1 PRODUCT NAME

Dimetapp Multi Symptom Cough Cold & Flu Liquid Filled Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each liquid filled capsule contains:
Paracetamol 300 mg, Dextromethorphan hydrobromide monohydrate 10 mg, Phenylephrine hydrochloride 5 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

For 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.

4.2 Dose and method of administration

Adults and children 12 years and over:

Two (2) capsules should be taken orally with water, every 4-6 hours as necessary.

Allow 4 - 6 hours between each dose.

Do not exceed 8 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 Multi Symptom Cough Cold & Flu Liquid Caps are contraindicated for use in patients:

- with known hypersensitivity to the active ingredients paracetamol, phenylephrine hydrochloride, or dextromethorphan hydrobromide monohydrate 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 impaired hepatic function
- with respiratory insufficiency and respiratory depression

Dimetapp Multi Symptom Cough Cold & Flu Liquid Caps should not be used during an acute asthma attack.

Dimetapp Multi Symptom Cough Cold & Flu Liquid Caps are contraindicated for use in children under 12 years of age.

4.4 Special warnings and precautions for use

Dimetapp Multi Symptom Cough Cold & Flu 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
- history of asthma

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

Dimetapp Multi Symptom Cough Cold & Flu 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.

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.
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.

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
Refer to section 4.2 Dose and method of administration, section 4.3 contraindications, section 4.8 Undesirable effects, and section 5.2 Pharmacokinetic properties.

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 hepatotoxicity
- 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 Multi Symptom Cough Cold & Flu 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 Contraindications” 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.

4.6 Fertility, pregnancy and lactation

Pregnancy
Category B2: The active ingredients in Dimetapp Multi Symptom Cough Cold & Flu 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 Multi Symptom Cough Cold & Flu 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 Multi Symptom Cough Cold & Flu Liquid Caps are not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

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 Multi Symptom Cough Cold & Flu Liquid Caps if pregnant, trying to become pregnant or breastfeeding.

**Fertility**

Not available

4.7 **Effects on ability to drive and use machines**

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 containing products:

**Cardiac disorders**

Palpitations, tachycardia or arrhythmias

**Gastrointestinal disorders**

Nausea, vomiting, stomach discomfort or constipation

**Immune system disorders**

Hypersensitivity

**Nervous system disorders**

Dizziness, mild drowsiness, fatigue, dystonias, headache, psychomotor hyperactivity, anxiety, tremors, (rarely) hallucinations

**Renal and urinary disorders**

Urinary retention

**Psychiatric disorders**

Agitation, anxiety, excitability, insomnia, irritability, nervousness, restlessness

**Skin and subcutaneous tissue disorders**

Rash, urticaria

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**
Haematological reactions

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:

**Cardiac disorders**
Bradycardia, palpitation, tachycardia

**Gastrointestinal disorders**
Nausea, vomiting

**Nervous system disorders**
Convulsion, dizziness, tremor, depressed level of consciousness, dysarthria, nystagmus, somnolence, myoclonus

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

**Vascular disorders**
Hypertension, increased blood pressure

**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.

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.

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 overdose (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.

5.3 Preclinical safety data

Not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin, Macrogol 400, Opacode white NSP-78-18022, Plasticizer A-810, Povidone, Propylene glycol, Purified water, Sodium metabisulfite, Sunset yellow FCF.

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 Multi Symptom Cough Cold & Flu Liquid Caps are shiny, orange-coloured, clear, oblong, soft gelatin capsules, printed with ‘DIMETAPP PE’ on one side in white ink in blister packs of 24s (marketed) and 48s (not marketed).

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

19 July 2012

10 DATE OF REVISION OF THE TEXT

21 May 2020

SUMMARY TABLE OF CHANGES

<table>
<thead>
<tr>
<th>Section changed</th>
<th>Section changed:</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>New data sheet in SmPC format</td>
</tr>
</tbody>
</table>