AUSTRALIAN PRODUCT INFORMATION

Codral® Original Day & Night tablets (Paracetamol, Pseudoephedrine hydrochloride, Triprolidine hydrochloride)

1 Name of the Medicine

Paracetamol

Pseudoephedrine Hydrochloride

Triprolidine Hydrochloride

2 Qualitative and Quantitative composition

Codral® Original Day & Night tablets contain two separate formulations: day tablets and night tablets.

Each Codral® Original Day & Night **day** tablet contains pseudoephedrine hydrochloride 30 mg, paracetamol 500 mg

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

Each Codral® Original Day & Night **night** tablet contains pseudoephedrine hydrochloride 30 mg, paracetamol 500 mg, triprolidine hydrochloride 1.25 mg

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

3 Pharmaceutical form

Codral® Original Day & Night day tablets are white, round, flat and uncoated with wide bevelled edges. They are scored and coded ‘P3F’ on one face, and the other face is plain.

Codral® Original Day & Night night tablets are turquoise, bevelled, capsule-shaped, flat and uncoated. They are scored on one face and coded ‘S3F’ each side of the score, and plain on the other face.

4 Clinical Particulars

4.1 Therapeutic Indications

Codral® Original Day & Night provides temporary relief from the symptoms of colds and flu. “Day” tablet relieves runny nose, nasal congestion, headache, body aches and pains, and fever. “Night” tablet relieves runny nose, pain, fever, headache and sneezing.

4.2 Dosage and administration

The recommended dosage of Codral® Original Day & Night for adults and children 12 years and over is:

- Day – take 2 day tablets in the morning and 2 tablets in the afternoon.
- Night – take 2 night tablets in the evening at bedtime.

Codral® Original Day & Night should not to be taken by children under 12 years of age.

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.

4.3 Contraindications

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 or uncontrolled hypertension or severe coronary artery disease
- taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days
- with severe acute or chronic kidney disease/renal failure.

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

Triprolidine 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.

Triprolidine is contraindicated for use in:

- newborns or premature infants
- lactating women
- patients taking monoamine oxidase inhibitors (MAOIs).

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

4.4 Special Warnings and Precautions for Use

High Anion Gap Metabolic Acidosis
Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or patients with malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

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 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.

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

Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

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 physician should be consulted.

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 drug should be

discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

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

Triprolidine 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, and in patients with respiratory conditions such as emphysema, chronic bronchitis, or acute or chronic bronchial asthma.

Pseudoephedrine is contraindicated for use in patients with severe acute or chronic kidney disease/renal failure (see section 4.3 Contraindications)

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

Severe skin reactions such as acute generalized exanthematous pustulosis(AGEP) have been reported very rarely with pseudoephedrine containing products. 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 formation of small pustules or rash occur, with or without pyrexia or erythema, then treatment with pseudoephedrine should be discontinued and a physician should be consulted. (see Section 4.8)

Use in elderly
The elderly may experience paradoxical excitation with triprolidine. The elderly are more likely to have CNS depressive side effects, including confusion.

Paediatric use
Children may experience paradoxical excitation with triprolidine.

Effects on laboratory tests
No data available.

4.5 Interactions with other medicines and other forms of interactions

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 paracetamol have been noted:
- anticoagulant drugs (warfarin) – dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period oftime
- 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 drugsor drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents
- paracetamol excretion may be affected andplasma concentrations altered when given with probenecid
- colestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol
  Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4)

The following interactions with triprolidine have been noted:
- 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
The pregnancy categorisation is 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.

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.

Triprolidine 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.

Use in lactation
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.
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 infant.

Triprolidine 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 the ability to drive and use machines

Triprolidine 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.

4.8 Adverse Effects (Undesirable Effects)

Adverse drug reactions identified during post-marketing experience are detailed in the table below. Additionally the following should be noted:

Adverse effects of pseudoephedrine include elevated blood pressure

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

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

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

CNS depressive effects of triprolidine 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 triprolidine may include appetite stimulation, muscle dyskinesias and activation of epileptogenic foci.

High doses of triprolidine may cause agitation, and irritability.

Side effects of triprolidine 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, the combination of pseudoephedrine and triprolidine, the combination of pseudoephedrine and paracetamol or the combination paracetamol, pseudoephedrine and triprolidine appear in the following tables. The frequency category was estimated from spontaneous reporting rates.

Adverse events that have been observed during clinical trials and/or post-marketing use are ranked under the following frequency: Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1000, <1/100); rare (>1/10000, <1/1000); very rare (<1/10000 and including isolated reports).

Frequency category	Adverse Event Preferred Term
Immune System Disorders	
Very Rare	*Anaphylactic reaction*
Very Rare	*Hypersensitivity*
Psychiatric Disorders	
Very Rare	*Hallucination*
Very Rare	*Anxiety*
Very Rare	*Euphoric mood*
Very Rare	*Insomnia*
Very Rare	*Nervousness*
Very Rare	*Restlessness*
Very Rare	*Hallucination visual*
Nervous System Disorders	
Very Rare	*Cerebrovascular accident**
Very Rare	*Dizziness*
Very Rare	*Headache*
Very Rare	*Paraesthesia*
Very Rare	*Psychomotor hyperactivity (in the paediatric population)*

Very Rare	*Somnolence*
Very Rare	*Tremor*
Very Rare	*Posterior Reversible Encephalopathy Syndrome (PRES) (see section 4.4)*
Very Rare	*Reversible Cerebral Vasoconstriction Syndrome (RCVS) (see section 4.4)*
Cardiac Disorders	
Very Rare	*Arrhythmia*
Very Rare	*Myocardial infarction**
Very Rare	*Palpitations*
Very Rare	*Tachycardia*
Respiratory, Thoracic, and Mediastinal Disorders	
Very Rare	*Epistaxis*
Gastrointestinal Disorders	
Very Rare	*Abdominal discomfort*
Very Rare	*Colitis ischaemic*
Very Rare	*Dry mouth*
Very Rare	*Nausea*
Very Rare	*Vomiting*
Very Rare	*Diarrhoea*
Skin and Subcutaneous Tissue Disorders	
Very Rare	*Pruritus*
Very Rare	*Angioedema*
Very Rare	*Pruritic rash*
Very Rare	*Rash*
Very Rare	*Urticaria*
Very Rare	*Acute generalised exanthematous pustulosis*
Very Rare	*Fixed eruption*[a]
Renal and Urinary Disorders	
Very Rare	*Dysuria*
Very Rare	*Urinary retention*
General Disorders and Administration Site Conditions	

Very Rare	*Fatigue*
Very Rare	*Feeling jittery*
Investigations	
Very Rare	*Blood pressure increased*
Very Rare	*Transaminases increased*
Metabolism and nutrition disorders	
Not known	*High anion gap metabolic acidosis*

a The common clinical term for PT Fixed eruption is fixed drug eruption.

* 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 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 Overdosage

If an overdose is taken or suspected, immediately contact the Poisons Information Centre (in Australia, call 13 11 26; 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.

Overdosage with paracetamol if left untreated can result in severe, sometimes fatal liver damage, and rarely, acute renal tubular necrosis.

5 Pharmacological Properties

5.1 Pharmacodynamics properties

Mechanisms of action
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.

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.

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

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

Triprolidine is highly selective for histamine$_1$-receptors but has little effect on histamine$_2$ or histamine$_3$ receptors. Triprolidine also activates 5-hydroxytryptamine (serotonin) and α-adrenergic receptors and blocks cholinergic receptors.

Clinical trials
No data available.

5.2 Pharmacokinetics

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.

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 150 mg/kg or 10 g 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.

After absorption from the gastro-intestinal tract, triprolidine hydrochloride is metabolised; a carboxylated derivative accounts for about half the dose excreted in the urine. Reported half-lives vary from 3 to 5 hours or more. Triprolidine is

distributed into breast milk.

5.3 Preclinical safety data

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 Pharmaceutical Particulars

6.1 List of excipients

Each Codral® Original Day & Night **day** tablet contains the excipients: microcrystalline cellulose, hydroxypropylcellulose, magnesium stearate, sodium starch glycollate, pregelatinised wheat starch, stearic acid.

Each Codral® Original Day & Night **night** tablet contains the excipients: brilliant blue FCF, microcrystalline cellulose, hydroxypropylcellulose, magnesium stearate, povidone, quinoline yellow.

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 25°C. Keep in a dry dark place.

6.5 Nature and Contents of Container

Codral® Original Day & Night tablets are available in blister packs of the following sizes:

- 24 tablets (S3) Pharmacist Only Medicine

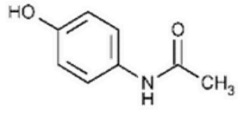
6.6 Special Precautions for disposal

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

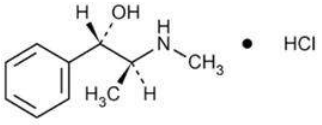
6.7 Physicochemical Properties

Chemical Structure

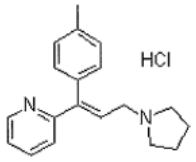
Paracetamol



Pseudoephedrine Hydrochloride



Triprolidine Hydrochloride



CAS number

Paracetamol

CAS Registry Number: 103-90-2

Pseudoephedrine Hydrochloride

CAS Registry Number: 345-78-8

Triprolidine Hydrochloride

CAS Registry Number: 6138-79-0

7 Medicine Schedule (Poisons Standard)

Schedule 3

8 Sponsor

Kenvue Pacific Australia
New Zealand
Sydney, NSW, Australia and
Auckland New Zealand

®Registered trademark

9 Date of First Approval

11 May 2016

10 Date of Revision

13 October 2026

Summary table of changes

Section Changed	Summary of new information
4.3	Additional contraindications added
4.4, 4.5, 4.8	Additional warning statements added
8	Update Sponsor details
4.4 & 4.8	Additional warning statement added for AGEP