

Data Sheet

Benadryl* Nighttime Oral Liquid

Product description

Each 5 mL of Benadryl* Nighttime oral liquid contains dextromethorphan hydrobromide 10 mg and diphenhydramine hydrochloride 12.5 mg.

Benadryl* Nighttime also contains: ammonium glycyrrhizinate, anhydrous citric acid, liquid glucose, glycerol, menthol, saccharin sodium, sodium benzoate, sodium citrate, sucrose, purified water, brilliant scarlet 4R, Caramel HGP, Nature Identical Raspberry Flavour 08-3326,

Pharmacology

Pharmacokinetics

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.

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 $72 \pm 26\%$.

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 $78 \pm 3\%$. 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.

Pharmacodynamics/Mechanism of action

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.

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

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

Indications

Benadryl* Nighttime provides relief from the symptoms of dry raspy coughs and the symptoms of a cold.

Contraindications

Benadryl* Nighttime is contraindicated for use in patients with:

- known hypersensitivity or idiosyncratic reaction to dextromethorphan, 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.

Benadryl* Nighttime is also contraindicated for use in patients taking monoamine oxidase inhibitors (MAOIs). (See Interactions with other medicines.)

Precautions

Benadryl* Nighttime should not be used in patients with:

- breathing problems such as emphysema or chronic bronchitis
- risk of developing respiratory failure, eg asthma, chronic obstructive airways disease and pneumonia
- persistent or chronic cough such as with smoking, asthma or emphysema
- cough accompanied by excessive secretions (mucus)
- renal or hepatic impairment
- epilepsy
- glaucoma
- history of asthma.

Benadryl* Nighttime should not be given during an acute attack of asthma.

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.

Use in children

Diphenhydramine may cause excitability, especially in children. Benadryl Nighttime* should not be used for children under 2 years of age.

Use in pregnancy

Category A: Dextromethorphan and diphenhydramine 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. It is not known whether dextromethorphan is excreted in breast milk. Therefore, Benadryl* Nighttime 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

Benadryl* Nighttime 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.

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, hypertension, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering and tremor.

Serum levels of dextromethorphan may be increased by the concomitant use of inhibitors of cytochrome P450 2D6, such as the antiarrhythmics quinidine and amiodarone, antidepressants such as fluoxetine and paroxetine, or other drugs which inhibit cytochrome P450 2D6 such as haloperidol and thioridazine.

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

Diphenhydramine possesses anticholinergic activity which may be potentiated by other drugs with strong anticholinergic effects 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.

Adverse reactions

Side effects with usual doses of dextromethorphan are uncommon but may include mild drowsiness, fatigue, dystonias, dizziness and gastrointestinal disturbances (nausea or vomiting, stomach discomfort, or constipation).

Side effects that may occur with high doses (overdosage) of dextromethorphan include excitation, confusion, psychosis, nervousness, irritability, restlessness, "serotonin syndrome", severe nausea and vomiting, and respiratory depression.

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

Body as a Whole: headache, photosensitivity

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, wheezing

Skin: pruritis, rash, urticaria

Special Senses: blurred vision, tinnitus

Urogenital system: urinary retention.

Somnolence was the most frequently reported adverse effect.

Dosage

The recommended doses of Benadryl* Nighttime are:

- 2 to 6 years 2.5 mL
- 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 4 doses in 24 hours.

Benadryl* Nighttime should not be used for children under 2 years.

Overdosage

In case of overdose, immediately contact the Poisons Information Centre for advice. (In Australia, call 13 11 26; in New Zealand call 0800 764 766).

Presentation

Benadryl* Nighttime is a red-brown, viscous liquid with raspberry flavour. It is available in bottles of 100 mL and 200 mL.

Restricted Medicine

Store below 30°C.

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