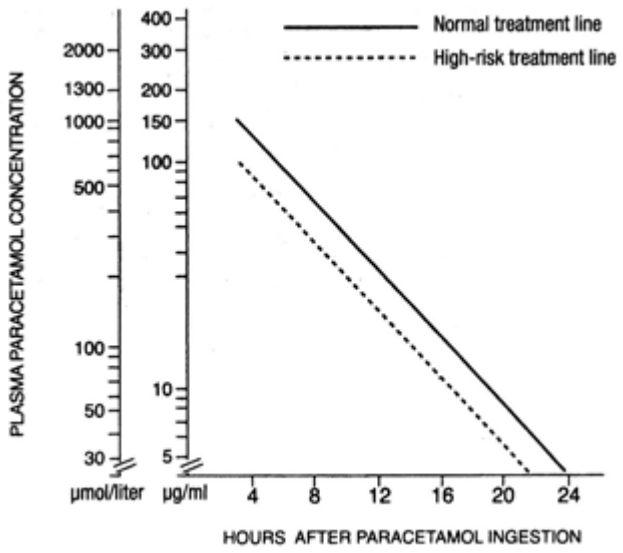
Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 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 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.



Source: Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th Ed.

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.

Pseudoephedrine

Overdosage may result in nausea, vomiting, sympathomimetic symptoms including central nervous system stimulation, insomnia, tremor, mydriasis, anxiety, agitation, hallucinations, seizures, palpitations, tachycardia, hypertension, and reflex bradycardia. Other effects may include dysrhythmias, hypertensive crisis, intracerebral haemorrhage, myocardial infarction, psychoses, rhabdomyolysis, hypokalaemia, and ischemic bowel infarction. Drowsiness has been reported with overdose in children.

REGISTRATION NUMBER

30/5.8/0419

Nam.Reg.No.: 04/5.8/0292
NS 1

IDENTIFICATION

A clear purple syrup with a grape odour.

PRESENTATION

Glass bottles containing 30 ml or 100 ml of syrup

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light.

KEEP OUT OF REACH OF CHILDREN

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

JANSSEN PHARMACEUTICA (PTY) LTD

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DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION INSERT

- the date on the registration certificate: 07 January 1997
- the date of the most recently revised Professional Information Insert as approved by advisory clinical committee: 23 July 2019