NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Maxiclear® Day and Night + Cough Film Coated Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each data tablets contains: Paracetamol 500 mg, Phenylephrine hydrochloride 5 mg, Dextromethorphan hydrobromide monohydrate 10 mg

Each night table contains: Paracetamol 500 mg, Phenylephrine hydrochloride 5 mg, Dextromethorphan hydrobromide monohydrate 10 mg

3. PHARMACEUTICAL FORM

Film coated tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Day tablet: For non-drowsy, temporary relief from the symptoms of the common cold and flu including headaches, body aches and pains, blocked nose, fever and dry irritated coughs.

Night tablet: For temporary relief from the symptoms of the common cold and flu including headaches, body aches and pains, blocked and runny nose, fever and dry irritated coughs. The night tablet allows rest.

4.2 Dose and method of administration

Adults and children 12 years and over: Take 2 red/brown (day) tablets every 4 -6 hours and 2 blue (night) tablets at night time as necessary.

Do not exceed 6 day tablets and 2 night tablets in 24 hours.

Do not take the night tablets within 4 hours of taking the day tablets.

Adults: Keep to the recommended dose. Do not take this medicine for longer than a few days at a time unless advised to by a doctor.

Adolescents: Do not take this medicine for longer than 48 hours at a time unless advised by a healthcare

professional.

Do not give to children under 12 years of age.

4.3 Contraindications

Maxiclear® Day and Night + Cough Film Coated Tablets are contraindicated for use in patients:

- with known hypersensitivity to the active ingredients paracetamol, phenylephrine hydrochloride, dextromethorphan hydrobromide monohydrate or chlorphenamine maleate or substances of similar chemical structure or any other ingredient in the product
- taking prescription medication for depression, psychiatric or emotional conditions e.g. a monoamine oxidase inhibitor (MAOI), selective serotonin reuptake inhibitor (SSRI) or for Parkinson's disease, or for 2 weeks after stopping the medication.
- with severe hypertension or coronary artery disease
- with narrow-angle glaucoma
- with stenosing peptic ulcer
- with symptomatic prostatic hypertrophy
- with bladder neck obstruction
- with pyloroduodenal obstruction
- with impaired hepatic function
- with respiratory insufficiency and respiratory depression
- with chronic airway disease
- taking other antihistamines

Maxiclear® Day and Night + Cough Film Coated Tablets should not be used during an acute asthma attack.

Maxiclear® Day and Night + Cough Film Coated Tablets are contraindicated for use in:

- children under 12 years of age
- lactating women

4.4 Special warnings and precautions for use

Maxiclear® Day and Night + Cough Film Coated Tablets should be used with caution in patients with:

- impaired renal function
- hypertension
- hyperthyroidism
- diabetes mellitus
- coronary heart disease
- ischaemic heart disease

- glaucoma
- prostatic hypertrophy
- epilepsy
- history of asthma

Maxiclear® Day and Night + Cough Film Coated Tablets should not be used for chronic persistent cough accompanying a disease state, or cough associated with excessive secretions

Maxiclear® Day and Night + Cough Film Coated Tablets should not be given to patients with or at risk of developing respiratory failure, e.g. asthma, chronic obstructive airways disease, and pneumonia.

The chlorphenamine component 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.

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 the underlying cause of HAGMA in patients with multiple risk factors.

Serotonin Syndrome
Serotonergic effects, including the development of a potentially life-threatening serotonin syndrome, have been reported for dextromethorphan with concomitant administration of serotonergic agents, such as selective serotonin re-uptake inhibitors (SSRls), drugs which impair metabolism of serotonin (including monoamine oxidase inhibitors (MAOls)) and CYP 2D6 inhibitors.

Serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/ or gastrointestinal symptoms. If serotonin syndrome is suspected, treatment with Maxiclear® Day and Night + Cough Film Coated Tablets should be discontinued.

Patients should stop use and ask a doctor if cough lasts for more than few days, comes back, or is accompanied by fever, rash or persistent headache. These could be signs of a serious condition.

This product should not be taken with another cough and cold medicine unless directed by a doctor.

Patients should not exceed the recommended dosage.

Cases of dextromethorphan abuse and dependence have been reported. Caution is particularly recommended for adolescents and young adults as well as in patients with a history of drug abuse or

psychoactive substances.

This product should be kept out of reach of children. This product should not be taken longer than few days unless directed by a doctor.

Use in children and elderly
Children and the elderly may experience paradoxical excitation with the antihistamine chlorphenamine maleate in Maxiclear® Day and Night + Cough Film Coated Tablets. The elderly are more likely to have central nervous system (CNS) depressive side effects, including confusion.

4.5 Interaction with other medicines and other forms of interaction

- Anticoagulant drugs (warfarin) – dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period of time
- Drugs that induce liver microsomal enzymes (e.g. alcohol, anticonvulsants), and other potentially hepatotoxic drugs, may increase the risk of paracetamol-induced hepatoxicity
- 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.
- Paracetamol excretion may be affected and plasma concentration altered when given with probenecid.
- Colestyramine reduces the absorption of paracetamol if given 1 hour of paracetamol.
- Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) may cause a serious increase in blood pressure or hypertensive crisis, hyperpyrexia, convulsion and may prolong and intensify the anticholinergic and CNS depressive effects.
- 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 phenylephrine.

- Urinary alkalinisers decrease elimination of phenylephrine.

- Central nervous system (CNS) depressants (alcohol, sedatives, opioid analgesics, hypnotics) may cause an increase in CNS depressant effects.

- Selective Serotonin Reuptake Inhibitors (SSRIs) or tricyclic antidepressants may result in a "serotonin syndrome" with changes in mental status, hypertension, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering and tremor. Tricyclic antidepressants may also prolong and intensify the anticholinergic and CNS depressive effects.

- Serum levels of dextromethorphan may be increased by the concomitant use of inhibitors of cytochrome P450 2D6, such as antiarrhythmics quinidine and amiodarone, antidepressants such as fluoxetine and paroxetine, or other drugs which inhibit cytochrome P450 2D6 such as haloperidol and thioridazine.

- Chlorphenamine when taken concomitantly with phenytoin may cause a decrease in phenytoin elimination

Maxiclear® Day and Night + Cough Film Coated Tablets are contraindicated for use in patients taking medications for depression, psychiatric, or emotional conditions, or Parkinson's disease, or for 2 weeks after stopping the medication.

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).

4.6 Fertility, pregnancy and lactation

Pregnancy
Category: B2

The active ingredients in Maxiclear® Day and Night + Cough Film Coated Tablets have 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 fetus having been observed.

Studies in animals are inadequate or maybe lacking, but available data show no evidence of an increased occurrence of fetal damage for the active ingredient phenylephrine.

Maxiclear® Day and Night + Cough Film Coated Tablets should be used in pregnancy only if the potential benefits to the patient are weighed against the possible risk to the fetus.

Breast-feeding
Maxiclear® Day and Night + Cough Film Coated Tablets are contraindicated for use in women who are breastfeeding.

Chlorphenamine maleate is excreted in breast milk.

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.

Since it is not known whether phenylephrine is distributed in milk, the drug should be used with caution in nursing women.

It is not known whether dextromethorphan is excreted in breast milk or whether it has a harmful effect on the breastfeeding infant.

It is recommended to consult a healthcare professional before using Maxiclear® Day and Night + Cough Film Coated Tablets if pregnant, trying to become pregnant or breastfeeding.

Fertility
No data available

4.7 Effects on ability to drive and use machines

Chlorphenamine may cause drowsiness or sedation. Be cautious about driving a vehicle or operating machinery within 8 hours of taking this medicine. If still affected do not drive a vehicle or operate machinery. Avoid alcohol.

Risk of impairment is increased when dextromethorphan is taken concurrently with alcohol or medicines that can impair reaction times.

4.8 Undesirable effects

The following adverse reactions may be associated with the use of paracetamol/ phenylephrine/ dextromethorphan/ chlorphenamine containing products:

Cardiac disorders
Palpitations, tachycardia or arrhythmias, bradycardia, extrasystoles.

Gastrointestinal disorders
Nausea, vomiting, stomach discomfort or constipation, diarrhoea, dry mouth.

General disorders and administration site conditions
Fatigue, malaise.

Eye disorder
Vision blurred, dryness of eyes, visual disturbance.

Immune system disorders
Hypersensitivity, anaphylactic shock.

Nervous system disorders
Dizziness, mild drowsiness, fatigue, dystonias, headache, psychomotor hyperactivity, anxiety, tremors, (rarely) hallucinations, sedation, somnolence, appetite stimulation, muscle dyskinesias and activation of epileptogenic foci. 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 in the morning after a night-time dose.

Renal and urinary disorders
Urinary hesitance and retention, dysuria.

Psychiatric disorders
Agitation, anxiety, excitability, insomnia, irritability, nervousness, restlessness, confusional state, euphoric mood.

Skin and subcutaneous tissue disorders
Rash, urticaria, drug eruption, photosensitivity reaction.

Very rare cases of serious skin reactions (including severe cutaneous reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and acute generalised exanthematous pustulosis) have been reported.

Vascular disorders
Hypertension, increased blood pressure.

Blood and lymphatic system
Agranulocytosis, haemolytic anaemia, hypoplastic anaemia, thrombocytopenia, haematological reactions.

Respiratory, thoracic and mediastinal disorders
Dry throat, nasal dryness

High anion gap metabolic acidosis with frequency "Not known"
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).

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

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

Symptoms which may be associated with high doses (overdosage) of paracetamol/ phenylephrine/ dextromethorphan/ chlorphenamine:

Cardiac disorders
Bradycardia, palpitation, tachycardia.

Gastrointestinal disorders
Nausea, vomiting, dry mouth, abdominal discomfort.

Nervous system disorders
Convulsion, dizziness, tremor, depressed level of consciousness, dysarthria, nystagmus, somnolence, nervousness, insomnia, agitation, irritability, ataxia, coma, lethargy, sedation, myoclonus.

Psychiatric disorders
Agitation, anxiety, insomnia, irritability, nervousness, restlessness, excitability, confusional state, psychotic disorder, serotonin syndrome, delirium, hallucination.

Vascular disorders
Hypertension, increased blood pressure, circulatory collapse, flushing, hypotension, pallor.

Respiratory, thoracic and mediastinal disorders
Respiratory depression, apnoea, dyspnoea, dry throat, nasal dryness, respiratory arrest, respiratory failure.

Eye disorders
Vision blurred

General disorders and administration site conditions
Fatigue, hyperpyrexia, hyperthermia

Investigations
Heart rate abnormal

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

Dextromethorphan overdose may be associated with nausea, vomiting, dystonia, agitation, confusion, somnolence, stupor, nystagmus, cardiotoxicity (tachycardia, abnormal ECG including QTc prolongation), ataxia, toxic psychosis with visual hallucinations, hyperexcitability. In the event of massive overdose the following symptoms may be observed: coma, respiratory depression, convulsions.

Management
Activated charcoal can be administered to asymptomatic patients who have ingested overdoses of dextromethorphan within the preceding hour. For patients who have ingested dextromethorphan and are sedated or comatose, naloxone, in the usual doses for treatment of opioid overdose, can be considered. Benzodiazepines for seizures and benzodiazepines and external cooling measures for hyperthermia from serotonin syndrome can be used.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

Phenylephrine has direct sympathomimetic activity and is an effective decongestant in the upper respiratory tract. It elicits a response in the effector tissue by directly stimulating alpha adrenergic adrenoreceptors.

Sympathomimetic agents are used as nasal decongestants to provide symptomatic relief. They act by causing vasoconstriction resulting in redistribution of local blood flow, which reduces oedema of the nasal mucosa, thus improving ventilation, drainage and nasal stuffiness.

Dextromethorphan is a non-opioid cough suppressant. It is 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 histamine1-receptor sites, preventing the histamine-receptor interaction and subsequent mediator release.

Chlorphenamine maleate is a highly lipophilic molecule that readily crosses the blood-brain barrier. Chlorphenamine maleate is highly selective for histamine1-receptors but has little effect on histamine2 or histamine3 receptors. Chlorphenamine maleate also activates 5-hydroxytryptamine (serotonin) and

α-adrenergic receptors and blocks cholinergic receptors.

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. Paracetamol crosses the placenta and is present in breast milk. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing doses. The elimination half-life of paracetamol varies from about 1 to 3 hours.

Paracetamol is metabolised predominantly in the liver and excreted in the urine mainly as the inactive glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. 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.

Phenylephrine is a synthetic sympathomimetic amine, which acts directly on alpha adrenergic receptors. It has a low oral bioavailability owing to irregular absorption and first-pass metabolism in the GI tract and liver by the enzyme monoamine oxidase (MAO). Following oral administration nasal decongestion may occur within 15 or 20 minutes and may persist for 2-4 hours. The half-life of phenylephrine is 2-3 hours.

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.

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, with peak plasma concentrations occurring about 2.5 to 6 hours after oral administration. Chlorphenamine appears to undergo considerable first-pass metabolism. Bioavailability is low, values of 25 to 50% having been reported. About 70% of chlorphenamine in the circulation is bound to plasma proteins. There is wide inter-individual variation in the pharmacokinetics of chlorphenamine; half-life values ranging from 2 to 43 hours have been reported. Chlorphenamine is widely distributed in the body and enters the CNS.

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

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose, Povidone, Maize starch, Colloidal anhydrous silica, Pregelatinised maize starch, Sodium starch glycollate, Purified talc, Magnesium stearate, Hypromellose, Macrogol 6000, Titanium Dioxide, Colour Iron oxide red, Colour Indigo Carmine lake.

6.2 Incompatibilities

Not available.

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 containing:

- 16 film coated tablets (12 day tablets and 4 night tablets)
- 24 film coated tablets (18 day tablets and 6 night tablets)
- 32 film coated tablets (24 day tablets and 8 night tablets)
- 40 film coated tablets (30 day tablets and 10 night tablets)
- 48 film coated tablets (36 day table and 12 night tablets)
- 64 film coated tablets (48 day tablets and 16 night tablets)

6.6 Special precautions for disposal

Return unused and expired medicines to your local pharmacy for disposal.

7. MEDICINE SCHEDULE

Restricted medicine.

8. SPONSOR

AFT Pharmaceuticals Limited
PO Box 33-203
Takapuna
Auckland 0740
Phone: 0800 423 823

9. DATE OF FIRST APPROVAL

08/05/2025

10. DATE OF REVISION OF THE TEXT

01/08/2025

Summary table of changes

Section changed	Summary of new information
4.4, 4.5 and 4.8	Safety warnings on high anion gap metabolic acidosis have been added.