**Professional information for SINUTAB Sinus Allergy Congestion & Pain**

**SCHEDULING STATUS:**

**S2**

## 1. NAME OF THE MEDICINE

SINUTAB Sinus Allergy Congestion & Pain tablets

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

| | |
|---|---|
| Pseudoephedrine hydrochloride | 30 mg |
| Chlorphenamine maleate | 2 mg |
| Paracetamol | 500 mg |

Sugar free

## 3. PHARMACEUTICAL FORM

Tablets.

A slightly mottled, peach coloured, round, biconvex tablet.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

For the symptomatic relief of sinus pain, including maxillary, frontal or facial pain and the relief of associated malaise, fever and congestion of the nasal, sinus and Eustachian tube mucosa.

For the symptomatic relief of allergic rhinitis (hay fever), vasomotor rhinitis, influenza and the common cold.

## 4.2 Posology and method of administration

**Posology:**

Adults and children over 12 years:

Two tablets every six to eight hours.

Do not exceed eight tablets in 24 hours.

Not to be used in children below the age of 12 years.

**DO NOT EXCEED THE RECOMMENDED DOSE.**

## 4.3 Contraindications

- Hypersensitivity to chlorphenamine maleate, paracetamol, pseudoephedrine, or to any of the ingredients (see section 4.8).
- Contraindicated in children under 12 years of age.
- Paracetamol should not be used in patients with severe liver and renal disease.
- Pseudoephedrine should be avoided in patients undergoing inhalation anaesthesia.
- SINUTAB Sinus Allergy Congestion & Pain should not be given concurrently with any monoamine oxidase inhibitor (MAOI) for depression or within 14 days of stopping such treatment. The concomitant use of these medicines may cause a rise in blood pressure and/or hypertensive crisis.
- Contraindicated in most types of cardiovascular disease, including angina and hypertension, and in hyperthyroidism, phaeochromocytoma, closed angle glaucoma and diabetes mellitus.

## 4.4 Special warnings and precautions for use

**SINUTAB Sinus Allergy Congestion & Pain contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdosage and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be**

**contacted immediately.**

Do not use with any other medicines containing paracetamol.

Do not use continuously for more than seven days. If symptoms persist or get worse, or if new symptoms occur, irrespective of therapy used, patients should stop use and consult your doctor. Dosages in excess of those recommended may cause severe liver, or kidney damage.
Consult your doctor if no relief is obtained with the recommended dosage.

Patients with a persistent respiratory condition such as emphysema, chronic bronchitis, bronchial asthma, or where cough is accompanied by excessive secretions should be advised to consult a doctor before using SINUTAB Sinus Allergy Congestion & Pain.

While taking SINUTAB Sinus Allergy Congestion & Pain, avoid alcoholic beverages and consult a doctor prior to taking with central nervous system depressants (see section 4.5).

**Paracetamol**

Patients with impaired kidney or liver function should take paracetamol under medical supervision only.
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 SINUTAB Sinus Allergy Congestion & Pain should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Chronic alcohol users should ask their doctor whether they should take paracetamol or other pain

relievers or fever reducers.

**Chlorphenamine maleate:**

Chlorphenamine should be given with care to patients with glaucoma, urinary retention, prostatic hypertrophy or pyloroduodenal obstruction. Caution is advised in patients with epilepsy and severe cardiovascular disorders.

Elderly patients are more susceptible to the central nervous system depressant and lowering of blood pressure effects even at dose quantities effective for treatment.

The warning signs of damage caused by ototoxic medicines may be masked by chlorphenamine.

Chlorphenamine may cause drowsiness.

Chlorphenamine may enhance the sedative effect of central nervous system depressants including alcohol, barbiturates, hypnotics, analgesics, sedatives and tranquillisers. Care should be taken when taking medicines containing tricyclic anti-depressants or atropine together.

**Pseudoephedrine hydrochloride**

SINUTAB Sinus Allergy Congestion & Pain should not be used by patients with cardiovascular disease in particular those with coronary heart disease and hypertension, hyperthyroidism, liver disease, renal disease, difficulty in urination and/or enlargement of the prostate, glaucoma or diabetes. (See section 4.3)

SINUTAB Sinus Allergy Congestion & Pain should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported with pseudoephedrine-containing medicines, such as SINUTAB Sinus Allergy Congestion & Pain. 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.

### 4.5 Interaction with other medicines and other forms of interaction

Combinations containing any of the following medicines, depending on the amount, may also interact with SINUTAB Sinus Allergy Congestion & Pain.

Chlorphenamine may enhance the effects of central nervous system depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics, and other medicines with anti-cholinergic properties such as tricyclic anti-depressants.

Cardiac dysrhythmias may occur when pseudoephedrine is used prior to anaesthesia with inhalation anaesthetics such as chloroform, cyclopropane, enflurane, halothane, isoflurane, methoxyflurane, and trichloroethylene or concurrently with digitalis glycosides.

Anticholinergic effects may be potentiated when SINUTAB Sinus Allergy Congestion & Pain is used concurrently with anticholinergics or other medicines with anticholinergic activity.

Concurrent use with SINUTAB Sinus Allergy Congestion & Pain may also potentiate the cardiovascular effects of sympathomimetic amines. Pseudoephedrine may reverse the action of cardiovascular medicines and therefore special care is advisable in patients receiving such therapy.

Antihypertensive effects may be reduced when these medicines are used concurrently with sympathomimetic amines.

Concurrent use of beta-adrenergic blocking agents with sympathomimetic amines may result in significant hypertension and excessive bradycardia with possible heart block.

CNS stimulants used concurrently with pseudoephedrine may result in additive CNS stimulation to excessive levels, which may cause unwanted effects, such as nervousness, irritability insomnia, or possibly convulsions or cardiac dysrhythmias.

Doxapram used concurrently with SINUTAB Sinus Allergy Congestion & Pain may increase the pressor effects of either doxapram or sympathomimetic amines.

Monoamine oxidase inhibitors used concurrently with antihistamines may prolong and intensify the anticholinergic and CNS depressant effects of SINUTAB Sinus Allergy Congestion & Pain.

Concurrent use of MAOIs with sympathomimetic amines may prolong and intensify the cardiac stimulant and vasopressor effects of pseudoephedrine. These medicines should not be administered during or within 14 days following the administration of a MAO inhibitor.

The risk of hepatotoxicity with single toxic doses or prolonged use of high doses of paracetamol may be increased in alcoholics or in patients regularly taking other hepatotoxic medicines or hepatic enzyme inducers.

Prolonged concurrent use of paracetamol with other NSAIDs may also increase the risk of adverse renal effects.

Paracetamol may competitively inhibit the hepatic glucuronidation and decrease the clearance of zidovudine; zidovudine may also inhibit the hepatic glucuronidation of paracetamol.

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

**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. Patients should consult a doctor or pharmacist before use if they are taking warfarin or other coumarin derivatives.

## 4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

## 4.7 Effects on ability to drive and use machines

SINUTAB Sinus Allergy Congestion & Pain may cause drowsiness and impaired concentration which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents. Patients should be warned not to drive a motor vehicle, operate dangerous machinery, or climb dangerous heights, as impaired decision making could lead to accidents.

## 4.8 Undesirable effects

**Paracetamol:**

**Blood and lymphatic system disorders**

*Less frequent:* neutropenia, pancytopenia, leucopenia, thrombocytopenia

**Immune system disorders**

*Less frequent:* sensitivity/allergic reactions resulting in skin rash, laryngeal oedema, angioedema and anaphylaxis

**Skin and subcutaneous tissue disorders**

*Less frequent:* erythematous rash, urticarial rash

**Gastrointestinal disorders**

*Less frequent:* mucosal lesions, pancreatitis

**General disorders and administration site conditions**

*Less frequent:* fever

**Chlorphenamine maleate:**

### Blood and lymphatic system disorders

*Less frequent:* agranulocytosis, leucopenia, haemolytic anaemia and thrombocytopenia

### Immune system disorders

*Less frequent:* hypersensitivity reactions such as pruritus or rash

### Psychiatric disorders

*Less frequent:* nervousness, euphoria, irritability, nightmares, hallucinations

### Nervous system disorders

*Frequent:* sedation, varying from slight drowsiness to deep sleep, including lassitude, dizziness and incoordination

*Less frequent:* insomnia, tremors, convulsions, headache, blurred vision, paraesthesias extrapyramidal effects

### Ear and labyrinth disorders

*Less frequent:* tinnitus

### Vascular disorders

*Less frequent:* hypertension, hypotension

### Respiratory, thoracic and mediastinal disorders

*Less frequent:* thickened respiratory-tract secretions and tightness of the chest

### Gastrointestinal disorders

*Less frequent:* nausea, vomiting, dry mouth, constipation, gastric reflux, diarrhoea, epigastric pain

**Musculoskeletal and connective tissue disorders**

*Less frequent:* myalgia

**Renal and urinary disorders**

*Less frequent:* urinary difficulty and retention

**General disorders and administration site conditions**

*Less frequent:* Sweating, hair loss

**Pseudoephedrine hydrochloride:**

**Metabolism and nutrition disorders**

*Less frequent:* decreased appetite, hypokalaemia, altered metabolism

**Psychiatric disorders**

*Frequent:* fear, anxiety, insomnia, confusion, irritability, psychotic states

**Nervous system disorders**

*Frequent:* restlessness, tremor, dizziness

*Less frequent:* cerebral haemorrhage, headache

**Cardiac disorders**

*Less frequent:* pulmonary oedema, cardiac dysrhythmias, anginal pain, palpitations, and cardiac arrest

**Vascular disorders**

*Less frequent:* hypertension, reflex bradycardia, tachycardia, hypotension, fainting

**Respiratory, thoracic and mediastinal disorders**

*Less frequent:* dyspnoea

**Gastrointestinal disorders**

*Less frequent:* nausea, vomiting, hypersalivation

**Renal and urinary disorders**

*Less frequent:* difficulty in micturition, urinary retention

**General disorders and administration site conditions**

*Frequent:* weakness, sweating, tolerance with dependence

**Investigations**

*Less frequent:* changes in blood sugar levels

**Chlorphenamine/Pseudoephedrine/Paracetamol combination**

**Nervous system disorders:**

*Frequent:*

Dizziness, somnolence

**Gastrointestinal disorders:**

*Frequent:*

Dry mouth

**General disorders and administration site conditions:**

*Frequent:*

Asthenia

**Post-marketing experience:**

The following adverse drug reactions were identified during post-marketing experience with chlorpheniramine, paracetamol, pseudoephedrine by frequency category estimated from clinical trials or epidemiology studies:

Immune system disorders:

*Frequency unknown:* Anaphylactic reaction, hypersensitivity.

Psychiatric disorders:

*Frequency unknown:* Anxiety, euphoric mood, hallucination, visual hallucination, restlessness.

Nervous system disorders:

*Frequency unknown:* Cerebrovascular accident, headache, paraesthesia, psychomotor hyperactivity, tremor.

Cardiac disorders:

*Frequency unknown:* Dysrhythmia, myocardial infarction, palpitations, tachycardia.

Gastrointestinal disorders:

*Frequency unknown:* Abdominal pain, colitis ischaemic, diarrhoea, vomiting.

Skin and subcutaneous tissue disorders:

*Frequency unknown:* Acute generalised exanthematous pustulosis, angioedema, fixed eruption, pruritus, rash, pruritic rash, urticaria.

Renal and urinary disorders:

*Frequency unknown:* Dysuria, urinary retention.

Investigations:

*Frequency unknown:* Increased blood pressure, increased transaminases.

**Reporting of suspected adverse reactions:**

Reporting suspected adverse reactions after authorisation of SINUTAB Sinus Allergy Congestion & Pain is important. It allows continued monitoring of the benefit/risk balance of SINUTAB Sinus Allergy Congestion & Pain. 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

## 4.9 Overdose

See section 4.4 and 4.8.

**Paracetamol:** 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 an overdosage, consult a doctor immediately, or take the person to a hospital directly. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5-10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning, do not reflect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and

death.

Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac dysrhythmias have been reported.

**Treatment for 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.

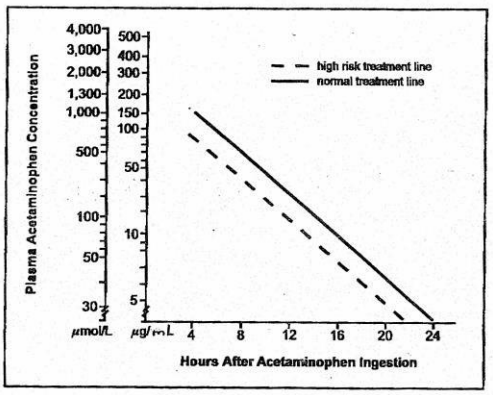
**N-acetylcysteine** should be administered to all cases of suspected overdose as soon as possible, preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

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



Adapted from Smilkstein et al. Ann Emerg Med 1991;20:1059

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.

**Chlorphenamine maleate**

Chlorphenamine overdosage may be fatal especially in infants and children. The main symptoms being central nervous system stimulation and anti-muscarinic effects, including ataxia, excitement, hallucinations, muscle tremor, convulsions, dilated pupils, dry mouth, flushed face and hyperpyrexia. Deepening coma, cardiorespiratory collapse, and death may occur within 18 hours. The usual symptoms in adults are central nervous system depression with drowsiness, coma and convulsions. Hypotension may also occur.

**Pseudoephedrine hydrochloride:**

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, dysrhythmias,

myocardial infarction and cerebral haemorrhage.

**Treatment of overdose:**

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.

Consult a doctor or take the patient to the nearest hospital immediately.

Specialised treatment is essential as soon as possible.

The latest information regarding the treatment of overdosage can be obtained from the nearest poison centre.

## 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 analgesics and antipyretics: paracetamol, combinations excl. psycholeptics

ATC code: N02BE51

SINUTAB Sinus Allergy Congestion & Pain has analgesic, anti-pyretic, decongestant and antihistaminic properties.

## 5.2 Pharmacokinetic properties

**Absorption:**

***Chlorphenamine***

Chlorphenamine is slowly absorbed from the gastrointestinal tract and its absorption is sensitive to various gastrointestinal local conditions such as foods, fluid volume and formulations. The small intestine is considered the primary site of absorption due to the available surface area and the basic nature of the parent chlorphenamine. Complete absorption from the gastrointestinal tract was demonstrated by a low amount of medicine detected in faeces for 48 hours post-administration. The oral bioavailability of chlorphenamine, however, is incomplete due to extensive gut and hepatic first pass metabolism, with the medicine reaching peak plasma concentrations of ~ 32 ng/mL in adults with a 4 mg oral dose at approximately 6 hours.

***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.

***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.

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.

**Distribution:**

***Chlorphenamine***

Chlorphenamine undergoes a rapid and extensive distribution to the lungs, kidneys, liver, milk and brain. The apparent volume of distribution is approximately 7 L/kg for adults after oral dosing. Chlorphenamine is highly protein bound (~ 70 %).

***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 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.

**Biotransformation:**

***Chlorphenamine***

Chlorphenamine undergoes extensive gut and hepatic first pass metabolism with an absolute bioavailability of 25 to 50 %. It is extensively metabolised in the liver by demethylation to mono- and didesmethylchlorpheniramine. It also undergoes oxidative deamination to polar metabolites, an alcohol and an acid. Metabolism of chlorphenamine has been shown to be mediated by the cytochrome P450 isozyme CYP2D6.

***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*.

***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.

**Elimination:**

***Chlorphenamine***

Mean half lives in adults administered a 4 mg oral tablet range from 20 to 30 hours. Variability in the half-life of chlorphenamine and its metabolites has been historically attributed to the tubular

reabsorption of non-ionised medicine from alkaline urine. The protonation of chlorphenamine in acidic urine limits reabsorption of charged medicine, whereas the excretion of uncharged medicine in alkaline urine is dependent upon urine flow rate. Recent studies have shown that differences in CYP2D6 polymorphism in individuals who are poor and extensive metabolisers of the medicine are responsible for such variation.

Chlorphenamine metabolites are excreted primarily in urine. Total body clearance ranges from 4,4 – 7,9 mL/min/kg in adults. Long half-lives of up to 330 hours have been seen in patients with renal impairment. Urinary excretion is dependent on urine pH and flow with 20 – 26,5 % of unchanged medicine being excreted in acidic urine in 24 hours but only 0,3 – 0,4 % being excreted in alkaline urine. Less than 1 % of medicine is excreted in the faeces. Age, dialysis, urinary pH and flow influence the elimination kinetics.

***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.

***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.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Calcium phosphate dihydrate

Colloidal silicon dioxide

Crospovidone

F D & C yellow no. 6 (colourant, E110)

Magnesium stearate

Povidone

Pregelatinised maize starch

Stearic acid

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months.

### 6.4 Special precautions for storage

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

Protect from light and moisture.

Do not remove tablets from the outer carton until required for use.

### 6.5 Nature and contents of container

PVC/Aluminium blister packs containing 20 tablets.

### 6.6 Special precautions for disposal and other handling

None.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

Johnson & Johnson (Pty) Ltd.

241 Main Road

Retreat

7945

SOUTH AFRICA

## 8. REGISTRATION NUMBER

37/5.8/0260

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 November 2005

## 10. DATE OF REVISION OF THE TEXT

20 April 2022