DIMETAPP COUGH COLD & FLU DECONGESTANT DAY & NIGHT

1 PRODUCT NAME

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Filled Capsule

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Day Liquid Capsule Contains:
Paracetamol 300 mg, Dextromethorphan hydrobromide monohydrate 10 mg, Phenylephrine hydrochloride 5 mg

Each Night Liquid Capsule Contains:
Paracetamol 300 mg, Dextromethorphan hydrobromide monohydrate 10 mg, Phenylephrine hydrochloride 5 mg, Chlorphenamine maleate 2 mg

Excipient(s) with known effect:
- Sorbitol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Liquid filled capsule

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The daytime capsules provide temporary relief from the symptoms of the common cold and flu such as nasal congestion, headaches, muscular aches, fever, body aches and pains, sore throat, stuffy, runny noses and dry irritating coughs.

The night time capsule also provides temporary relief from the major symptoms of cold and flu and also contain an antihistamine to relieve runny nose, sneezing, itching of the nose and throat, itchy watery eyes due to cold and flu symptoms, and therefore allows a good night's sleep.

4.2 Dose and method of administration

Adults and children 12 years and over:

Day: Two (2) orange capsules should be taken orally with water, every 4-6 hours (Morning, midday & afternoon) as necessary.

Night: Two (2) green capsules should be taken orally with water at bedtime as necessary.

Allow 4- 6 hours between each dose.

Do not exceed 6 orange day liquid capsules and 2 green night liquid capsules in 24 hours.

Adults should not take this product for more than a few days at a time except on medical advice.

Children and adolescents 12 years and over should not use this product for more than 48 hours, except on medical advice.

Do not use in children under 12 years.

4.3 Contraindications

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps 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
- taking other antihistamines

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps should not be used during an acute asthma attack.

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps are contraindicated for use in:

- children under 12 years of age
- lactating women

4.4 Special warnings and precautions for use

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps 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

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps should not be used for chronic persistent cough accompanying a disease state, or cough associated with excessive secretions

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps 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 in the night time capsule 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.

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 (SSRIs), drugs which impair metabolism of serotonin (including monoamine oxidase inhibitors (MAOIs)) 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 Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps 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 Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps. 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.

  Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps 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.

  Refer to section 4.3 for additional information.

- 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

4.6 Fertility, pregnancy and lactation

Pregnancy
Category B2:

The active ingredients in Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps 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.

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps should be used in pregnancy only if the potential benefits to the patient are weighed against the possible risk to the fetus.

Breast-feeding
Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps are contraindicated for use by 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 Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps if pregnant, trying to become pregnant or breastfeeding.

Fertility
Not available

4.7 Effects on ability to drive and use machines

NIGHT CAPSULES ONLY: May cause drowsiness or sedation in some people. 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 Generalized 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

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://nzphvc.otago.ac.nz/reporting/

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

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.

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

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 150mg/kg or 10g 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

Not available

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The Day capsule contains Macrogol 400, Povidone, Sodium metabisulfite, Propylene glycol, Gelatin, Sunset yellow FCF, Opacode WB water based Monogramming Ink NSP-78-18022 White, Sorbitol Special-Glycerin blend, and Water – purified.

The Night capsule contains Macrogol 400, Povidone, Sodium metabisulfite, Propylene glycol, Gelatin, Brilliant Blue FCF, Opacode WB water based Monogramming Ink NSP-78-18022 White, Sorbitol Special-Glycerin blend, and Water – purified.

6.2 Incompatibilities

Not available

6.3 Shelf life

2 Years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Dimetapp Cough Cold & Flu Decongestant Day & Night Liquid Caps are clear soft gelatin capsules in blister pack of 24s (contains 1 blister). The product is available in pack sizes of 24 and 48 liquid capsules.

One (1) blister pack contains 18 Orange DAY capsules and 6 green NIGHT capsules.

Day liquid caps: Clear, orange-coloured, oblong, soft gelatin capsules, printed with 'DIMETAPP PE' on one side in white ink.

Night liquid caps: Clear, green-coloured, oblong, soft gelatin capsules, printed with 'DIMETAPP PE' on one side in white ink.

6.6 Special precautions for disposal

Not available

7 MEDICINE SCHEDULE

Restricted Medicine

8 SPONSOR

Pfizer New Zealand Limited
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AUCKLAND 1140
New Zealand
☎Toll Free 0800 447 400
Web: www.dimetapp.co.nz

9 DATE OF FIRST APPROVAL

24 May 2012

10 DATE OF REVISION OF THE TEXT

21 May 2020

SUMMARY TABLE OF CHANGES

Section changed	Summary of changes
All	New data sheet in SmPC format