

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Noumed Night Time Cold & Flu Relief

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Noumed Night Time Cold & Flu Relief tablet contains the active ingredients:

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

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

3. PHARMACEUTICAL FORM

Noumed Night Time Cold & Flu Relief is a pink, round, uncoated tablet with a break-line.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Noumed Night Time Cold & Flu Relief is indicated for temporary relief from symptoms of cold and flu: nasal congestion, runny nose, headache, body aches and pains, fever, itchy or watery eyes, and sneezing. Assists rest by providing relief from these symptoms.

4.2 Dose and method of administration

Adults & Children 12 years and over

Take 2 tablets every 4 to 6 hours when necessary. Do not halve the tablet.

No more than 4 doses should be taken in 24 hours.

This medicine should not be taken with other medicines containing paracetamol unless advised to do so by a doctor or pharmacist.

Use in Adults

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

Use in Children

Do not give to children under 12 years of age. This medicine should not be taken for more than a few days at a time except on medical advice.

NEW ZEALAND DATA SHEET

4.3 Contraindications

Noumed Night Time Cold & Flu Relief is contraindicated for use in patients with the following conditions:

- Known hypersensitivity or idiosyncratic reaction to paracetamol, pseudoephedrine, chlorphenamine (or substances of a similar chemical structure) or any of the other ingredients in this medicine.
- Uncontrolled hypertension or severe coronary artery disease.
- Taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days.
- Narrow-angle glaucoma
- Stenosing peptic ulcer
- Symptomatic prostatic hypertrophy
- Bladder neck obstruction
- Pyloroduodenal obstruction

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

4.4 Special warnings and precautions for use

Noumed Night Time Cold & Flu Relief should be used with caution in patients with the following conditions:

- Impaired hepatic function
- Impaired renal function
- Hypertension
- Hyperthyroidism
- Diabetes mellitus
- Coronary heart disease
- Ischaemic heart disease
- Glaucoma
- Prostatic hypertrophy
- Epilepsy

Effects on sleep

Chlorphenamine 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.

This product contains pseudoephedrine which may cause sleeplessness if taken up to several hours before going to bed.

NEW ZEALAND DATA SHEET

Ischaemic colitis

Some cases of ischaemic colitis have been reported with pseudoephedrine. Discontinue the product and seek medical advice if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Serious skin reactions

Serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported very rarely in patients receiving paracetamol. Patients should be informed about the signs of serious skin reactions and use of the product should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

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

There have been rare cases of posterior reversible encephalopathy (PRES)/reversible cerebral vasoconstriction syndrome (RCVS) reported with sympathomimetic drugs, including pseudoephedrine. Symptoms reported included sudden onset of severe headache, nausea, vomiting, and visual disturbances. Most cases improved or resolved within a few days following appropriate treatment. This product should be discontinued immediately, and medical advice sought if signs/symptoms of PRES/RCVS develop.

Ischaemic optic neuropathy

Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. The product should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

Use in elderly

The elderly may experience paradoxical excitation with chlorphenamine. The elderly are more likely to have central nervous system (CNS) depressive side effects, including confusion.

Paediatric use

No data available.

Effects on laboratory tests

No data available.

NEW ZEALAND DATA SHEET

4.5 Interaction with other medicines and other forms of interaction

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.
- High anion gap metabolic acidosis from pyroglutamic acid (5-oxoprolinemia) has been reported with concomitant use of therapeutic doses of paracetamol and flucloxacillin. Patients reported to be most at risk are elderly females with underlying disease such as sepsis, renal function abnormality, and malnutrition.

The following interactions with pseudoephedrine have been noted:

- Antidepressant medication e.g. 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
- Antihypertensives e.g. methyldopa and beta-blockers – may cause an increase in blood pressure
- Urinary acidifiers enhance elimination of pseudoephedrine
- Urinary alkalinisers decrease elimination of pseudoephedrine

NEW ZEALAND DATA SHEET

The following interactions with chlorphenamine 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

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in Pregnancy

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.

Noumed Night Time Cold & Flu Relief should not be used in pregnancy unless the potential benefits to the patient are weighed against the possible risk to the foetus.

Use in 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.

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.

Chlorphenamine is excreted in breast milk.

Therefore, Noumed Night Time Cold & Flu Relief is not recommended for breastfeeding mothers (see also Contraindications).

NEW ZEALAND DATA SHEET

4.7 Effects on ability to drive and use machines

CNS depressive effects of chlorphenamine 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.

4.8 Undesirable effects

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 of pseudoephedrine 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.

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

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

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

Adverse drug reactions identified during post-marketing experience with paracetamol, pseudoephedrine, and the combination appear in the following table. The frequency category was estimated from spontaneous reporting rates.

NEW ZEALAND DATA SHEET

Adverse events that have been observed during clinical trials and/or post-marketing use are ranked under the following frequency: Very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), rare ($\geq 1/10,000$ and $< 1/1,000$), very rare ($< 1/10,000$).

System Organ Class	
Frequency Category	Adverse Event Preferred Term
Blood and Lymphatic System Disorders	
Unknown	Thrombocytopenia
Unknown	Agranulocytosis
Immune System Disorder	
Very rare	Anaphylactic reaction
Very rare	Hypersensitivity
Psychiatric Disorder	
Very rare	Anxiety
Very rare	Euphoric mood
Very rare	Restlessness
Very rare	Insomnia
Very rare	Hallucinations
Very rare	Hallucination, visual
Nervous System Disorder	
Very rare	Cerebrovascular accident*
Very rare	Headache
Very rare	Paraesthesia
Very rare	Psychomotor hyperactivity (in the paediatric population)
Very rare	Tremor
Very rare	Posterior Reversible Encephalopathy Syndrome
Very rare	Reversible Cerebral Vasoconstriction Syndrome
Eye Disorders	
Unknown	Ischaemic optic neuropathy
Cardiac Disorders	
Very rare	Arrhythmia
Very rare	Myocardial infarction*
Very rare	Palpitations
Very rare	Tachycardia
Gastrointestinal Disorders	
Very rare	Abdominal discomfort
Very rare	Colitis ischaemic
Very rare	Diarrhoea
Very rare	Vomiting
Skin and Subcutaneous Tissue Disorders	
Very rare	Pruritus
Very rare	Acute generalised exanthematous pustulosis
Very rare	Angioedema
Very rare	Pruritic rash
Very rare	Rash
Very rare	Urticaria
Very rare	Fixed eruption

NEW ZEALAND DATA SHEET

Renal and Urinary Disorders

Very rare Dysuria

Very rare Urinary retention

General Disorders and Administration Site Conditions

Very rare Feeling jittery

Very rare Anxiety

Investigations

Very rare Blood pressure increased

Very rare Transaminases increased

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

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 professionals are asked to report any suspected adverse reactions <https://pophealth.my.site.com/carmreportnz/s/>

4.9 Overdose

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

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.

NEW ZEALAND DATA SHEET

Chlorphenamine competes with histamine at central and peripheral histamine₁-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 histamine₁-receptors but has little effect on histamine type-2 or histamine type-3 receptors. Chlorphenamine also activates 5-hydroxytryptamine (serotonin) and α -adrenergic receptors and blocks cholinergic receptors.

Clinical trials

No data available.

5.2 Pharmacokinetic properties

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral administration.

Pseudoephedrine is readily absorbed from the gastrointestinal tract.

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, with peak plasma concentrations occurring about 2.5 to 6 hours after oral administration. Bioavailability is low, values of 25 to 50 % having been reported. 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 has been reported in children compared to adults.

Distribution

Paracetamol is distributed into most body tissues. Plasma protein binding is negligible at usual therapeutic doses but increases with increasing doses.

Small amounts of pseudoephedrine are distributed into breast milk.

Chlorphenamine is widely distributed in the body and enters the CNS. About 70 % of chlorphenamine in the circulation is bound to plasma proteins.

Metabolism

Paracetamol is metabolised extensively in the liver. 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 overdose (more than 150 mg/kg or 10 g total

NEW ZEALAND DATA SHEET

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 incompletely metabolised (less than 1 %) in the liver to an inactive metabolite by N-demethylation.

Chlorphenamine maleate is metabolised extensively. Metabolites include desmethyl- and didesmethylchlorphenamine.

Excretion

Paracetamol is excreted in the urine mainly as inactive glucuronide and sulfate conjugates. Less than 5% is excreted unchanged. The elimination half-life varies from about 1 to 3 hours.

Pseudoephedrine 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.

Unchanged chlorphenamine 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. There is wide inter-individual variation in the pharmacokinetics of chlorphenamine; half-life values ranging from 2 to 43 hours have been reported. 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.

NEW ZEALAND DATA SHEET

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Crospovidone
- Erythrosine aluminium lake (Night tablets only)
- Magnesium stearate
- Microcrystalline cellulose
- Povidone
- Pregelatinised maize starch
- Stearic acid
- Purified water

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30 °C. Keep out of reach of children.

6.5 Nature and contents of container

The tablets are presented in PVC/PVDC/Aluminium blister packs which are enclosed in a carton. Each blister pack contains 10 and 12 tablets.

The pack sizes are:

- 10 tablets (1 x 10 tablet blister pack in a carton)
- 12 tablets (1 x 12 tablet blister pack in a carton)
- 20 tablets (2 x 10 tablet blister packs in a carton)
- 24 tablets (2 x 12 tablet blister packs in a carton)

Not all pack sizes are marketed.

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements by taking to your local pharmacy.

NEW ZEALAND DATA SHEET

7. MEDICINE SCHEDULE Controlled

Drug C3.

8. SPONSOR

Noumed Pharmaceuticals Limited

Auckland, New Zealand

Freephone 0800 527 545

9. DATE OF FIRST APPROVAL

TBC

10. DATE OF REVISION OF THE TEXT

26 March 2024

SUMMARY TABLE OF CHANGES

Section changes	Summary of new information
All	New