NEW ZEALAND DATA SHEET

1 PRODUCT NAME
Codral® Original Day & Night

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. Do not halve tablet.

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. Do not halve tablet.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Codral® Original Day & Night tablets provide temporary relief from the symptoms of cold and flu: runny nose, nasal congestion, headache, body aches and pains, and fever. The night tablets also provide relief from sneezing and itchy or watery eyes, and assist rest by providing relief from these symptoms.

4.2 Dose and method of 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. Do not halve tablet.
Night – take 2 night tablets in the evening at bedtime. Do not halve tablet.

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

Use in adults
Codral® Original Day & Night should not be taken for more than a few days at a time except on medical advice.

Use in children
Codral® Original Day & Night should not be administered to children under 12 years of age.

For children over 12 years old, Codral® Original Day & Night should not be taken for more

than 48 hours except on medical advice.

4.3 Contraindications

This product is contraindicated for use in patients with the following conditions:

- known hypersensitivity or idiosyncratic reaction to paracetamol, pseudoephedrine, triprolidine (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 to '4.5 Interactions with other medicines and other forms of interactions' for additional information.

4.4 Special warnings and precautions for use

Identified precautions

Use in 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

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.

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

Respiratory conditions

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

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

Paediatric use
No data available.

Effects on laboratory tests
No data available.

4.5 Interaction with other medicines and other forms of interaction

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
- Antihypertensives e.g. beta-blockers, methyldopa ‑ pseudoephedrine may antagonise the effect of certain classes of antihypertensives and 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 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 triprolidine 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

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.

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.

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

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.

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.

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 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 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.

Adverse reactions with triprolidine:

- CNS stimulatory effects of triprolidine may include anxiety, hallucinations, appetite stimulation, muscle dyskinesias and activation of epileptogenic foci.
- High doses of triprolidine may cause nervousness, tremor, insomnia, 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, and the combination appear in the following table. 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 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥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 Disorders	
Very Rare	*Anaphylactic reaction*

Very Rare	*Hypersensitivity*
Psychiatric Disorders	
Very Rare	*Anxiety*
Very Rare	*Euphoric mood*
Very Rare	*Restlessness*
Very Rare	*Insomnia*
Very Rare	*Hallucination*
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*
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*
Respiratory, Thoracic, and Mediastinal Disorders	
Very Rare	*Epistaxis*
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*
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 post-authorisation 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 reactions
https://pophealth.my.site.com/carmreportnz/s/

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

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 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.

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 Pharmacokinetic properties

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.

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.

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
36 months

6.4 Special precautions for storage
Store below 25°C. Keep in a dry, dark place.

6.5 Nature and contents of container
Blister packs of 24 tablets.

6.6 Special precautions for disposal
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE
Class C3 Controlled Drug

8. SPONSOR
JNTL Consumer Health (New Zealand) Limited
PO Box 147247
Ponsonby
Auckland 1144

9. DATE OF FIRST APPROVAL
Date of publication in the New Zealand Gazette of consent to distribute the medicine: 12 April 2024

10. DATE OF REVISION OF THE TEXT
12 April 2024

Summary table of changes

Section changed	Summary of new information
Whole data sheet	New data sheet