DIMETAPP COUGH COLD & FLU DAYTIME/NIGHTIME

1 PRODUCT NAME

Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Filled Capsule

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Day Liquid Filled Capsule Contains:
Paracetamol 300 mg, Dextromethorphan hydrobromide monohydrate 10 mg

Each Night Liquid Filled Capsule Contains:
Paracetamol 300 mg, Dextromethorphan hydrobromide monohydrate 10 mg, Doxylamine succinate 6.25 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 and nightime capsule in Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps provide relief from the symptoms of colds and flu including headaches, body aches and pains, sore throat and dry irritating coughs. Reduces fever. The nightime capsules also provide relief from runny nose, sneezing and itchy, watery eyes.

4.2 Dose and method of administration

Adults and children 12 years and over:

Daytime – Take 2 orange capsules with water every 4-6 hours (Morning, midday and afternoon) as necessary.

Nightime – Take 2 blue capsules with water at bedtime as necessary.

Allow 4-6 hours between the Daytime and Nightime dose.

Do not exceed 6 orange daytime capsules and 2 blue nightime capsules in 24 hours.

Adults should not take this product for more than a few days at a time except on medical advice. Children should not use for more than 48 hours, except on medical advice.

Do not use in children under 12 years.

4.3 Contraindications

Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps are contraindicated for use in patients:

- with known hypersensitivity to the active ingredients paracetamol, dextromethorphan hydrobromide monohydrate or doxylamine succinate 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 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 Daytime/Nightime Liquid Caps should not be used during an acute asthma attack.

Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps are contraindicated for use in lactating women.

Do not use in children under 12 years.

4.4 Special warnings and precautions for use

Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps should be used with caution in patients with:

- impaired renal function
- epilepsy
- history of asthma

Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps should not be used for chronic persistent cough accompanying a disease state, or for cough associated with excessive secretions.

Dimetapp Cough Cold & Flu Daytime/Nightime 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.

This product 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 Daytime/Nightime 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 medicines 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.

Use in children and elderly
Children and the elderly may experience paradoxical excitation with the antihistamine doxylamine succinate in Dimetapp Cough Cold & Flu Daytime/Nightime 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

- 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 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 within1 hour of paracetamol

- Monoamine oxidase inhibitors (MAOIs), may increase the risk of serious side effects such as hypertensive crisis, hyperpyrexia and convulsions. Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) may prolong and intensify the anticholinergic and CNS depressive effects.

  Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps are contraindicated for use in patients taking medications for depression, psychiatric, or emotional conditions, or for Parkinson's disease, or for 2 weeks after stopping the medication.

  Refer to section 4.3 for additional information.

- CNS depressants (including alcohol, sedatives, narcotic analgesics, hypnotics and tranquillizers) may increase the CNS depressant or sedation 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

4.6 Fertility, pregnancy and lactation

Pregnancy

Category A: The active ingredients in Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps have been taken by a large number of pregnant women and women of child bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Breast-feeding

The active ingredients in Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps are excreted in breastmilk. Therefore, Dimetapp Cough Cold & Flu Daytime/Nightime Liquid Caps are not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

It is recommended to consult a healthcare professional before using Dimetapp Cough Cold & Flu Daytime/Nightime 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. 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/ dextromethorphan/ doxylamine containing products:

Immune system disorders
hypersensitivity, skin rashes

Gastrointestinal disturbances
nausea or vomiting, stomach discomfort or constipation

Central nervous system
mild drowsiness, fatigue, dystonias, dizziness, anxiety, hallucinations, appetite stimulation, muscle dyskinesias and activation of epileptogenic foci. 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 in the morning after a night-time dose.

Anticholinergic effects
dryness of the eyes, mouth and nose, blurred vision, urinary hesitancy and retention, constipation and tachycardia

Blood and lymphatic system
haematological reactions

Skin and subcutaneous tissue disorders
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.

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/dextromethorphan/doxylamine:

Gastrointestinal disorders
Nausea, vomiting

Nervous system disorders
Depressed level of consciousness, dizziness, dysarthria, nystagmus, somnolence, nervousness, tremor, insomnia, agitation irritability, CNS depression, myoclonus

Psychiatric disorders
Excitability, confusional state, psychotic disorder, serotonin syndrome, restlessness

Respiratory, thoracic and mediastinal disorders
Respiratory depression

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.

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.

Doxylamine succinate competes with histamine at central and peripheral histamine1-receptor sites, preventing the histamine-receptor interaction and subsequent mediator release.

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

Doxylamine succinate is highly selective for histamine1-receptors but has little effect on histamine2 or histamine3 receptors. Doxylamine succinate also activate 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 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.

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.

Doxylamine succinate is readily absorbed from the gastrointestinal tract. Following oral administration, the mean peak plasma concentration occurs after 2-3 hours. It has an elimination half-life of about 10 hours in healthy adults. It is excreted in the urine as unchanged doxylamine (60%) and metabolites (nordoxylamine and dinordoxylamine).

The major metabolic site is the liver and major metabolic pathways are N-demethylation, N-oxidation, hydroxylation, N-acetylation, N-desalkylation and ether cleavage.

5.3 Preclinical safety data

Not available

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The Day capsule contains Macrogol 400, propylene glycol, povidone, gelatin, glycerol, sorbitol, sunset yellow FCF CI15985, water – purified and opacode monogramming ink NSP-78-18022 white.

The Night capsule contains Macrogol 400, propylene glycol, povidone, gelatin, glycerol, sorbitol, brilliant blue FCF CI42090, water – purified and opacode monogramming ink NSP-78-18022 white.

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 Daytime/Nightime Liquid Caps are soft gelatin capsules in blister packs of 8s (not marketed), 24s (marketed; contains 1 blister) and 48s (marketed; contains 2 blister packs).

One (1) blister pack contains 18 Orange DAYTIME capsules and 6 blue NIGHTIME capsules.

Daytime caps: Shiny, clear, orange-coloured, oblong, soft capsules, printed with 'DIMETAPP' on one side in white ink.

Nightime caps: Shiny, clear, blue-coloured, oblong, soft capsules, printed with 'DIMETAPP' 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
P O Box 3998
AUCKLAND 1140
New Zealand
☎Toll Free 0800 447 400
Web: www.dimetapp.co.nz

9 DATE OF FIRST APPROVAL

23 July 2009

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