NEW ZEALAND DATA SHEET

DIMETAPP COUGH & COLD COLOUR FREE

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1 PRODUCT NAME

Dimetapp Cough & Cold Colour Free Elixir

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL of oral liquid contains:
Brompheniramine maleate 2 mg, Phenylephrine hydrochloride 5 mg, Dextromethorphan hydrobromide monohydrate 10 mg.

Excipient(s) with known effect:
- Sodium benzoate
- Sorbitol
- Ethanol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Elixir

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dimetapp Cough & Cold Colour Free temporarily suppresses dry coughs and relieves common cold symptoms like nasal congestion, runny nose, sneezing and itchy, watery eyes.

4.2 Dose and method of administration

Children 6 to under 12 years:	5 mL Every 4 hours, as necessary
Adults and children 12 years and over:	10 mL Every 4 hours, as necessary

Do not exceed 6 doses in any 24 hour period.

Do not use in children under 6 years of age.

Use in children aged 6 to 11 years only on the advice of a doctor, pharmacist or nurse practitioner.

4.3 Contraindications

Dimetapp Cough & Cold Colour Free is contraindicated for use in patients:

- With known hypersensitivity to the active ingredients, brompheniramine maleate, phenylephrine hydrochloride and Dextromethorphan hydrobromide monohydrate 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 Parkinson's disease, or for 2 weeks after stopping the medication. If you are unsure if your prescription medication contains any of these drugs, ask a doctor or pharmacist before taking this product.
- 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 Colour Free is also contraindicated for use in:

- children under 6 years of age
- lactating women

4.4 Special warnings and precautions for use

Dimetapp Cough & Cold Colour Free should be used with caution in patients with:

- impaired renal function
- epilepsy
- cardiovascular disease (including ischaemic heart disease, hypertension, bradycardia, tachycardia, arteriosclerosis, and coronary artery disease)
- thyroid disease
- diabetes mellitus
- glaucoma
- prostatic hypertrophy

Dimetapp Cough & Cold Colour Free should not be used in chronic persistent cough accompanying a disease state, or cough associated with excessive secretions.

Dimetapp Cough & Cold Colour Free 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.

This product may cause drowsiness or sedation 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 Colour Free 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. 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 brompheniramine maleate in Dimetapp Cough & Cold Colour Free. The elderly are more likely to have central nervous system (CNS) depressive side effects, including confusion.

Serious adverse events may occur in children in case of overdose including neurological disorders. Caregivers should be advised not to exceed the recommended dose.

4.5 Interaction with other medicines and other forms of interaction

The following interactions with brompheniramine maleate, phenylephrine hydrochloride and Dextromethorphan hydrobromide monohydrate have been noted:

- Antidepressant medication e.g. tricyclic antidepressants – may cause a serious increase in blood pressure or hypertensive crisis, intensify anticholinergic effect
- Do not use if you are now taking a prescription monoamine oxidase inhibitor (MAOI), a selective serotonin reuptake inhibitor (SSRI), or other medications for depression, psychiatric, or emotional conditions, or Parkinson's disease, or for 2 weeks after stopping the medication. If you are not sure if your prescription medication contains one of these drugs, ask a doctor or pharmacist before taking this product – may cause

a serious increase in blood pressure or hypertensive crisis, hyperpyrexia and convulsion
- Other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psycho stimulants – may cause an increase in blood pressure and additive effects
- Use with certain antihypertensive agents may diminish their antihypertensive effect
- Central nervous system (CNS) depressants (alcohol, sedatives, opioid analgesics, hypnotics) – may cause an increase in 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 B2:

The active ingredients in Dimetapp Cough & Cold Colour Free 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.

Breast-feeding
Dimetapp Cough & Cold Colour Free is 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 Colour Free if pregnant, trying to become pregnant or breastfeeding.

Fertility
Not Available.

4.7 Effects on ability to drive and use machines

Brompheniramine 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 brompheniramine maleate/phenylephrine hydrochloride/dextromethorphan containing products:

Eye Disorders
Vision blurred, visual disturbance, dry eyes

Gastrointestinal disorders
Constipation, diarrhoea, dry mouth, nausea, vomiting

General disorders and administration site conditions
Fatigue, malaise

Immune system disorders
Anaphylactic shock, hypersensitivity

Nervous system disorders
Coordination abnormal, dizziness, headache, sedation, somnolence, psychomotor hyperactivity, anxiety, hallucinations, 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.

Psychiatric disorders
Confusional state, euphoric mood, excitability, irritability, nervousness, restlessness, insomnia, tremors

Renal and Urinary disorders
Dysuria, urinary retention, urinary hesitancy

Respiratory, thoracic and mediastinal disorders
Dry throat, nasal dryness or dry nose

Blood and lymphatic system
Agranulocytosis, haemolytic anemia, hypoplastic anemia, thrombocytopenia

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

Vascular disorders
Increased blood pressure, hypertension

Cardiac disorders

Palpitations, tachycardia, bradycardia, extrasystoles

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 brompheniramine maleate/phenylephrine hydrochloride/Dextromethorphan hydrobromide monohydrate:

Eye disorders
Vision blurred

Gastrointestinal disorders
Dry mouth, abdominal discomfort, nausea, vomiting

General Disorders and Administration Site Conditions
Fatigue, hyperpyrexia, hyperthermia

Investigations
Heart rate abnormal

Nervous System disorders
Ataxia, depressed level of consciousness, coma, convulsion, dizziness, tremor, somnolence, lethargy, sedation, dysarthria, nystagmus, myoclonus

Psychiatric disorders
Anxiety, agitation, delirium, excitability, hallucination, insomnia, nervousness, irritability, restlessness, psychiatric disorder, confusional state, serotonin syndrome

Respiratory, thoracic and mediastinal disorders
Apnea, dyspnea, dry throat, nasal dryness, respiratory arrest, respiratory failure, respiratory depression

Vascular disorder
Circulatory collapse, flushing, hypotension, pallor, increased blood pressure, hypertension

Cardiac disorder
Bradycardia, palpitations, tachycardia

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Brompheniramine maleate is an antihistamine which is structurally similar to histamine. It is an alkylamine with a propylamine side chain.

Brompheniramine competes with histamine at histamine receptor sites. By occupying the histamine receptor sites, it prevents histamine from activating the site. Brompheniramine is an H-1 histamine receptor inhibitor, acting on the H-1 histamine receptors to block histamine-induced vascular responses. It has no effect on histamine-induced gastric secretion (H-2 histamine receptor).

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 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.

5.2 Pharmacokinetic properties

Brompheniramine maleate appears to be well absorbed from the gastrointestinal tract after oral doses. Peak plasma concentrations are achieved within about 5 hours. An elimination half-life of about 25 hours has been reported. Unchanged drug and metabolites are excreted primarily in the urine.

Phenylephrine has low oral bioavailability owing to irregular absorption and first-pass

metabolism by monoamine oxidase in the gut and liver. The bioavailability of phenylephrine following oral administration is approximately 38% relative to IV administration. Because of extensive first-pass metabolism, there is considerable interindividual and possible intraindividual variation in oral bioavailability of the drug. Following oral administration of phenylephrine (1 or 7.8 mg), peak serum concentrations occur at 0.75 – 2 hours or nasal decongestion may occur within 15 to 20 minutes and may persist for 2 – 4 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

Citric acid – anhydrous, Ethanol, Glycerol, Propylene glycol, Saccharin sodium, Sodium benzoate, Sorbitol solution (70%) crystallising, Water – purified, Artificial grape flavour #5-8994 and Grape flavour artificial 11540.

6.2 Incompatibilities

Not available

6.3 Shelf life

5 Years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Dimetapp Cough & Cold Colour Free is a clear, colourless liquid with grape flavour and odour, packed in bottles.

Marketed pack sizes:	25 mL (Professional sample), 100 mL and 200 mL
Not marketed pack sizes:	45 mL (Professional sample) and 50 mL

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

18 July 2002

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