NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Difflam Dry Cough + Antibacterial + Anti-inflammatory Lozenges

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each lozenge contains dextromethorphan hydrobromide monohydrate 10 mg, cetylpyridinium chloride 1.33 mg and benzydamine hydrochloride 1.5 mg.

Excipients with known effect:
Sucralose and isomalt.

For full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Blackcurrant flavour: A violet coloured, circular, flat surface lozenge with round edges.

Pineapple lime flavour: A light green coloured, circular, flat surface lozenge with round edges.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For fast temporary relief from the symptoms of dry, tickly cough in association with sore throat, tonsillitis, pharyngitis, swelling, redness and inflammatory conditions.

4.2 Dose and method of administration

For buccal use. Slowly dissolve lozenges in the mouth, one at a time. Do not chew or swallow whole.

Age	**Dosage**	**How often**
Adults and children 12 years & over	1-2 lozenges	Every 4 hours as required (maximum 12 lozenges per 24 hours)
Children 6 – 11 years	1 lozenge	Every 4-6 hours as required (maximum 6 lozenges per 24 hours)
Children under 6 years	Do not use	

4.3 Contraindications

DIFFLAM is contraindicated in:

- Children under the age of 6 years
- In the last 3 months of pregnancy
- Hypersensitivity to dextromethorphan hydrobromide, cetylpyridinium chloride, benzydamine hydrochloride, other NSAIDs, salicylic acid or any of the excipients listed in section 6.1 List of excipients
- Patients taking a monoamine oxidase inhibitor (MAOI) or antidepressant medicine who have taken them in the previous two weeks
- Patients taking a selective serotonin re-uptake inhibitor (SSRI), other medications for depression, psychiatric, or emotional conditions, or Parkinson's disease
- Bronchial asthma
- Chronic obstructive pulmonary disease
- Pneumonia
- Respiratory insufficiency
- Respiratory depression
- Breastfeeding.

4.4 Special warnings and precautions for use

Avoid drinking alcoholic beverages while using dextromethorphan. Dextromethorphan potentiates the inhibitory effect of alcohol on the central nervous system.

In cases of productive cough with considerable mucus production (e.g., patients with conditions such as bronchiectasis, cystic fibrosis) or in patients with neurological illness associated with a markedly reduced cough reflex (such as stroke, Parkinson's disease and dementia) antitussive treatment should be administered with particular caution and only after careful benefit-risk assessment (refer to section 4.5 Interaction with other medicines and other forms of interaction).

Dextromethorphan 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.

Dextromethorphan is not recommended in patients suffering from chronic cough as occurs with smoking, asthma or patients suffering from an acute asthma attack, or where cough is accompanied by excessive secretions.

Causes of chronic cough should be excluded if symptoms are persistent. Any accompanying symptoms should be appropriately investigated and treated. Patients should be advised to stop use and seek medical advice if their cough lasts more than 7 days, returns or is accompanied by a fever, rash or persistent headache.

Concomitant use of DIFFLAM with other medicines intended to treat the symptoms of the common cold is not recommended.

DIFFLAM contains isomalt, which may have a laxative effect or cause diarrhoea and patients with rare hereditary problems of fructose intolerance should not take this medicine.

Drug dependence, tolerance and potential for abuse

Prolonged use of dextromethorphan may lead to drug dependence even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse (including alcohol misuse) or mental health disorder (e.g., major depression). Caution is particularly recommended for adolescents and young adults as well as in patients with a history of drug abuse or psychoactive substances.

Drug withdrawal syndrome

Drug withdrawal syndrome may occur following prolonged use of dextromethorphan. The drug withdrawal syndrome is characterised by some or all of the following: Restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

Metabolism by CYP2D6 substrates

Dextromethorphan is metabolised by hepatic cytochrome P450 2D6 (CYP2D6). The activity of this enzyme is genetically determined. About 10% of the general population are poor metabolisers of CYP2D6. Poor metabolisers and patients with concomitant use of CYP2D6 inhibitors may experience exaggerated and/or prolonged effects of dextromethorphan. Caution should therefore be exercised in patients who are slow metabolisers of CYP2D6 or use CYP2D6 inhibitors (see also section 4.5 Interaction with other medicines and other forms of interaction).

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 CYP2D6 inhibitors.

Serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. If serotonin syndrome is suspected, treatment with DIFFLAM should be discontinued.

4.5 Interaction with other medicines and other forms of interaction

Dextromethorphan possesses weak serotonergic properties. Thereby dextromethorphan may increase the risk of serotonin toxicity (serotonin syndrome) particularly if taken with other serotonergic agents, such as MAOIs, SSRIs and CYP2D6 inhibitors. Especially pre-treatment or concomitant treatment with medicines that impair metabolism of serotonin, such as antidepressants of the MAO inhibitor type, may result in the development of a serotonin syndrome.

Dextromethorphan should not be used in patients taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days. The use of dextromethorphan with, or within two weeks of taking MAOIs, may increase the risk of serious side effects such as hypertensive crisis, hyperpyrexia and convulsions (see Section 4.3 Contraindications).

Dextromethorphan when used with SSRI's (such as fluoxetine) or tricyclic antidepressants (such as clomipramine and imipramine) may result in a "serotonin syndrome" with changes in mental status (e.g. agitation, excitement, confusion), hypertension, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering and tremor.

Concomitant use of dextromethorphan and other CNS depressants (e.g. alcohol, narcotic analgesics and tranquillizers) may increase the CNS depressant effects of these drugs.

If dextromethorphan is used in combination with secretolytics in patients with pre-existing chest disease such as cystic fibrosis and bronchiectasis who are affected by mucus hypersecretion reduced cough reflex can lead to serious accumulation of mucus.

CYP2D6 inhibitors

Dextromethorphan is metabolised by CYP2D6 and has an extensive first-pass metabolism. Concomitant use of potent CYP2D6 enzyme inhibitors can increase the dextromethorphan concentrations in the body to levels multi-fold higher than normal. This increases the patient's risk for toxic effects of dextromethorphan (agitation, confusion, tremor, insomnia, diarrhoea and respiratory depression) and development of serotonin syndrome. Potent CYP2D6 enzyme inhibitors include fluoxetine, paroxetine, quinidine and terbinafine.

In concomitant use with quinidine, plasma concentrations of dextromethorphan have increased up to 20-fold, which has increased the CNS adverse effects of the agent. Amiodarone, flecainide and propafenone, sertraline, bupropion, methadone, cinacalcet, haloperidol, perphenazine and thioridazine also have similar effects on the metabolism of dextromethorphan.

If concomitant use of CYP2D6 inhibitors and dextromethorphan is necessary, the patient should be monitored, and the dextromethorphan dose may need to be reduced.

Alcohol

Drinking alcoholic beverages whilst using dextromethorphan is not recommended. Taking DIFFLAM with medicines containing e.g. propylene glycol or ethanol may lead to accumulation of ethanol and induce adverse effects, particularly in young children with low or immature metabolic capacity.

4.6 Fertility, pregnancy and lactation

Category: B2

Fertility

Based on available non-clinical experience and observations in humans there are no reported harmful effects of the use of dextromethorphan on reproduction or foetal development.

Pregnancy

If the patient is trying to become pregnant or is during the first 6 months of pregnancy DIFFLAM is not recommend. DIFFLAM is contraindicated in the last 3 months of pregnancy.

Although dextromethorphan has been in widespread use for many years without apparent ill-consequence, there are no specific data on its use during pregnancy.

Breast-feeding/ Lactation

There is insufficient information on the excretion of benzydamine in human milk. It is not known whether dextromethorphan or its metabolites are excreted in human milk. Therefore, Difflam is not recommended for use in nursing mothers.

4.7 Effects on ability to drive and use machines

Dextromethorphan may cause mild drowsiness and can impair cognitive function that may affect a patient's ability to drive safely or operate machinery. Patients are therefore advised to exercise caution before driving or use of machinery until they know DIFFLAM does not adversely affect their performance.

4.8 Undesirable effects

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The following rate values have been used: Very common (≥ 1/10), Common (≥ 1/100 to <1/10), Uncommon (≥1/1,000 to<1/100), Rare (≥1/10,000 to <1/1,000) and Very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Undesirable Effect**
Gastrointestinal Disorders	Common	Nausea, Vomiting, Constipation
	Rare	Gastrointestinal upset, Burning mouth, Dry mouth
	Not known	Hypoaesthesia oral
Nervous System Disorders	Very common	Somnolence, Dizziness
	Rare	Dizziness, drowsiness, mental confusion
	Not known	Vertigo, Slurred speech and Nystagmus, Dystonia especially in children
Immune System Disorders	Not known	Hypersensitivity, Urticaria, Fixed drug eruption, Anaphylactic reaction, Angioedema, Bronchospasm
Psychiatric Disorders	Common	Confusion
	Very rare	Drug dependence (see section 4.4 Special warnings and precautions for use)
	Not known	Hallucinations
Respiratory, Thoracic & Mediastinal Disorders	Very rare	Laryngospasm
General Disorders and Administration Site Conditions	Common	Fatigue
	Not known	Drug withdrawal syndrome (see section 4.4 Special warnings and precautions for use)
Skin and Subcutaneous Tissue Disorders	Uncommon	Photosensitivity
	Very rare	Angioedema
	Not known	Skin reactions such as rash with pruritis

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

Signs and Symptoms

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.

Restlessness and excitability may develop into agitation with increasing overdose. In addition, symptoms such as psychotic disorders like disorientation and delusions up to confusional or paranoid states, changes in blood pressure, impaired concentration and consciousness up to coma as a sign of severe intoxication, slurred speech, changes in mood such as dysphoria and euphoria, dysarthria, increased muscle tone, vision disturbance, convulsions, as well as respiratory depression, and light-headedness may occur.

Dextromethorphan may increase the risk of serotonin syndrome, and this risk is increased by overdose, particularly if taken with other serotonergic agents.

Cases of fatal outcomes have been reported with combination overdose with dextromethorphan and other drugs (combination poisoning)

Benzydamine
No overdosage with the lozenge formulation has been reported. However, very rarely in children excitation, convulsions, sweating, ataxia, tremor and vomiting have been reported after the oral administration of benzydamine dosages about 100 times higher than those of the lozenge.

Cetylpyridinium chloride
May cause corrosive damage to the gastrointestinal tract, leading to pain, nausea, vomiting and diarrhoea. Signs of toxicity may also include euphoria, slurred speech, muscular incoordination, impairment of consciousness and coma.

Management

The mainstay of treatment is supportive and symptomatic care. Adequate hydration must be maintained. If necessary, close intensive care monitoring with symptom-related treatment should be initiated.

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 children who have ingested cetylpyridinium chloride, overdosage could lead to hypoglycaemia which should be treated with either oral or intravenous glucose.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dextromethorphan: A non-opioid cough suppressant which has a central action on the cough centre in the medulla. It has no analgesic properties and little sedative activity. The onset of antitussive effect occurs within an hour and the duration of action is approximately 3 – 6 hours.

Benzydamine: Clinical studies demonstrate that benzydamine is effective in relieving suffering from localised irritation processes of the mouth and pharynx. In addition, benzydamine possesses a moderate local anaesthetic effect.

Cetylpyridinium chloride: A cationic antiseptic with activity against both gram-positive and gram-negative organisms.

Pharmacotherapeutic group: Cough suppressant
ATC code: R05DA09

5.2 Pharmacokinetic properties

Dextromethorphan

Dextromethorphan is well absorbed from the gastrointestinal tract.

It undergoes rapid and extensive first-pass metabolism in the liver after oral administration. Genetically controlled O-demethylation (CYD2D6) is the main determinant of dextromethorphan pharmacokinetics in human volunteers. It appears that there are distinct phenotypes for this oxidation process resulting in highly variable pharmacokinetics between subjects. Unmetabolised dextromethorphan, together with the three demethylated morphinan metabolites dextrorphan (also known as 3-hydroxy-N-methylmorphinan), 3- hydroxymorphinan and 3-methoxymorphinan have been identified as conjugated products in the urine. Dextrorphan, which also has antitussive action, is the main metabolite. In some individuals, metabolism proceeds more slowly, and unchanged dextromethorphan predominates in the blood and urine.

It is excreted in the urine as unchanged dextromethorphan and demethylated metabolites, including dextrorphan. 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.

Benzydamine

Oral doses of benzydamine are well absorbed and plasma drug concentrations reach a peak fairly rapidly and then decline with a half-life of approximately 13 hours. Benzydamine is primarily metabolised by oxidation, dealkylation, and conjugation into hydroxy, dealkylated, and N-oxide metabolites. In general, however, when used at the recommended doses the levels at which benzydamine is absorbed or exposed into the body are usually not sufficient to produce systemic pharmacological effects. Excretion occurs mainly in the urine and mostly in the form of inactive metabolites or conjugation products.

Cetylpyridinium chloride

Oral doses are generally poorly absorbed and therefore relatively large amounts of the compound are eliminated in faeces. No readily available data regarding its metabolism is available.

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Blackcurrant flavour:
Beta-cyclodextrin
Sucralose
Citric acid anhydrous
Sodium chloride
Menthol
Isomalt
Patent blue V
Blackcurrant flavour RFF 50207
Carmoisine

Pineapple Lime flavour:
Beta-cyclodextrin
Sucralose
Citric acid anhydrous
Sodium chloride
Menthol
Isomalt
Patent blue V
Pineapple flavour Singapore SN657103
Lime oil RFF 51217
Quinoline yellow

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30°C

6.5 Nature and contents of container

Blackcurrant flavour: Blister pack, PVC/PVDC/Aluminium foil: 16 or 24 lozenges
Pineapple lime flavour: Blister pack, PVC/PVDC/Aluminium foil: 16 lozenges

6.6 Special precautions for disposal

No special requirements.

7. MEDICINE SCHEDULE

Restricted medicine

8. SPONSOR

iNova Pharmaceuticals (New Zealand) Limited
C/- Simpson Grierson,
88 Shortland Street
AUCKLAND 1141
Telephone: 0508 375 394

9. DATE OF FIRST APPROVAL

26 March 2026

10. DATE OF REVISION OF THE TEXT

26 March 2026

SUMMARY TABLE OF CHANGES

Section changed:	**Summary of new information:**
All	New data sheet