AUSTRALIAN PRODUCT INFORMATION

CODRAL ORIGINAL DAY & NIGHT + DRY COUGH CAPSULES (Paracetamol, Dextromethorphan hydrobromide monohydrate, Pseudoephedrine hydrochloride, Chlorphenamine maleate)

1 NAME OF THE MEDICINE

Paracetamol
Pseudoephedrine hydrochloride
Dextromethorphan hydrobromide
monohydrate Chlorphenamine maleate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Codral® Original Day & Night + Dry Cough capsules contain two separate formulations: day capsules and night capsules.

Each **day** capsule contains paracetamol 500 mg, pseudoephedrine hydrochloride 30 mg, dextromethorphan hydrobromide monohydrate 10 mg

Each **night** capsule contains paracetamol 500 mg, chlorphenamine maleate 2 mg, dextromethorphan hydrobromide monohydrate10 mg.

Day and Night capsules also contain lactose.

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

3 PHARMACEUTICAL FORM

The day capsules are blue green/white opaque hard gelatin with 'Day' printed in black.

The night capsules are reddish orange/white opaque hard gelatin with 'Night' printed in black.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Codral® Original Day & Night + Dry Cough provide temporary relief of cold and flu symptoms. The day capsules temporarily relieve headache, body aches and pains, blocked nose, fever and dry irritated coughs without causing drowsiness. The night capsules temporarily relieve headache, body aches and pains, blocked nose, fever and dry irritated coughs and a runny nose.

4.2 DOSE AND METHOD OF ADMINISTRATION

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

- Day dosage – take one or two green capsules in the morning, at midday and in the afternoon as required.
- Night dosage – take one or two red capsules at bedtime as required.

Each dose should be taken at least 4 to 6 hours apart. Do not exceed four doses in 24 hours.

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

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

For children over 12 years old, Codral® Original Day & Night + Dry Cough should not be taken for more than 48 hours except on medical advice.

4.3 CONTRADINDICATIONS

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 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.

Dextromethorphan is contraindicated for use in patients:
- with known hypersensitivity or idiosyncratic reaction to dextromethorphan (or any of the other ingredients in the product).
- taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days.

Chlorphenamine 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.

Chlorphenamine is contraindicated for use in:
- newborns or premature infants
- lactating women
- patients taking monoamine oxidase inhibitors (MAOIs).

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.

Identified 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 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.

Dextromethorphan should not be used for chronic persistent cough accompanying a disease state, or for cough associated with excessive secretions.

Dextromethorphan should not be given to patients with or at risk of developing respiratory failure, e.g. asthma, chronic obstructive airways disease, and pneumonia. Caution is needed in patients with a history of asthma and it should not be given during an acute attack.

Chlorphenamine may cause drowsiness and may increase the effects of alcohol. Drowsiness may continue the following day.

Use with caution in patients with epilepsy.

While taking this product, avoid alcoholic beverages and consult a healthcare professional prior to taking with central nervous system depressants.

Patients with a persistent respiratory condition such as emphysema, chronic bronchitis, acute or chronic bronchial asthma, where cough is accompanied by excessive secretions, glaucoma or prostate hyperplasia with residual urine formation (adult products) should be advised to consult a physician before using this product.

Talk to your doctor or pharmacist: if you have been told that you are a slow metaboliser of CYP2D6 or are taking any other medicines. Patients should not use with any other product containing paracetamol.

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

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 hepatic impairment

Use with caution in patients with hepatic impairment or severe hepatic dysfunction.

Use in renal impairment

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

Use in the elderly

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

Paediatric use

Children may experience paradoxical excitation with chlorphenamine.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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
- 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 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 dextromethorphan have been noted:

- Dextromethorphan should not be used in patients taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days. The use of dextromethorphan with, or within two weeks of taking MAOIs, may increase the risk of serious side effects such as hypertensive crisis, hyperpyrexia and convulsions.
- Dextromethorphan when used with SSRIs (such as fluoxetine) or tricyclic antidepressants (such as clomipramine and imipramine) may result in a “serotonin syndrome” with changes in mental status, hypertension, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering and tremor.
- Serum levels of dextromethorphan may be increased by the concomitant use of inhibitors of cytochrome P450 2D6, such as the antiarrhythmics quinidine and amiodarone, antidepressants such as fluoxetine and paroxetine, or other drugs which inhibit cytochrome P450 2D6 such as haloperidol and thioridazine.

- Metoprolol is a CYP2D6 substrate and metabolism of dextromethorphan has been shown to be prolonged when the two drugs are administered concomitantly.
- Isavuconazole is a moderate inhibitor of CYP3A4 and a mild inducer of CYP2B6. When administered concomitantly with dextromethorphan, the AUC and Cmax of dextromethorphan has been observed to increase by 18% and 17%, respectively.
- Concomitant use of dextromethorphan with SSRI agents may lead to Serotonin Syndrome.
- Concomitant use of dextromethorphan and other CNS depressants (e.g. alcohol, narcotic analgesics and tranquillizers) may increase the CNS depressant effects of these drugs.

The following interactions with chlorphenamine 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
- when taken concomitantly with phenytoin may cause a decrease in phenytoin elimination.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No data available

Use in pregnancy: Category B2

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.

Dextromethorphan 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.

Chlorphenamine 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.
It is not known whether dextromethorphan is excreted in breast milk or whether it has a harmful effect on the breastfeeding infant. Therefore it is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Chlorphenamine 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

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.

4.8 ADVERSE EFFECTS (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
- 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.

Side effects with usual doses of dextromethorphan are uncommon but may include mild drowsiness, fatigue, dystonias, dizziness and gastrointestinal disturbances (nausea or vomiting, stomach discomfort, or constipation).

Side effects that may occur with high doses (overdosage) of dextromethorphan include excitation, confusion, psychosis, nervousness, irritability, restlessness, “serotonin syndrome”, severe nausea and vomiting, and respiratory depression.

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.

Central Nervous System (CNS) effects

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.

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.

Anticholinergic effects

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.

Post-Marketing Data

Adverse drug reactions ADRs identified with single ingredient chlorphenamine, dextromethorphan, pseudoephedrine and paracetamol are included in the following tables. The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000

Not known (cannot be estimated from the available data)

Table 1. Adverse Drug Reactions Identified During Post-Marketing Experience with Chlorphenamine, Dextromethorphan, Paracetamol or the combination by Frequency Category Estimated from Spontaneous Reporting Rates

System Organ Class Frequency Category	Adverse Event Preferred Term
Metabolism and Nutrition Disorders	
Not known	*High anion gap metabolic acidosis*
Immune System Disorders	
Very rare	*Anaphylactic reaction*
Very rare	*Hypersensitivity*
Psychiatric Disorders	
Very rare	*Insomnia*
Nervous System Disorders	
Very rare	*Psychomotor hyperactivity*
Gastrointestinal Disorders	
Very rare	*Abdominal pain*
Very rare	*Diarrhoea*

Very rare	*Nausea*
Very rare	*Vomiting*
Skin and Subcutaneous Tissue Disorders	
Very rare	*Angioedema*
Very rare	*Fixed eruption**
Very rare	*Pruritus*
Very rare	*Rash*
Very rare	*Rash pruritic*
Very rare	*Urticaria*
Investigations	
Very rare	*Transaminases increased*

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

Table 2. Adverse Drug Reactions Identified During Post-Marketing Experience with Dextromethorphan, Paracetamol, Pseudoephedrine by Frequency Category Estimated from Estimated from Spontaneous Reporting Rates

System Organ Class Frequency Category	Adverse Event Preferred Term
Metabolism and Nutrition Disorders	
Very rare	*Decreased appetite*
Not known	*High anion gap metabolic acidosis*
Immune System Disorders	
Very rare	*Anaphylactic reaction*
Very rare	*Hypersensitivity*
Psychiatric Disorders	
Very rare	*Agitation*
Very rare	*Anxiety*
Very rare	*Euphoric mood*
Very rare	*Hallucination*
Very rare	*Hallucination, visual*
Very rare	*Insomnia*
Very rare	*Irritability*
Very rare	*Restlessness*
Nervous System Disorders	
Very rare	*Cerebrovascular accident*
Very rare	*Headache*
Very rare	*Paraesthesia*
Very rare	*Psychomotor hyperactivity*
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)*
Eye Disorders	
Very rare	*Mydriasis*
Cardiac Disorders	
Very rare	*Arrhythmia*
Very rare	*Myocardial infarction*
Very rare	*Palpitations*
Very rare	*Tachycardia*
Respiratory, Thoracic and Mediastinal Disorders	
Very rare	*Dyspnoea*
Gastrointestinal Disorders	
Very rare	*Abdominal pain*
Very rare	*Diarrhoea*
Very rare	*Colitis ischaemic*
Very rare	*Vomiting*

Skin and Subcutaneous Tissue Disorders	
Very rare	*Acute generalised exanthematous pustulosis*
Very rare	*Angioedema*
Very rare	*Fixed eruption**
Very rare	*Pruritus*
Very rare	*Rash*
Very rare	*Rash erythematous*
Very rare	*Rash pruritic*
Very rare	*Urticaria*
Renal and Urinary Disorders	
Very rare	*Dysuria*
Very rare	*Urinary retention*
Investigations	
Very rare	*Blood pressure increased*
Very rare	*Transaminases increased*
Very rare	*Transaminases increased*

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

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: https://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

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.

Fatal cases of dextromethorphan overdose have been reported very rarely.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

There is no available information on the pharmacodynamic properties for the combination of chlorpheniramine, dextromethorphan, paracetamol and pseudoephedrine in humans. The information presented below describes the pharmacodynamic properties of the single active ingredients.

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.

Dextromethorphan is a non-opioid cough suppressant. It is the methylated dextrorotatory analogue of levorphanol, a codeine analogue. Dextromethorphan acts centrally on the cough centre in the medulla and nucleus tractus solaris to increase the cough threshold. It does not have classical analgesic, sedative or respiratory depressant effects at usual antitussive doses. Chlorphenamine competes with histamine at central and peripheral histamine$_1$-receptor sites, preventing the histamine-receptor interaction and subsequent mediator release.

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

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

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

There is no available information on the pharmacokinetic properties for the combination of chlorpheniramine, dextromethorphan, paracetamol and pseudoephedrine in humans. The information presented below describes the pharmacokinetic properties of the single active ingredients.

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.

Dextromethorphan is well absorbed from the gastrointestinal tract after oral administration. It is metabolised in the liver, exhibiting polymorphic metabolism involving the cytochrome P450 isoenzyme (CYP 2D6). It is excreted in the urine as unchanged dextromethorphan and demethylated metabolites, including dextrorphan, which has some cough suppressant activity. The plasma elimination half-life of dextromethorphan is 1.2 to 3.9 hours. However, the rate of metabolism varies between individuals according to phenotype (extensive v poor metabolisers), with half-life being as long as 45 hours in patients who are poor metabolisers.

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 central nervous system (CNS).

Chlorpheniramine 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.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Each **day** capsule contains the following excipients: allura red AC, brilliant blue FCF, gelatin, lactose, magnesium stearate, quinoline yellow, colloidal anhydrous silica, silicon dioxide, sodium lauryl sulfate, purified talc, titanium dioxide, Opacode Black A-10259.

Each **night** capsule contains the following excipients: allura red AC, brilliant blue FCF, gelatin, lactose, magnesium stearate, colloidal anhydrous silica, silicon

dioxide, sodium lauryl sulfate, purified talc, titanium dioxide, Opacode Black A-10259.

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C

6.5 NATURE AND CONTENTS OF CONTAINER

Blister packs of 24 capsules (18 Day capsules, 6 Night capsules)

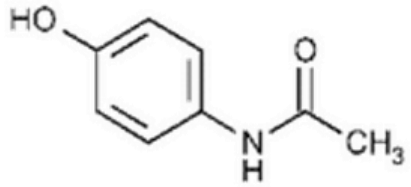
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy

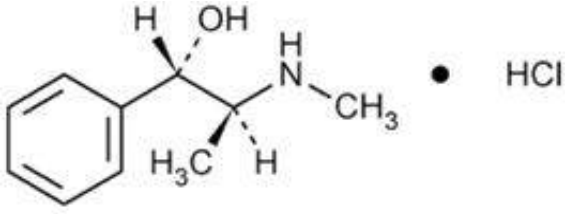
6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

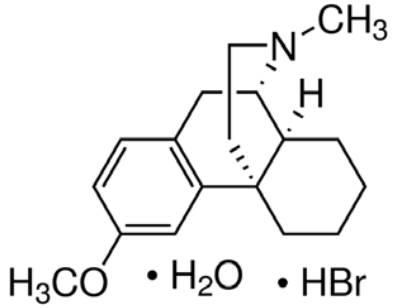
Paracetamol:



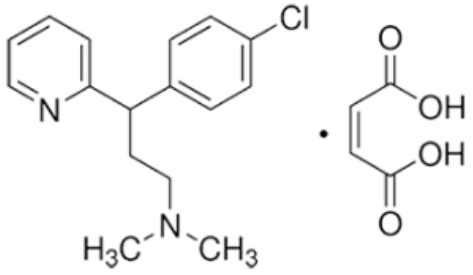
Pseudoephedrine Hydrochloride:



Dextromethorphan hydrobromide monohydrate:



Chlorphenamine maleate:



CAS number

Paracetamol:
103-90-2

Pseudoephedrine hydrochloride:
345-78-8

Dextromethorphan hydrobromide monohydrate: 125-69-9

Chlorphenamine maleate:
113-92-8

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

4 October 2006

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

5.1,5.2	Inclusion of information regarding combination vs single ingredient formulations
8	Updated Sponsor details
4.4	Additional warning statement added for AGEP