AUSTRALIAN PRODUCT INFORMATION – CODRAL DRY COUGH & COLD WITH ANTIHISTAMINE

1 NAME OF THE MEDICINE

Diphenhydramine hydrochloride

Ammonium chloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL of CODRAL® Dry Cough & Cold With Antihistamine contains diphenhydramine hydrochloride 12.5 mg and ammonium chloride 125mg.

CODRAL® Dry Cough & Cold With Antihistamine also contains: sugars, benzoates, saccharin and sodium.

For full list of ingredients, refer to section 6.1

3 PHARMACEUTICAL FORM

CODRAL® Dry Cough & Cold With Antihistamine is a clear to slightly opalescent red liquid with a raspberry flavour. Each 5 mL of CODRAL® Dry Cough & Cold With Antihistamine contains diphenhydramine hydrochloride 12.5 mg and ammonium chloride 125mg.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

CODRAL® Dry Cough & Cold With Antihistamine provides relief from the symptoms of coughs and nasal congestion due to common cold.

4.2 DOSE AND METHOD OF ADMINISTRATION

The recommended doses of CODRAL® Dry Cough & Cold With Antihistamine are:

6 to 12 years	5 mL
Adults and children over 12 years	10 mL

The recommended dose should be taken every 4 hours as required. Do not exceed 6 doses in 24 hours.

CODRAL® Dry Cough & Cold With Antihistamine should not be used for children under 6 years, and should be used under the advice of a doctor for children 6-11 years.

4.3 CONTRAINDICATIONS

1. Known hypersensitivity or idiosyncratic reaction to diphenhydramine (or substances of similar chemical structure) or any of the other ingredients in the product
2. Narrow-angle glaucoma

3. Stenosing peptic ulcer
4. Symptomatic prostatic hypertrophy
5. Bladder neck obstruction
6. Pyloroduodenal obstruction.
7. Severe liver failure or renal impairment
8. Children under the age of 6 years (see Use in children)
9. Patients taking monoamine oxidase inhibitors (MAOIs) (see Interactions with other medicines)

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

CODRAL® Dry Cough & Cold With Antihistamine should be used with caution in patients with:

- breathing problems such as emphysema or chronic bronchitis
- persistent or chronic cough such as with smoking, asthma or emphysema
- cough accompanied by excessive secretions (mucus)
- glaucoma
- Prostate hyperplasia with urinary retention

Concomitant treatment

Precaution is recommended if other sedating antihistamines are taken concomitantly.

Mental Alertness

Diphenhydramine 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 (see Interactions with other medicines).

Hepatic impairment

CODRAL® Dry Cough & Cold With Antihistamine should be used with caution in patients with hepatic impairment.

Epilepsy

CODRAL® Dry Cough & Cold With Antihistamine should be used with caution in patients with epilepsy impairment.

Renal impairment

CODRAL® Dry Cough & Cold With Antihistamine should be used with caution in patients with renal impairment

Use in the elderly

No data available.

Paediatric use

Diphenhydramine may cause excitability, especially in children. CODRAL® Dry Cough & Cold With Antihistamine should not be used for children under 2 years of age and should be used under the advice of a doctor for children 6-11 years.

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Diphenhydramine possesses anticholinergic activity which may be potentiated by other drugs with strong anticholinergic effects such as MAOIs and tricyclic antidepressants (TCAs), resulting in increased anticholinergic adverse effects.

Diphenhydramine may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics.

Diphenhydramine may potentiate the effects of certain Beta Blockers such as metoprolol due to inhibition of CYP2D6 mediated metabolism.

4.6 FERTILITY, PREGNANCY AND LACTATION

Use in pregnancy – Pregnancy Category A

Diphenhydramine and ammonium chloride have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Use in lactation

Diphenhydramine is excreted in breast milk. Therefore, CODRAL® Dry Cough & Cold With Antihistamine is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Effects on fertility

No data available

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Due to diphenhydramine's potential for sedation, caution should be used when driving a motor vehicle or operating machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following rare side effects have been associated with diphenhydramine hydrochloride use:

Body as a Whole: headache, photosensitivity, asthenia

Cardiovascular system: hypotension, palpitations, tachycardia

Digestive System: constipation, diarrhoea, dry mouth, dry throat, dyspepsia, nausea, vomiting.

Nervous system: agitation/ excitation, anxiety, confusion, convulsions, disturbed coordination, dizziness, hallucinations, insomnia, irritability, nervousness, paresthesia, somnolence/ sedation, tremor. Impaired performance (impaired driving performance, poor work performance, uncoordination, reduced motor skills and impaired information processing), appetite stimulation, muscle dyskinesias and activation of epileptogenic foci.

Respiratory System: dryness of nose, thickening of bronchial secretions, tightness of chest or throat, wheezing

Skin: pruritis, rash, urticaria

Special Senses: dryness of the eyes, blurred vision, tinnitus

Urogenital system: urinary hesitancy and retention.

Somnolence was the most frequently reported adverse effect.

Nausea and vomiting have been reported with high doses of ammonium chloride.

Post Marketing Data

Adverse drug reactions (ADRs) identified during post-marketing experience with the combination of ammonium chloride and diphenhydramine (with or without menthol and sodium citrate) are included in Table 2 and Table 3. The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000
Not known (cannot be estimated from the available data)	

Adverse Drug Reactions Identified during Post Marketing Experience with Ammonium Chloride and Diphenhydramine Hydrochloride with or without Menthol, Sodium Citrate Frequency Category Estimated from Clinical Trials or Epidemiology Studies

SOC Frequency Category	**Adverse Event Preferred Term**
Immune System Disorders	
Not known	Angioedema
Not known	Hypersensitivity
Psychiatric Disorders	
Not known	Confusional state
Not known	Irritability
Not known	Nervousness
Nervous System Disorders	
Not known	Agitation, coordination abnormal, convulstion, headache, insomnia, paraesthesia, sedation, tremor
Eye Disorders	
Not known	Vision blurred

Ear and labyrinth Disorders	
Not Known	Tinnitus
Cardiac Disorders	
Not known	Palpitations, tachycardia
Vascular Disorders	
Not known	Hypotension
Respiratory, Thoracic and Mediastinal Disorders	
Not known	Chest discomfort, dry throat, nasal dryness
Gastrointestinal Disorders	
Not known	Abdominal pain, application site reaction, constipation, diarrhoea, dyspepsia, nausea, vomiting
Skin and Subcutaneous Tissue Disorders	
Not known	Pruritus, rash, urticaria

Adverse Drug Reactions Identified during Post Marketing Experience with Ammonium Chloride and Diphenhydramine Hydrochloride with or without Menthol, Sodium Citrate Frequency Category Estimated from Spontaneous Reporting Rates

SOC Frequency Category	**Adverse Event Preferred Term**
Immune System Disorders	
Very rare	Angioedema
Very rare	Hypersensitivity
Psychiatric Disorders	
Very rare	Confusional state
Very rare	Irritability
Very rare	Nervousness
Nervous System Disorders	
Very rare	Agitation, coordination abnormal, convulstion, headache, insomnia, paraesthesia, sedation, tremor
Eye Disorders	
Very rare	Vision blurred
Ear and labyrinth Disorders	
Very rare	Tinnitus
Cardiac Disorders	
Very rare	Palpitations, tachycardia
Vascular Disorders	
Very rare	Hypotension

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at: https://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

As an antihistamine, diphenhydramine hydrochloride antagonizes endogenous histamine by competitively and reversibly blocking the histamine H1 receptor.

As an antitussive, diphenhydramine hydrochloride selectively suppresses the central cough mechanism, thus raising the threshold for afferent (incoming) cough pulses.

Ammonium chloride is an expectorant that has an irritant effect on mucous membranes.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Diphenhydramine hydrochloride is well absorbed from the gastro-intestinal tract, although high first-pass metabolism appears to affect systemic bioavailability. Following a single 50 mg oral dose, peak plasma concentrations of 66 ± 22 ng/mL were achieved in 2.3 ± 0.64 hours. Bioavailability of the oral form is reported to be 72 ± 26%.

Ammonium chloride is absorbed from the gastrointestinal tract. The ammonium ion is converted into urea in the liver or is attached to the amide nitrogen of glutamine for transport in the blood.

Distribution

Diphenhydramine hydrochloride is widely distributed throughout the body, including the central nervous system (CNS). It crosses the placenta and has been detected in breast milk. Diphenhydramine is highly bound to plasma proteins and total protein binding is reported to be 78 ± 3%. Volume of distribution is 4.5 ± 2.8 L/kg. Metabolism is extensive with approximately 50% of diphenhydramine hydrochloride metabolized in the liver to the inactive metabolite diphenylmethane, which suggests a large first-pass effect. Little, if any, diphenhydramine hydrochloride is excreted unchanged in the urine. The elimination half-life of diphenhydramine

hydrochloride is 8.5 ± 3.2 hours and may be prolonged with age. Total body clearance is 6.2 ± 1.7 mL/min-1/kg-1 and may be decreased with age.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

CODRAL® Dry Cough & Cold With Antihistamine in addition to the active ingredients contains: sucrose, glucose-liquid, glycerol, sodium citrate, raspberry flavour, citric acid monohydrate, saccharin sodium, menthol, Allura Red FC, Brilliant Blue FCF, sodium benzoate.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine. Refer to section 4.5: Interactions with other medicines and other forms of interactions.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C

6.5 NATURE AND CONTENTS OF CONTAINER

CODRAL® Dry Cough & Cold With Antihistamine is available in glass bottles with child resistant bottle caps.

Pack sizes

100mL

200mL

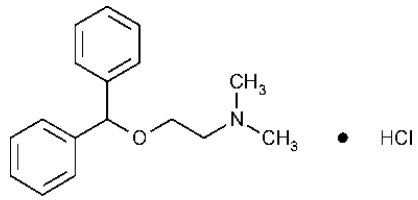
Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



Chemical Name: 2-(diphenylmethoxy)-N,N-dimethylethanamine hydrochloride.

CAS number

Diphenhydramine hydrochloride: 58-73-1

Ammonium chloride: 1215-02-9

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacist Only Medicine (S3)

8 SPONSOR

Johnson & Johnson Pacific
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45 Jones Street, Ultimo NSW 2007
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New Zealand: 0800 446 147
Overseas Customers +61 2 8260 8366

9 DATE OF FIRST APPROVAL

04 November 2020

10 DATE OF REVISION

N/A

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information