POLARAMINE®

dexchlorpheniramine maleate

DESCRIPTION
Polaramine (dexchlorpheniramine maleate) is the dextro-isomer of chlorpheniramine maleate. It is an antihistamine with anticholinergic properties.

Dexchlorpheniramine maleate (CAS no. 2438-32-6) is described chemically as (+)-2-[p-chloro-α-[2-(dimethylamino)ethyl]benzyl]pyridine maleate (1:1).

It has the empirical formula of C₁₆H₁₉ClN₂.C₄H₄O₄ and the following structural formula:

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Dexchlorpheniramine maleate is a white, odourless, crystalline powder which in aqueous solution has a pH of between 4 and 5. It is freely soluble in water, soluble in alcohol and in chloroform, but only slightly soluble in benzene or ether.

PHARMACOLOGY

Pharmacodynamics

Mechanism of Action:
Dexchlorpheniramine, the d-isomer of the racemic compound chlorpheniramine, is two times more active than chlorpheniramine. Dexchlorpheniramine does not prevent the release of histamine, but rather, competes with free histamine for binding at the H₁-receptor sites, and competitively antagonizes the effects of histamine on H₁-receptors in the GI tract, uterus, large blood vessels, and bronchial muscle. Blockade of H₁-receptors also suppresses the formation of oedema, flare, and pruritus that result from histaminic activity. Since dexchlorpheniramine binds to central and peripheral H₁-receptors, sedative effects are likely to occur. H₁-antagonists are structurally similar to anticholinergic agents and therefore possess the potential to exhibit anticholinergic properties of varying degrees. They also have antipruritic effects. Dexchlorpheniramine has high antihistaminic activity, moderate anticholinergic effects and minimal sedative effects. The drug does not possess antiemetic properties.

Pharmacokinetics:
The absorption, distribution, metabolism and elimination of dexchlorpheniramine have not been specifically described. However, since dexchlorpheniramine is the primary active isomer of the racemic compound chlorpheniramine, the pharmacokinetics of dexchlorpheniramine are likely to be similar to that of chlorpheniramine.
Dexchlorpheniramine is administered orally. H₁-antagonists are generally well absorbed from the GI tract. The onset of action of immediate release formulations of chlorpheniramine is about 30-60 minutes. The Cmax of chlorpheniramine occurs in about 2 hours, the maximum therapeutic effect in about 6 hours, and the duration of action lasts between 4-8 hours. Protein binding is approximately 72%. Chlorpheniramine is widely distributed in body tissues and fluids, and it crosses the placenta and is excreted into breast milk.

The metabolism of chlorpheniramine is extensive and rapid, first occurring in the gastric mucosa and then on first-pass through the liver, which may be saturable. N-dealkylation produces several metabolites, which are excreted in the urine along with the parent compound. The half-life in healthy adults and children is 20-24 hours and 10-13 hours, respectively. Excretion rates are dependent on the pH of urine and urinary flow, with the rate decreasing as the pH rises and urinary flow decreases.

INDICATIONS
POLARAMINE is indicated for symptomatic treatment of perennial and seasonal allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis, mild uncomplicated allergic skin manifestations of urticaria and angioedema. Polaramine may relieve itching due to skin conditions such as allergic eczema, pruritus ani, pruritus vulvae, atopic dermatitis, contact dermatitis, insect bites, dermographism and drug reactions, including serum sickness.

CONTRAINDICATIONS
Polaramine is contraindicated for use in:
• newborns and premature infants.
• patients taking monoamine oxidase inhibitors (MAOIs) (see “Interactions with other medicines” section)
• patients with a history of hypersensitivity to dexchlorpheniramine, to other drugs of similar chemical structure, or to any other excipients.

PRECAUTIONS
Polaramine may cause drowsiness and may add to the effects of alcohol. Drowsiness may continue the following day. Those affected should not drive or operate machinery; alcohol should be avoided.

Polaramine should be used with caution in patients with:
• narrow-angle glaucoma
• stenosing peptic ulcer
• prostatic hypertrophy
• bladder neck obstruction
• pyloroduodenal obstruction
• cardiovascular disease including hypertension
• increased intraocular pressure
• hyperthyroidism
• use with caution in patients with renal or hepatic impairment
• seizures

Polaramine may cause photosensitivity in some patients.

Use in Pregnancy (Category A)
Safety during pregnancy has not been established. Polaramine should be used during the first two trimesters of pregnancy only if clearly needed.

Dexchlorpheniramine maleate should not be used in the third trimester of pregnancy because newborn and premature infants may have severe reactions to antihistamines.
Polaramine has 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 of on the foetus having been observed.

**Use in Lactation**
Polaramine is excreted in breast milk. Therefore caution should be exercised when administered to nursing mothers.

**Paediatric use**
Children may experience paradoxical excitation with dexchlorpheniramine maleate. In children this may cause excitability.

Polaramine Syrup contains Sorbitol which may have a laxative effect or cause diarrhoea.

**Use in the elderly**
The elderly may experience paradoxical excitation with dexchlorpheniramine maleate. In patients over 60 years of age, antihistamines may cause dizziness, sedation and hypotension. Also they are more likely to have central nervous system (CNS) depressive side effects, including confusion.

**Interactions with other medicines**
The following interactions with Polaramine have been noted:
- central nervous system (CNS) depressants (alcohol, sedatives, opioid analgesics, hypnotics) may cause an increase in sedative effects of Polaramine
- concomitant administration with tricyclic antidepressants (TCAs) may result in additive antimuscarinic activity
- monoamine oxidase inhibitors (MAOIs) may prolong and intensify the anticholinergic and CNS depressive effects of some antihistamines and may cause a decrease in blood pressure
- oral anticoagulants may have their actions decreased by antihistamines.

**Effect on laboratory tests**
Antihistamines should be discontinued approximately 48 hours prior to skin testing procedures since these drugs may prevent or diminish otherwise positive reactions to dermal reactivity indicators.

**ADVERSE REACTIONS**
Slight to moderate drowsiness is the most frequent side effect of dexchlorpheniramine maleate.

Other reported reactions associated with antihistamine therapy in general include:

**General:** Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose and throat

**Cardiovascular:** Hypotension, hypertension, headache, palpitations, tachycardia, extrasystoles

**Haematological:** Haemolytic anaemia, hypoplastic anaemia, thrombocytopenia, agranulocytosis

**Gastrointestinal:** Epigastric distress, anorexia, nausea, vomiting, diarrhoea, constipation

**Genitourinary:** Urinary frequency, difficult urination, urinary hesitation and retention, early menses
Nervous System: Sedation, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitement, nervousness, tremor, irritability, insomnia, euphoria, paraesthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions, lassitude, depression, inability to concentrate, dilated pupils, hyporeflexia, hyporeflexia, xerostomia, hallucinations, appetite stimulation, anxiety, facial dyskinesias and seizures

Respiratory: Thickening of bronchial secretions, tightness of chest, wheezing, nasal stuffiness

DOSAGE AND ADMINISTRATION

Polaramine Tablets
Adults and children over 12 years: One tablet every 6 hours

Polaramine Syrup
Adults and children over 12 years: 5 mL every 6 hours
Children 6 - 12 years: 2 – 4 mL every 6 - 8 hours
Children 4 - 6 years: 1.75 – 2 mL every 6 - 8 hours
Children 2 - 4 years: 1.25 – 1.75 mL every 6 - 8 hours

Polaramine Syrup is not to be used in children under 2 years of age.

OVERDOSE
In case of overdose, immediately contact the Poisons Information Centre (in New Zealand, call 0800 764 766 [0800 POISON]) for advice.

Manifestations. Antihistamine overdose effects may vary from central nervous system depression (apnoea, arrhythmias, cardiovascular collapse, cyanosis, diminished mental alertness, sedation) to stimulation (convulsions, hallucinations, insomnia or tremors) to death. Other signs and symptoms may be ataxia, blurred vision, dizziness, hypotension and tinnitus. Stimulation is particularly likely in children, as are atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing; gastrointestinal symptoms and hyperthermia).

Treatment: Dialysis is of little value in antihistamine poisoning. Treatment of the signs and symptoms of an over dosage are symptomatic and supportive. Consider standard measures to remove any unabsorbed drug. There is no specific antidote. Measures to enhance excretion (urinary acidification, haemodialysis) are not recommended.

PRESENTATION AND STORAGE CONDITIONS
Polaramine is available for oral use as either as: film coated immediate release tablet (Polaramine Tablets) or as a syrup (Polaramine syrup).

Polaramine Tablets
Off-white, round, bevelled tablet with Flask and Bowl logo on one side, score on the other side. Available in blister packs of 20 and 40 tablets

Active: Dexchlorpheniramine maleate 2 mg
Inactive: Lactose, starch-maize, starch – pregelatinised maize, magnesium stearate

Store below 25°C

Polaramine Syrup
A clear, red syrup with an orange like odour. Available in a bottle of 100 mL.

Active: Dexchlorpheniramine maleate 2mg per 5 mL
Inactive: Sodium citrate, sodium chloride, sucrose, sorbitol solution (70 per cent), methyl hydroxybenzoate, propyl hydroxybenzoate, menthol, ethanol, water, brilliant scarlet 4R, apricot flavour, blood orange flavour.

Store below 25°C

MEDICINE CLASSIFICATION
Pharmacist Only Medicine

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