1.3.1.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

SINUGESIC 30 mg/ 500 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of SINUGESIC contains 30 mg pseudoephedrine hydrochloride and 500 mg paracetamol.

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

SINUGESIC is a round, yellow, convex tablet with a breakline on one side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

4.2. Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE.

Adults and children over 12 years:

One to two tablets every four to six hours.

Do not exceed eight tablets in 24 hours.

Children 6 to 12 years:

A half to one tablet every six hours.

Do not exceed four tablets in 24 hours.

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

Not recommended for children under 6 years.

Paediatric population

SINUGESIC is not recommended for children under 6 years (see section 4.3).

Method of administration

For oral administration.

4.3. Contraindications

SINUGESIC is contraindicated in:

- Patients with hypersensitivity to pseudoephedrine hydrochloride or paracetamol or to any excipients in SINUEGSIC (see section 6.1).

- Patients receiving monoamine oxidase inhibitors or within 14 days of its termination.
- Hyperexcitability and phaeochromocytoma.
- Patients with severe liver disease.
- Pregnancy or whilst breastfeeding.
- Children under 6 years.
- Severe renal impairment.
- Severe acute or chronic kidney disease/renal failure.
- Cardiovascular disease including hypertension or uncontrolled hypertension and peripheral vascular disease.
- Patients with diabetes mellitus.
- Patients with hyperthyroidism.
- Patients with closed-angle glaucoma or where intraocular pressure is raised.
- Concomitant use of other sympathomimetic decongestants.
- Concomitant use with beta-blockers (see section 4.5).

4.4. Special warnings and precautions for use

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

Pseudoephedrine hydrochloride

Hypersensitivity

Severe Skin reactions

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine hydrochloride containing products as in SINUGESIC. 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 localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of this medicine should be discontinued and appropriate measures taken if needed (see section 4.8).

If any of the following occur, the product should be stopped:

- Hallucinations.
- Restlessness.
- Sleep disturbances.

Ischaemic colitis

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

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)

Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3). Pseudoephedrine hydrochloride should be discontinued, and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

Risks of abuse

Pseudoephedrine hydrochloride, as contained in SINUGESIC, carries the risk of abuse. Prolonged administration has no cumulative effect, but continuous use can lead to tolerance resulting in an increased risk of overdosing. The recommended maximum dose and treatment duration should not be exceeded (see section 4.2).

Glucose-6-phosphate dehydrogenase deficiency

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

Paracetamol

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), drug reaction with eosinophilia and systemic symptoms (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 SINUGESIC must immediately be discontinued and appropriate treatment instituted (see section 4.8).

Concomitant use with flucloxacillin

Caution is advised if paracetamol, as contained in SINUGESIC, 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.

Alcohol

Chronic alcohol users should ask their healthcare provider whether they should take paracetamol or other pain relievers or fever reducers.

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

Do not use with any other product containing paracetamol.

Patients suffering from liver or kidney disease should take paracetamol only if instructed to do so by the doctor (see section 4.3).

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

Great care is also needed in patients with dysrhythmia, Prinzmetal's angina, thrombo-embolic disorders, tachycardia, occlusive vascular disorders including arteriosclerosis or aneurysms.

Anginal pain may be precipitated in patients with angina pectoris. Special care is also needed in the elderly who have pre-existing-coronary or cerebrovascular disease.

Due to possible increase in blood pressure special care is advisable in patients receiving antihypertensive therapy (see section 4.3 and 4.5).

Pseudoephedrine hydrochloride should be given with caution to patients with prostatic enlargement as it may increase difficulty in micturition.

Paediatric population

SINUGESIC should not be given to children under 6 years (see section 4.3).

4.5. Interaction with other medicines and other forms of interaction

Pseudoephedrine hydrochloride

- Pseudoephedrine hydrochloride should be avoided or used with extreme caution in patients undergoing anaesthesia with cyclopropane, halothane, or other halogenated anaesthetics, as they may induce ventricular fibrillation.
- An increased risk of dysrhythmias may also occur if pseudoephedrine hydrochloride is given to patients receiving cardiac glycosides, quinidine, or tricyclic antidepressants. The effects of pseudoephedrine hydrochloride may be diminished or enhanced by tricyclic antidepressants.
- There is an increased risk of vasoconstrictor or pressor effects in patients receiving ergot alkaloids or oxytocin.
- Special care is advisable in patients receiving antihypertensive therapy since pseudoephedrine hydrochloride increases blood pressure. It specifically reverses the antihypertensive effects of guanethidine with the risk of severe hypertension. The effects of pseudoephedrine hydrochloride are diminished by guanethidine, reserpine, methyldopa.
- Severe hypertension may also develop if pseudoephedrine hydrochloride is given with a beta blocker (see section 4.3).
- A combination with alpha-adrenoceptor blockers, such as phenoxybenzamine and phentolamine, may result in both antihypertensive and cardiac-accelerating effects.

- The effects of pseudoephedrine hydrochloride are enhanced by an MAOI and may result in hazardous hypertensive interactions (see section 4.3).
- The hypokalaemic effects of pseudoephedrine hydrochloride may be potentiated by corticosteroids, potassium-depleting diuretics, and aminophylline or theophylline.
- Appetite suppressants and amphetamine-like psychostimulants as there is a risk of hypertension.
- Concomitant use of SINUGESIC with sympathomimetic medicines such as decongestants may cause a rise in blood pressure (see section 4.3).

Paracetamol

- The absorption of paracetamol may be accelerated by metoclopramide.
- Excretion may be affected and plasma concentrations altered when administered with probenecid.
- Colestyramine reduces the absorption of paracetamol if given within one hour of paracetamol administration.
- Medicines which induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptive steroids, may increase the rate at which paracetamol, as contained in SINUGESIC, is metabolised, leading to a reduced plasma concentration of the medicine.
- Alcohol may reduce the capacity of the liver to metabolise paracetamol (see section 4.4).
- Chronic use of paracetamol enhances the effects of anticoagulants.
- Concurrent use of paracetamol, as contained in SINUGESIC, with NSAIDs may increase the risk of adverse renal effects. The prolonged combined use of these medicines may increase the risk of renal damage.
- 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).

4.6. Fertility, pregnancy and lactation

The use of SINUGESIC is contraindicated in pregnancy and lactation (see section 4.3).

Fertility

No data

4.7. Effects on ability to drive and use machines

Since adverse reactions such as headaches, dizziness and tremors have been reported in patients taking SINUGESIC, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that SINUGESIC does not adversely affect their ability to do so (see section 4.8).

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Blood and the lymphatic system disorders			Haematological reactions including thrombocytopenia*, leucopenia*, pancytopenia*, neutropenia*, and agranulocytosis* have been reported
Immune system disorders		Other hypersensitivity reactions* including cross-sensitivity that may occur with other sympathomimetics[#]	
Metabolism and nutrition disorders		Hyperglycaemia[#]	Altered metabolism including changes in blood sugar concentrations[#],

			reduced appetite#, anorexia#
Psychiatric disorders		Hallucinations (particularly in children)#	Fear#, anxiety#, restlessness#, insomnia#, sleep disturbance#, irritability#, psychotic states#, excitability#
Nervous system disorders	Headache#	Dizziness#	Tremor#, confusion#, posterior reversible encephalopathy syndrome (PRES)# (see section 4.4). Reversible cerebral vasoconstriction syndrome (RCVS)# (see section 4.4).
Eye disorders			Ischaemic optic neuropathy#
Cardiac disorders			Reflex bradycardia#, tachycardia and cardiac dysrhythmias#, anginal pain#, palpitations#, and cardiac arrest#
Vascular disorders			Hypertension#, hypotension with dizziness, fainting, and flushing#, cerebral haemorrhage#
Respiratory, thoracic and mediastinal disorders			Dyspnoea#, pulmonary oedema#
Gastrointestinal disorders		Dry mouth#	Pancreatitis*, hypersalivation#, nausea#, vomiting#, ischaemic colitis#
Skin and subcutaneous tissue disorders		Skin rashes*	Sweating#, severe skin reactions, including acute generalized exanthematous pustulosis (AGEP)*# fixed drug eruptions (FDE)* and Drug-induced hypersensitivity syndrome (DIHS)* (see section 4.4)

Musculoskeletal and connective tissue disorders			Weakness[#]
Renal and urinary disorders			Difficulty in micturition and urinary retention[#]
General disorders and administrative site conditions		Coldness of extremities[#]	

*Paracetamol
#Pseudoephedrine

c. Description of selected adverse reactions

Skin rashes and other hypersensitivity reactions occur less frequently. The rash usually appears as red areas or allergic wheals and may be accompanied by fever and involvement of the mucous membranes.

Effects on the cardiovascular system are complex. Stimulation of alpha-adrenergic receptors produces vasoconstriction with resultant hypertension. This vasoconstriction is sometimes sufficiently severe to produce gangrene when sympathomimetics are infiltrated into the digits. The rise in blood pressure may produce cerebral haemorrhage and pulmonary oedema.

There may also be a reflex bradycardia, but stimulation of β_1-adrenergic receptors of the heart may produce tachycardia and cardiac dysrhythmias, anginal pain, palpitations, and cardiac arrest; hypotension with dizziness, fainting, and flushing, may occur due to stimulation of the β_2-adrenergic receptors and the resulting vasodilatation. Prolonged administration has no cumulative effect, but tolerance with dependence may occur.

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

See section 4.4 and 4.8.

Pseudoephedrine overdosage:

Symptoms of pseudoephedrine hydrochloride overdosage include paranoid psychosis, delusions and hallucinations.

Paracetamol overdosage:

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed. Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 to 10 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, lethargy, sweating and abdominal pain.

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.

Abnormalities of glucose metabolism and metabolic acidosis may occur.

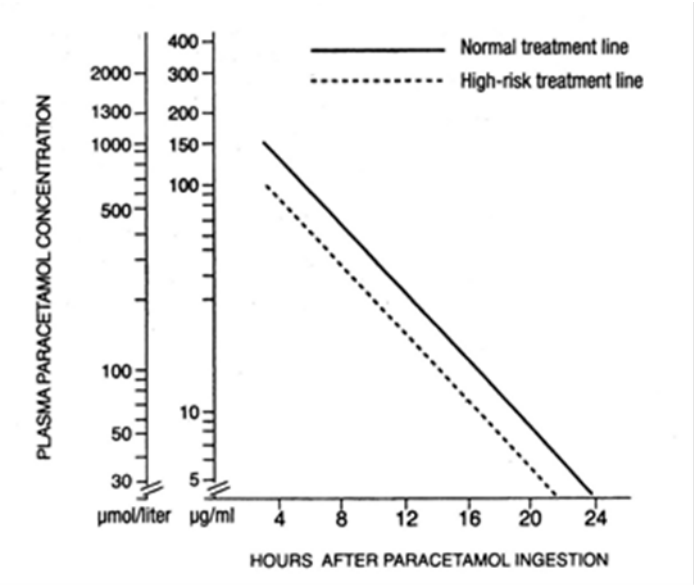
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac dysrhythmias have been reported.

Treatment

Specialised treatment is essential as soon as possible.

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given **intravenously** over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen hours. **The volume of intravenous fluid should be modified for children**. Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses. A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below. The nomogram should be used only in relation to a single acute ingestion. Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the “high risk treatment line”. Prothrombin index correlates best with survival. For overdose with an extended/modified release preparation the value of the nomogram is unknown. As there is no information on the plasma levels of paracetamol after an overdose of extended/modified release paracetamol preparations, all patients with suspected or known overdose with such

preparations should receive N-acetylcysteine. Because of lack of data for extended/modified release formulations, a level below the “treatment line” of the nomogram may not exclude the possibility of toxicity. Monitor all patients with significant ingestions for at least ninety-six hours.



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: Other cold preparations

ATC code: R05X

Mechanism of action

SINUGESIC has antipyretic, analgesic and decongestant 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 centre. Single-dose studies (12,5 mg/kg) of paracetamol in febrile children showed an onset of fever reduction within 15 to 30 minutes.

Pseudoephedrine hydrochloride

Pseudoephedrine hydrochloride 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 hydrochloride 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.

5.2. 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 to 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 mealtimes.

Pseudoephedrine hydrochloride

Pseudoephedrine hydrochloride is rapidly absorbed from the gastrointestinal tract. The oral bioavailability of pseudoephedrine hydrochloride is high, as determined by urine collections greater than 96 % of administered doses. When pseudoephedrine hydrochloride 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 hydrochloride 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 hydrochloride 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 hydrochloride

The apparent volume of distribution for pseudoephedrine hydrochloride ranges from 2,3 to 3,3 L/kg. Up to 0,7 % of a single 60 mg dose of pseudoephedrine hydrochloride may be distributed into breast milk over 24 hours. Pseudoephedrine hydrochloride 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 hydrochloride 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.

Biotransformation

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.

In adults, the majority of paracetamol is conjugated with glucuronic acid and, to a lesser extent, with sulfate. The glucuronide-, sulphate-, and glutathione-derived metabolites lack biologic activity. In premature infants, newborns, and young infants, the sulphate conjugate predominates. In adults with liver impairment of differing severity and aetiology, 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 hydrochloride

In adults, only a minor fraction of pseudoephedrine hydrochloride 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 to 60 %) and sulphate (25 to 35 %) conjugates, thiols (5 to 10 %) as cysteine and mercapturate metabolites, and catechols (3 to 6 %) that are excreted in the urine. Renal clearance of unchanged paracetamol is about 3,5 % of the dose.

Pseudoephedrine hydrochloride

Pseudoephedrine hydrochloride 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 halflife (t½) for both immediate- and extended-release pseudoephedrine hydrochloride ranges from 5,5 to 7,0 hours.

Oral clearance of pseudoephedrine hydrochloride is approximately 7,3 to 7,6 mL/min/kg.

Urinary pH affects the elimination t½ and clearance of pseudoephedrine hydrochloride 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 hydrochloride in urine ranged from 1,9 hours at pH 5,66 to 21 hours at pH 7,80.

Paediatrics

Pseudoephedrine hydrochloride

In children ages 6 to 12 years who receive a single dose of 30 or 60 mg pseudoephedrine hydrochloride 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 hydrochloride 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 hydrochloride 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 hydrochloride 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 hydrochloride 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 hydrochloride

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

Hepatic impaired

Pseudoephedrine hydrochloride

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

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Colloidal anhydrous silica, crospovidone, magnesium stearate, povidone K30, purified talc, quinolene yellow (C.I. 47005).

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store at or below 25 °C.

Keep well closed and protect from light.

Keep in original packaging until required for use.

6.5. Nature and contents of container

20 or 100 tablets are packed in a white low density polyethylene container with a white low density polyethylene cap, together with a leaflet.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Medical Hotline: 0800 118 088

8. REGISTRATION NUMBER

34/5.8/0196

9. DATE OF FIRST AUTHORISATION

11 October 2001

10. DATE OF REVISION OF TEXT

16 January 2026

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

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