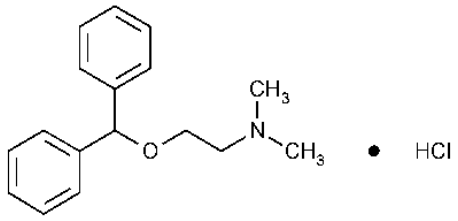
PRODUCT INFORMATION

BENADRYL ® Original Oral Liquid (New Formula)

Name of the Medicine

Diphenhydramine hydrochloride
Ammonium chloride

The chemical name for diphenhydramine hydrochloride is 2-(diphenylmethoxy)-*N,N*-dimethylethanamine hydrochloride. The chemical structure is:



CAS 58-73-1

The chemical formula for ammonium chloride is NH_4Cl. CAS 1215-02-9.

Product description

BENADRYL® Original is presented as a clear to slightly opalescent red liquid, with a raspberry odour.

Each 5 mL of BENADRYL® Original contains diphenhydramine hydrochloride 12.5 mg and ammonium chloride 125mg.

BENADRYL® Original also contains: sucrose, glucose-liquid, glycerol, sodium citrate, raspberry flavour, citric acid monohydrate, saccharin sodium, menthol, Allura Red FC, Brilliant Blue FCF, sodium benzoate.

Pharmacology

Pharmacodynamics
As an antihistamine, diphenhydramine hydrochloride antagonizes endogenous histamine by competitively and reversibly blocking the histamine H_1 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.

Pharmacokinetics
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%.

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.

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.

Indications

BENADRYL® Original provides relief from the symptoms of coughs and nasal congestion due to common cold.

Contraindications

BENADRYL® Original is contraindicated for use in patients with:

- known hypersensitivity or idiosyncratic reaction to diphenhydramine (or substances of similar chemical structure) or any of the other ingredients in the product
- narrow-angle glaucoma
- stenosing peptic ulcer
- symptomatic prostatic hypertrophy
- bladder neck obstruction
- pyloroduodenal obstruction.
- severe liver failure or renal impairment

BENADRYL® Original is also contraindicated for use in

- Children under the age of 6 years (see Use in children)
- Patients taking monoamine oxidase inhibitors (MAOIs) (see Interactions with other medicines)

Precautions

BENADRYL® Original 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)
- renal or hepatic impairment
- epilepsy
- glaucoma
- other sedating antihistamines

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).

Ammonium chloride is contraindicated in patients with hepatic or renal impairment.

Use in children
Diphenhydramine may cause excitability, especially in children. BENADRYL® Original 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.

Use in 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, BENADRYL® Original is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Interactions with other medicines

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.

Adverse reactions

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.

Dosage and Administration

The recommended doses of BENADRYL® Original 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.

BENADRYL® Original should not be used for children under 6 years, and should be used under the advice of a doctor for children 6-11 years.

Overdosage

In case of overdose, immediately contact the Poisons Information Centre for advice. (In Australia, call 13 11 26).

Presentation and Storage Conditions

BENADRYL® Original is a clear to slightly opalescent red liquid with a raspberry flavour. It is available in bottles of 100 mL and 200 mL.

Each 5 mL of BENADRYL® Original contains diphenhydramine hydrochloride 12.5 mg and ammonium chloride 125mg.

Store below 30°C.

Name and Address of Sponsor

Johnson & Johnson Pacific Pty Limited
45 Jones St
Ultimo NSW 2007
Australia
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Poison Schedule of the Medicine

(S3) Pharmacist Only Medicine

Date of first inclusion in the ARTG

16 July 2012

AUST R 199371

Date of most recent amendment

25 September 2015