AUSTRALIAN PRODUCT INFORMATION

PANADOL ALLERGY SINUS TABLETS

1 NAME OF THE MEDICINE

Paracetamol

Pseudoephedrine Hydrochloride

Chlorphenamine Maleate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Panadol Allergy Sinus Tablets contain pseudoephedrine hydrochloride 30 mg, paracetamol 500 mg, and chlorphenamine maleate 2 mg.

Excipient with known effect: sodium benzoate as a preservative.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Panadol Allergy Sinus Tablets are white, capsule-shaped tablets with flat edges, one face marked with 'PANADOL' and 'C&F C&F (upside down)' on the other side.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Panadol Allergy Sinus Tablets are used for the temporary relief of sinusitis symptoms, nasal congestion and allergic symptoms such as runny nose, sneezing, itchy and watery eyes.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults and children 12 years and over:

2 capsule-shaped tablets (caplets) taken with water every 6 hours as necessary, maximum 8 caplets within 24 hours.

Use in adults

Paracetamol should not be taken for more than a few days at a time except on medical advice.

Use in children aged 12 to 17 years

Paracetamol should not be taken for more than 48 hours except on medical advice. Do not use in children below 12 years of age.

Do not exceed the stated dose or frequency of dosing. Minimum dosage interval: 6 hours.

Should not be used with other medicines containing paracetamol, pseudoephedrine, chlorphenamine, decongestants or antihistamines, including cough and cold medicines.

Seek medical advice if symptoms persist for more than 7 days.

4.3 CONTRAINDICATIONS

This product is contraindicated for use in patients:

- With a previous history of hypersensitivity to paracetamol, pseudoephedrine, chlorphenamine, other antihistamines or any of the excipients included in the product.
- With severe hypertension or coronary artery disease.
- Who are taking Monoamine Oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days (see Section 4.5 Interactions with other medicines and other forms of interactions).
- With stenosing peptic ulcer.
- With symptomatic prostatic hypertrophy.
- With bladder neck obstruction.
- With pyloroduodenal obstruction.
- Who are taking other sympathomimetics (such as decongestants, appetite
- suppressants and amphetamine-like psychostimulants (see Section 4.5 Interactions with other medicines and other forms of interactions).
- With severe renal impairment.
- Narrow-angle glaucoma.
- Newborns or premature infants.
- Infants less than 12 months of age.
- Lactating women.

This product should not be used with other medicines containing paracetamol, pseudoephedrine, chlorphenamine or other medicines for the relief of colds, congestion or blocked nose.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified precautions

This product should be used with caution in patients with:

- Cardiovascular disease -coronary heart disease, ischaemic heart disease
- Arrhythmias
- Hypertension
- Prostatic hypertrophy

- Hyperthyroidism
- Diabetes mellitus
- Raised intra-ocular pressure including glaucoma
- Epilepsy
- Bronchitis
- Bronchiectasis
- Bronchial asthma
- Hepatic or renal impairment. Caution should be exercised in patients with kidney impairment and in those with hepatic impairment due to the paracetamol content of this medicine. Underlying liver disease increases the risk of paracetamol related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.
- In patients with glutathione depleted states such as sepsis, the use of paracetamol may increase the risk of metabolic acidosis
- Phaeochromocytoma

Use with caution in patients taking beta-blockers or other anti-hypertensives because of the pseudoephedrine content (see 4.5 Interactions with other medicines and other forms of interactions). Concurrent use of alcohol should be avoided due to the chlorphenamine content.

There have been reports of acute systemic vasoconstrictive with pseudoephedrine. Significant examples include:

Acute Coronary Syndrome (ACS): Symptoms include sudden chest pain, tightness, heavy sweating and dyspnoea at rest.

- Ischaemic colitis: Symptoms include sudden abdominal pain and rectal bleeding.
- Posterior reversible encephalopathy (PRES)/reversible cerebral vasoconstriction syndrome (RCVS): Symptoms included sudden onset of severe headache, nausea, vomiting, and visual disturbances. Most cases improved or resolved within a few days following appropriate treatment.

Pseudoephedrine should be discontinued immediately and medical advice sought if any signs/symptoms vasoconstrictive events develop.
Concurrent use with drugs which cause sedation, such as anxiolytics and hypnotics may cause an increase in sedative effects, therefore medical advice should be sought before taking chlorphenamine concurrently with these medicines (see 4.5 Interactions with other medicines and other forms of interactions).

This product should not be used with other antihistamine containing products, including antihistamine containing cough and cold medications, because of the chlorphenamine content.

Medical advice should be sought if the symptoms persist, or is accompanied by a high fever, skin rash or persistent headache.

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.
Patients should be advised not to drive or operate machinery if affected by dizziness.

Refer to 4.5 Interactions with other medicines and other forms of interactions for additional information.

Use in hepatic impairment

Caution should be exercised in patients with hepatic impairment due to the paracetamol content of this medicine.

Underlying liver disease increases the risk of paracetamol-related liver damage.

Patients who have been diagnosed with liver impairment must seek medical advice before taking this medication.

Use in renal impairment

Caution should be exercised in patients with kidney impairment due to the paracetamol content of this medicine.

Patients who have been diagnosed with kidney impairment must seek medical advice before taking this medication.

This product is contraindicated for use in patients with severe renal impairment.

Use in the elderly

No data available.

Paediatric use

Do not give to children under 12 years of age.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Paracetamol
The following interactions with paracetamol have been noted:

- The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol-containing products with increased risk of bleeding; occasional doses have no significant effect.
- Paracetamol absorption is increased by substances that increase gastric emptying, e.g. metoclopramide.

- Paracetamol absorption is decreased by substances that decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties, and narcotic analgesics.
- Paracetamol may increase chloramphenicol concentrations.
- The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents.
- Paracetamol excretion may be affected and plasma concentrations altered when given with probenecid.
- Colestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

Pseudoephedrine

The following interactions with pseudoephedrine have been noted:

- Antidepressant medication eg tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) – may cause a serious increase in blood pressure or hypertensive crisis.
- Concomitant administration of pseudoephedrine and MAOIs (or within two weeks of stopping of MAOI) may lead to hypertensive crisis. See Section 4.3 Contraindications.
- Other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psycho-stimulants which interfere with the catabolism of sympathomimetic amines may occasionally cause a rise in blood pressure. See 4.3 Contraindications.
- Pseudoephedrine may antagonise the effect of certain classes of antihypertensives (eg beta blockers, methyl-dopa, reserpine, debrisoquine, guanethidine). See Section 4.4 Special warnings and precautions for use.
- methyldopa and β-blockers – may cause an increase in blood pressure.
- urinary acidifiers enhance elimination of pseudoephedrine.
- urinary alkalinisers decrease elimination of pseudoephedrine.
- pseudoephedrine-containing products may antagonise the effect of certain classes of antihypertensives.

Chlorphenamine maletate

The following interactions with chlorphenamine maleta have been noted:

- Central nervous system (CNS) depressants (alcohol, sedatives, opioid analgesics, hypnotics) – may cause an increase in sedation effects.
- Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) – may prolong and intensify the anticholinergic and CNS depressive effects
- **Chlorphenamine** when taken with monoamine oxidase inhibitors (MAOIs) may cause a decrease in blood pressure
- **Chlorphenamine** when taken concomitantly with phenytoin may cause a decrease in phenytoin elimination and can lead to phenytoin toxicity

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No Data available.

Use in pregnancy – Pregnancy Category B2

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals are inadequate or may be lacking, but available data shows no evidence of an increased occurrence of foetal damage.

Paracetamol – Category A

Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

This product should be used in pregnancy only if the potential benefits to the patient are weighed against the possible risk to the foetus.

This product should not be used in pregnancy without medical advice.

Use in lactation.

This product should not be used whilst breastfeeding without medical advice Paracetamol is excreted in small amounts (< 0.2%) in breast milk but the effect of this on breast fed infants is unknown. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infants.

Pseudoephedrine is secreted in breast milk in small amounts. It has been estimated that 0.5% to 0.7% of a single dose of pseudoephedrine ingested by the mother will be excreted in the breast milk over 24 hours. Therefore, it is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Chlorphenamine Maleate and other histamines may inhibit lactation and is excreted in breast milk. Therefore it is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Chlorphenamine may cause drowsiness, dizziness, blurred vision and CNS depressive effects including sedation and impaired performance (impaired driving performance, incoordination, reduced motor skills and impaired information processing). Performance may be impaired in the absence of sedation and may persist the morning after a night time dose. Patients should be advised not to drive or operate machinery if affected. Due to Chlorphenamine content of this product, alcohol should be avoided. (See 4.5 Interactions with other medicines and other forms of interactions).

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adverse events from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by System Organ Class and frequency.

The following convention has been utilised for the classification of undesirable effects: very common (>/= 1/10), common (>= 1/100, <1/10), uncommon (>=1/1000, <1/100), rare (>= 1/10000, <1/1000), very rare (<1/10000), not known (cannot be estimated from the available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Paracetamol

Body System	Undesirable effect	Frequency
Blood and lymphatic system disorders	Thrombocytopaenia	Very rare
Immune System disorders	Anaphylaxis Cutaneous hypersensitivity reactions including among others, skin rashes, angioedema, Stevens Johnson syndrome and Toxic Epidermal Necrolysis	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs.	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

Pseudoephedrine

Body System	Undesirable effect	Frequency
Psychiatric disorders	Nervousness, Insomnia	Common
	Agitation, restlessness	Uncommon
	Hallucinations	Rare
Nervous System Disorders	Dizziness, tremors	Common
Cardiac Disorders	Tachycardia or arrhythmia, palpitations	Rare
Vascular disorders	Increased blood pressure[1]	Rare
Gastrointestinal Disorders	Vomiting, Dry Mouth, Nausea	Common
Skin and Subcutaneous Tissue Disorders	Rash, Allergic dermatitis[2]	Rare
Renal and Urinary Disorders	Dysuria, Urinary retention[3]	Uncommon

1. Increases in systolic blood pressure have been observed. At therapeutic doses, the effects of pseudoephedrine on blood pressure are not clinically significant.
2. A variety of allergic skin reactions, with or without systemic features such as bronchospasm and angioedema have been reported following use of pseudoephedrine.
3. Urinary retention is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Chlorphenamine maleate

Body System	Undesirable Effect	Frequency

Nervous system disorders	Sedation, somnolence Disturbance in attention, abnormal coordination, dizziness, headache	Very common Common
Eye disorders	Blurred vision	Common
Gastrointestinal disorders	Nausea, dry mouth	Common
General disorders and administration site conditions	Fatigue	Common
CNS stimulatory effects	Anxiety, hallucinations, appetite stimulation, muscle dyskinesias, and activation of epileptogenic foci.	Common
Anticholinergic effects	Dryness of the eyes and nose, blurred vision, urinary hesitancy and retention, constipation and tachycardia	Common
Immune system disorders	Allergic reactions, angioedema, anaphylactic reactions	Not known
Metabolism and nutritional disorders	Anorexia	Not known
Psychiatric disorders	Confusion*, excitation*, irritability*, nightmares*	Not known
Vascular disorders	Hypotension	Not known
Respiratory, thoracic and mediastinal disorders	Thickening of bronchial secretions	Not known
Gastrointestinal disorders	Vomiting, abdominal pain, diarrhoea, dyspepsia	Not known
Skin and subcutaneous disorders	Exfoliative dermatitis, rash, urticaria, photosensitivity	Not known
Musculoskeletal and connective tissue disorder	Muscle twitching, muscle weakness	Not known
General disorders and administration site conditions	Chest tightness	Not known

*Children and the elderly are more susceptible to neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Poisons Information Centre

If an overdose is taken or suspected, immediately contact the Poisons Information Centre (in Australia, call 131 126) for advice, or the patient should go to the hospital straight away even if they feel well because of the risk of delayed, serious liver damage. See Section 4.8 Adverse effects (undesirable effects).

Treatment-Paracetamol

Paracetamol overdose may cause liver failure which can lead to liver transplant or death. Acute pancreatitis has been observed with hepatic dysfunction.

Immediate medical management is required in the event of overdose, even if the symptoms of overdose are not present.

Administration of N-acetylcysteine or methionine may be required.

Treatment-Pseudoephedrine
Pseudoephedrine overdose may result in symptoms due to central nervous system and cardiovascular stimulation e.g. excitement, restlessness, hallucinations, hypertension and arrhythmias. In severe cases, psychosis, convulsions, coma and hypertensive crisis may occur. Serum potassium levels may be low due to the extracellular to intracellular shifts in potassium.

Treatment should consist of standard supportive measures.

Treatment-Chlorphenamine maleate
Overdose is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include paradoxical excitation, toxic psychosis, convulsions, apnoea, dystonic reactions and cardiovascular collapse including arrhythmias.

Treatment should be symptomatic and supportive and directed toward specific symptoms. Convulsions and marked CNS stimulation should be treated with parenteral diazepam.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Paracetamol is a p-aminophenol derivative that exhibits analgesic and antipyretic activity. It does not possess anti-inflammatory activity. Paracetamol is thought to produce analgesia through a central inhibition of prostaglandin synthesis.

Pseudoephedrine has direct- and indirect- sympathomimetic activity and is an effective decongestant in the upper respiratory tract. It is a stereoisomer of ephedrine and has a similar action, but has been found to have less pressor activity and fewer central nervous system (CNS) effects.

Sympathomimetic agents are used as nasal decongestants to provide symptomatic relief. They act by causing vasoconstriction resulting in redistribution of local blood flow to reduce oedema of the nasal mucosa, thus improving ventilation, drainage and nasal stuffiness.

Chlorphenamine Maleate competes with histamine at central and peripheral histamine$_1$-receptor sites, preventing the histamine-receptor interaction and subsequent mediator release.

It is a highly lipophilic molecule that readily crosses the blood-brain barrier. It is highly selective for histamine$_1$-receptors but has little effect on histamine$_2$ or histamine$_3$-receptors.

Chlorphenamine Maleate also activates 5-hydroxytryptamine (serotonin) and α-adrenergic receptors and blocks cholinergic receptors.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Paracetamol
Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral administration. Paracetamol is distributed into most body tissues. Plasma protein binding is negligible at usual therapeutic doses but increases with increasing doses. The elimination half-life varies from about 1 to 3 hours.

Paracetamol is metabolised extensively in the liver and excreted in the urine mainly as inactive glucuronide and sulphate conjugates. Less than 5% is excreted unchanged. The metabolites of paracetamol include a minor hydroxylated intermediate which has hepatotoxic activity. This intermediate metabolite is detoxified by conjugation with glutathione, however, it can accumulate following paracetamol over dosage (more than 150mg/kg or 10g total paracetamol ingested) and if left untreated can cause irreversible liver damage.

Paracetamol is metabolised differently by premature infants, newborns, infants and young children compared to adults, the sulphate conjugate being predominant.

Pseudoephedrine
Pseudoephedrine is readily absorbed from the gastrointestinal tract. It is largely excreted unchanged in the urine together with small amounts of its hepatic metabolite. It has a half- life of about 5-8 hours; elimination is enhanced and half-life reduced accordingly in acid urine. Small amounts are distributed into breast milk.

Chlorphenamine maleate
Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract,

with peak plasma concentrations occurring about 2.5 to 6 hours after oral administration. Chlorphenamine appears to undergo considerable first-pass metabolism. Bioavailability is low, values of 25 to 50% having been reported. About 70% of Chlorphenamine in the circulation is bound to plasma proteins. There is wide inter-individual variation in the pharmacokinetics of Chlorphenamine; half-life values

ranging from 2 to 43 hours have been reported. Chlorphenamine is widely distributed in the body and enters the CNS.

Chlorphenamine maleate is metabolised extensively. Metabolites include desmethyl- and didesmethylChlorphenamine. Unchanged drug and metabolites are excreted primarily in the urine; excretion is dependent on urinary pH and flow rate. Only trace amounts have been found in the faeces.

A duration of action of 4 to 6 hours has been reported; this is shorter than may be predicted from pharmacokinetic parameters.

More rapid and extensive absorption, faster clearance, and a shorter half-life have been reported in children compared to adults.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Panadol Allergy Sinus Tablets contain the excipients:

- Purified talc
- Maize starch
- Pregelatinised maize starch
- Stearic acid
- Povidone
- Silicon dioxide
- Sodium benzoate

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine. Refer to Section 4.5 – Interactions with other medicines and other forms of interactions.

6.3 SHELF LIFE

3 Years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Panadol Allergy Sinus Tablets are available in blister packs of the following sizes:

- 24 tablets

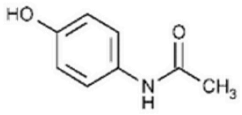
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

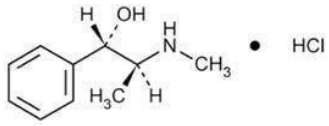
6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

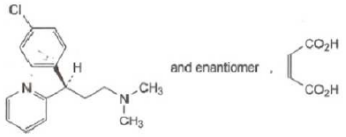
Paracetamol



Pseudoephedrine Hydrochloride



Chlorphenamine Maleate



CAS number

Paracetamol

CAS Registry Number: 103-90-2

Pseudoephedrine Hydrochloride

CAS Registry Number: 345-78-8

Chlorphenamine Maleate

CAS Registry Number: 113-92-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 3 Pharmacist Only Medicine

8 SPONSOR

Haleon Australia Pty Ltd
Sydney, Australia

9 DATE OF FIRST APPROVAL

18 February 1992

10 DATE OF REVISION

11 September 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
ALL	New PI format
Section 4.4	Updated information for acute vasoconstrictive events with pseudoephedrine