SUMMARY OF PRODUCT CHARACTERISTICS
AMMONIUM CHLORIDE138.0MG/ DIPHENHYDRAMINE HYDROCHLORIDE 14.08MG PER 5ML SYRUP
(COFSYL ORIGINAL COUGH SYRUP)

1. NAME OF THE MEDICINE

Generic name: Diphenhydramine hydrochloride and Ammonium chloride
Trade name: Cofsyl Original

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of COFSYL Original Syrup contains:
Ammonium Chloride…….…..….138.0mg
Diphenhydramine Hydrochloride……14.08mg
Excipients with known effect:
Sodium Benzoate……..…….……0.20%w/v
Sucrose……..1250mg
Sorbitol……..750mg
Refer to Section 6.1 for the full list of excipients.

3. PHARMACEUTICAL FORM

Cofsyl Original is a dark, brown-coloured syrup with a faint odour of kola champagne, menthol and peppermint,

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Cofsyl Original provides relief from the symptoms of coughs and nasal congestion due to common colds.

4.2 DOSE AND METHOD OF ADMINISTRATION

The recommended doses of COFSYL Original are:

1 to 12 years…….2 . 5 - 5.0 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.
Cofsyl Original should not be used for children under 1 year without the advice of a doctor or pharmacist.

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 1 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

Patients with the following conditions should be advised to consult a physician before using Cofsyl Original:

- 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

Patients should not use any other products containing diphenhydramine, even ones used on skin. If symptoms persist, worsen, or if new symptoms appear, stop use and consult a physician.

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).

Diphenhydramine may enhance the sedative effects of central nervous system depressants including sedatives and tranquilizers. Consult a healthcare professional prior to taking central nervous system depressants.

Hepatic impairment: Cofsyl Original should be used with caution in patients with hepatic impairment.

Epilepsy: Cofsyl Original should be used with caution in patients with epilepsy impairment.

Renal impairment: Cofsyl Original 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. Cofsyl Original be used under the advice of a doctor for children for children under 1 years.

Use in other populations

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine

Sorbitol is a source of fructose. If you (or your child) have hereditary fructose intolerance (HFI), a rare genetic disorder, you (or your child) must not receive this medicine. Patients with HFI cannot break down fructose, which may cause serious side effects.

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 are both Pregnancy Category A. There are no adequate and well-controlled studies for the combination of ammonium chloride and diphenhydramine (with or without menthol and sodium citrate) in pregnant or breast-feeding women. This product should not be used during pregnancy unless the potential benefit of treatment to the mother outweighs the possible risks to the developing fetus. A physician should be consulted before use if pregnant.

Use in lactation

Diphenhydramine is excreted in breast milk. Therefore, COFSYL® Original is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant. A physician should be consulted before breastfeeding.

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, incoordination, 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 and 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 Spontaneous Reporting Rates

SOC Frequency Category	**Adverse Event Preferred Term**
Immune System Disorders	
Very rare	Angioedema
Very rare	Hypersensitivity
Psychiatric Disorders	
Very rare	Confused state, Hallucination, Irritability, Nervousness
Nervous System Disorders	
Very rare	Agitation, coordination abnormal, convulsions, dizziness headache, insomnia, paraesthesia, sedation, somnolence, tremor
Eye Disorders	
Very rare	Blurred vision
Ear and labyrinth Disorders	
Very rare	Tinnitus
Cardiac Disorders	
Very rare	Palpitations, tachycardia
Vascular Disorders	
Very rare	Hypotension
Respiratory, Thoracic and Mediastinal Disorders	
Very rare	Chest discomfort, dry throat, nasal dryness
Gastrointestinal Disorders	
Very rare	Abdominal pain, application site reaction, constipation, diarrhoea, dry mouth, dyspepsia, nausea, vomiting
Skin and Subcutaneous Tissue Disorders	
Very rare	Pruritus, rash, urticaria
Renal and Urinary Disorders	
Very rare	Urinary retention
General Disorders and Administrative Site Conditions	
Very rare	Asthenia

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 to the manufacturer via the Cospharm website. *See details in section 10.*

4.9 OVERDOSE

Keep out of reach of children. In the event of an overdose, seek medical attention immediately.

5. PHARMOCOLOGICAL 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%. The volume of distribution is 4.5 ± 2.8 L/kg.

Metabolism
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.

Excretion
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 decrease with age.

5.3 PRECLINICAL SAFETY

DATA Genotoxicity

No data available

Carcinogenicity
No data available

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS
Cofsyl Original Syrup contains:
Sodium benzoate, Sucrose, Sodium citrate, Liquid Sorbitol, Glycerine, Colour: Liquid Caramel (9.01mg/5ml), Peppermint Essence (0.5mg/5ml), Menthol (0.94mg), Citric acid monohydrate, Saccharin Sodium, Kola champagne(6mg/5ml) and Purified water

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
Unopened: 24 months.
After opening: Use within 45 days of opening

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 30°C, protect from light and moisture. Keep out of children's reach

6.5 NATURE AND CONTENTS OF CONTAINER
Cofsyl Original Syrup is available in 100ml and/or 200ml amber glass bottle with a black PP cap. A 20ml measuring cup is included.
Not all packs sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
Any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

7. CATEGORY FOR DISTRIBUTION
Prescription Only Medicines, (POM)

8. PHARMACOLOGICAL CLASSIFICATION
22.2.5 Cough and cold preparations: Combination products

9. MARKETING AUTHORIZATION NUMBER(S)
Zimbabwe: TBA

10. PRINCIPAL AND MANUFACTURER

Cospharm

Cospharm Pharmaceuticals
Stand No.: 12896 Madokero Industrial Area, Harare, Zimbabwe
www.cospharm.org

11. DATE OF PUBLICATION

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