NEW ZEALAND DATA SHEET

1 PRODUCT NAME
Codral® Original Cold & Flu

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Codral® Original Cold & Flu tablets contain paracetamol 500 mg and pseudoephedrine hydrochloride 30mg.

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM
Codral® Original Cold & Flu tablets are white, flat, round and uncoated. They are scored and coded 'P3F' on one face, and the other face is plain.

Do not halve tablet.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Codral® Original Cold & Flu tablets is Indicated for temporary relief from the symptoms of cold and flu: runny nose, nasal congestion, headache, body aches and pains, and fever.

4.2 Dose and method of administration
The recommended dosage of Codral® Original Cold & Flu tablets for adults and children 12 years and over is 2 tablets every 4 to 6 hours as necessary. Do not exceed 8 tablets in 24 hours. Do not halve tablet.

Codral® Original Cold & Flu tablets should not be taken by children under 12 years of age.

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

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

For children over 12 years old, Codral® Original Cold & Flu 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 (or substances of a similar chemical structure) or any of the other ingredients in the product.
- Uncontrolled hypertension or severe coronary artery disease
- Taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days.

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

Effects on sleep

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

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

No data available.

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.

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.

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.

4.7 Effects on ability to drive and use machines
No data available.

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 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	*Hallucinations*
Very rare	*Hallucination, visual*

Nervous System Disorders	
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 pustuloisis*
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 increase*

* 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 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.

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.

5.3 Preclinical safety data

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Codral® Original Cold & Flu tablets contain the excipients: microcrystalline cellulose, hydroxypropylcellulose, magnesium stearate, sodium starch glycollate, pregelatinised wheat starch, stearic acid.

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 30°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