PANADOL® SINUS DAY & NIGHT TABLETS
PRODUCT INFORMATION

Product description

PANADOL SINUS DAY tablet is a white, film-coated capsule-shaped tablet with flat edges, front and back faces marked with DAY.

PANADOL SINUS NIGHT tablet is a white, film-coated round tablet with flat edges, front and back faces marked with NIGHT.

Ingredients

ACTIVE INGREDIENTS:	**DAY TABLETS**	**NIGHT TABLETS**
Paracetamol	500 mg	500 mg
Pseudoephedrine Hydrochloride	30 mg	30 mg
Chlorpheniramine Maleate	None present	2 mg

EXCIPIENTS:

DAY TABLETS	**NIGHT TABLETS**
Talc - purified	Talc - purified
Starch - Maize	Starch - Maize
Starch – Pregelatinised Maize	Starch – Pregelatinised Maize
Stearic Acid	Stearic Acid
Povidone	Povidone
Sodium Benzoate	Sodium Benzoate
Hypromellose	Hypromellose
Glycerol Triacetate	Glycerol Triacetate
Titanium Dioxide	Titanium Dioxide
Carnauba Wax	Carnauba Wax
Water - purified	Water - purified
	Silica – Colloidal Anhydrous

Pharmacology

Pharmacokinetics:
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 sulfate 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 overdosage (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 sulfate conjugate being predominant.

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.

Chlorpheniramine maleate is absorbed relatively slowly from the gastrointestinal tract, with peak plasma concentrations occurring about 2.5 to 6 hours after oral administration. Chlorpheniramine appears to undergo considerable first-pass metabolism. Bioavailability is low, values of 25 to 50% having been reported. About 70% of chlorpheniramine in the circulation is bound to plasma proteins. There is wide inter-individual variation in the pharmacokinetics of chlorpheniramine; half-life values ranging from 2 to 43 hours have been reported. Chlorpheniramine is widely distributed in the body and enters the CNS.

Chlorpheniramine maleate is metabolised extensively. Metabolites include desmethyl- and didesmethylchlorpheniramine. 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.

Pharmacodynamics/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.

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

Chlorpheniramine Maleate is a highly lipophilic molecule that readily crosses the blood-brain barrier.

Chlorpheniramine Maleate is highly selective for histamine$_1$-receptors but has little effect on histamine$_2$ or histamine$_3$ receptors. [Name of antihistamine] also activate 5-hydroxytryptamine (serotonin) and α-adrenergic receptors and blocks cholinergic receptors.

Indications

PANADOL SINUS DAY & NIGHT is used for the fast, effective temporary relief of sinus pain and congestion day & night. Reduces fever. The NIGHT formula also relieves runny nose, sneezing, itchy and watery eyes and allows rest.

Contraindications

Paracetamol is contraindicated for use in patients with known hypersensitivity or idiosyncratic reaction to paracetamol (or any of the other ingredients in the product);

Pseudoephedrine is contraindicated for use in patients:
- with known hypersensitivity or idiosyncratic reaction to pseudoephedrine (or any of the other ingredients in the product);
- with severe hypertension or coronary artery disease;
- taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days.

Chlorpheniramine Maleate is contraindicated for use in patients with:
- a history of hypersensitivity to the substance or substances of similar chemical structure (or any of the other ingredients in the product)
- narrow-angle glaucoma
- stenosing peptic ulcer
- symptomatic prostatic hypertrophy
- bladder neck obstruction
- pyloroduodenal obstruction

Chlorpheniramine Maleate is contraindicated for use in:
- newborns or premature infants
- [For promethazine] infants less than 12 months of age
- lactating women
- patients taking monoamine oxidase inhibitors (MAOIs)

Refer to 'Interactions with other medicines' for additional information

Precautions

Paracetamol should be used with caution in patients with:
- impaired hepatic function
- impaired renal function

Pseudoephedrine should be used with caution in patients with:
- hypertension
- hyperthyroidism
- diabetes mellitus
- coronary heart disease
- ischaemic heart disease
- glaucoma
- prostatic hypertrophy
- severe hepatic or renal dysfunction.

Chlorpheniramine Maleate may cause drowsiness and may increase the effects of alcohol. Drowsiness may continue the following day. Those affected should not drive or operate machinery; alcohol should be avoided.

Use with caution in patients with renal or hepatic impairment and in patients with epilepsy.

Refer to 'Interactions with other medicines' for additional information

Use in children and the elderly
Children and the elderly may experience paradoxical excitation with [name of antihistamine]. The elderly are more likely to have central nervous system (CNS) depressive side effects, including confusion. (See contraindications).

Use in pregnancy
Category A: Paracetamol has 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.

Category B2: Pseudoephedrine has 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.

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

Lactation
Paracetamol is excreted in small amounts (< 0.2%) in breast milk. 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.

Chlorpheniramine Maleate 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.

Interaction with other medicines

The following interactions with paracetamol have been noted:

- Anticoagulant drugs (warfarin) - dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period of time
- 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.

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
- other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants – may cause an increase in blood pressure and additive effects
- methyldopa and β-blockers – may cause an increase in blood pressure
- urinary acidifiers enhance elimination of pseudoephedrine
- urinary alkalinisers decrease elimination of pseudoephedrine

The following interactions with Chlorpheniramine Maleate 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
- **dexchlorpheniramine** when taken with monoamine oxidase inhibitors (MAOIs)may cause a decrease in blood pressure
- **chlorpheniramine** when taken concomitantly with phenytoin may cause a decrease in phenytoin elimination

Adverse reactions

Side effects of paracetamol are rare and usually mild, although haematological reactions have been reported. Skin rashes and hypersensitivity reactions occur occasionally. Overdosage with paracetamol if left untreated can result in severe, sometimes fatal liver damage and rarely, acute renal tubular necrosis.

Adverse effects include:
- cardiovascular stimulation – elevated blood pressure, tachycardia or arrhythmias
- central nervous system (CNS) stimulation – restlessness, insomnia, anxiety, tremors and (rarely) hallucinations
- skin rashes and urinary retention

Children and the elderly are more likely to experience adverse effects than other age groups.

Central Nervous System (CNS) effects
CNS depressive effects of Chlorpheniramine Maleate include sedation and impaired performance (impaired driving performance, poor work 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.

CNS stimulatory effects of Chlorpheniramine Maleate may include anxiety, hallucinations, appetite stimulation, muscle dyskinesias and activation of epileptogenic foci.

High doses of Chlorpheniramine Maleate may cause nervousness, tremor, insomnia, agitation, and irritability.

Anticholinergic effects
Side effects of Chlorpheniramine Maleate associated with cholinergic blockage include dryness of the eyes, mouth and nose, blurred vision, urinary hesitancy and retention, constipation and tachycardia.

Dosage

Adults and children over 12 years:
2 caplets / tablets taken with fluid every 6 hours as necessary, maximum 8 caplets / tablets within 24 hours. Do not take PANADOL SINUS DAY within 6 hours of PANADOL NIGHT.

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

Use in children
Paracetamol should not be taken for more than 48 hours except on medical advice.

Overdosage

If an overdose is taken or suspected, immediately contact the Poisons Information Centre (in Australia, call 131 126; in New Zealand call 0800 764 766) for advice, or go to a hospital straight away even if you feel well because of the risk of delayed, serious liver damage.

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Presentation

Description:	PANADOL SINUS DAY tablet is a white, film-coated capsule-shaped tablet with flat edges, front and back faces marked with DAY. PANADOL SINUS NIGHT tablet is a white, film-coated round tablet with flat edges, front and back faces marked with NIGHT.
Pack size:	*blister packs of 24*
Poisons Schedule:	*S3*
Manufactured by:	GlaxoSmithKline Australia Pty Ltd trading as GlaxoSmithKline Consumer Healthcare 82 Hughes Avenue, Ermington, NSW, Australia 2115

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