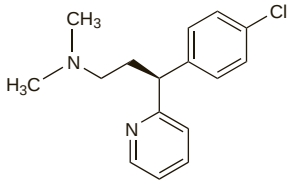
## Dexchlorpheniramine Maleate *(BANM, rINNM)*

Dekschlorfeniramino maleatas; Dekskloorifeniramiinimaleaatti; Dexchlorfeniramin-maleinát; Dexchlorphenamine Maleate; Dexchlorphéniramine, Maléate de; Dexchlorpheniramini maleas; Dexklorfeniraminmaleat; Dexklórfeniramin-maleát; Maleato de dexclorfeniramina.

Дексхлорфенирамина Малеат

*CAS — 25523-97-1 (dexchlorpheniramine); 2438-32-6 (dexchlorpheniramine maleate).*
*ATC — R06AB02.*
*ATC Vet — QR06AB02.*



*(dexchlorpheniramine)*

**Pharmacopoeias.** In *Eur.* (see p.vii), *Jpn*, and *US*.
**Ph. Eur. 6.2** (Dexchlorpheniramine Maleate). A white or almost white, crystalline powder. Very soluble in water; freely soluble in alcohol, in dichloromethane, and in methyl alcohol. A 1% solution in water has a pH of 4.5 to 5.5. Protect from light.
**USP 31** (Dexchlorpheniramine Maleate). A white, odourless, crystalline powder. Soluble 1 in 1.1 of water, 1 in 2 of alcohol, 1 in 1.7 of chloroform, and 1 in 2500 of ether; slightly soluble in benzene. pH of a 1% solution in water is between 4.0 and 5.0. Store in airtight containers. Protect from light.

### Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561. Exfoliative dermatitis may develop. Injections may be irritant and cause transient hypotension or stimulation of the CNS.

**Effects on the blood.** There are several old and isolated reports of blood dyscrasias after use of chlorphenamine maleate; these include agranulocytosis,[1,2] thrombocytopenia,[3] pancytopenia,[4] and aplastic anaemia.[5] Haemolytic anaemia has occurred after use of dexchlorpheniramine maleate.[6] The association with antihistamine use has been questioned in some of these cases.[7]

1. Shenfield G, Spry CJF. Unusual cause of agranulocytosis. *BMJ* 1968; **ii:** 52–3.
2. Hardin AS. Chlorpheniramine and agranulocytosis. *Ann Intern Med* 1988; **108:** 770.
3. Eisner EV, *et al.* Chlorpheniramine-dependent thrombocytopenia. *JAMA* 1975; **231:** 735–6.
4. Deringer PM, Maniatis A. Chlorpheniramine-induced bone-marrow suppression. *Lancet* 1976; **i:** 432.
5. Kanoh T, *et al.* Aplastic anaemia after prolonged treatment with chlorpheniramine. *Lancet* 1977; **i:** 546–7.
6. Duran-Suarez JR, *et al.* The I antigen as an immune complex receptor in a case of haemolytic anaemia induced by an antihistaminic agent. *Br J Haematol* 1981; **49:** 153–4.
7. Spry CJF. Chlorpheniramine-induced bone-marrow suppression. *Lancet* 1976; **i:** 545.

**Effects on the senses.** Chlorphenamine has been reported to affect the senses of smell and taste.[1]

1. Schiffman SS. Taste and smell in disease. *N Engl J Med* 1983; **308:** 1275–9.

**Extrapyramidal disorders.** Facial dyskinesias have been reported[1,2] after oral doses of chlorphenamine maleate.

1. Thach BT, *et al.* Oral facial dyskinesia associated with prolonged use of antihistaminic decongestants. *N Engl J Med* 1975; **293:** 486–7.
2. Davis WA. Dyskinesia associated with chronic antihistamine use. *N Engl J Med* 1976; **294:** 113.

### Interactions

As for the sedating antihistamines in general, p.563.

**Antiepileptics.** For a report of the effect of chlorphenamine on *phenytoin*, see p.499.

### Pharmacokinetics

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, peak plasma concentrations occurring about 2.5 to 6 hours after oral doses. Bioavailability is low, values of 25 to 50% having been reported. Chlorphenamine appears to undergo considerable first-pass metabolism. About 70% of chlorphenamine in the circulation is bound to plasma proteins. There is wide interindividual variation in the pharmacokinetics of chlorphenamine; values ranging from 2 to 43 hours have been reported for the half-life. Chlorphenamine is widely distributed in the body, and enters the CNS.

Chlorphenamine maleate is extensively metabolised. Metabolites include desmethyl- and didesmethylchlorphenamine. Unchanged drug and metabolites are excreted primarily in the urine; excretion is dependent on urinary pH and flow rate. Only trace amounts have been found in the faeces.

A duration of action of 4 to 6 hours has been reported; this is shorter than may be predicted from pharmacokinetic parameters.

More rapid and extensive absorption, faster clearance, and a shorter half-life have been reported in children.

◊ References.


1. Rumore MM. Clinical pharmacokinetics of chlorpheniramine. *Drug Intell Clin Pharm* 1984; **18:** 701–7.
2. Paton DM, Webster DR. Clinical pharmacokinetics of H -receptor antagonists (the antihistamines). *Clin Pharmacokinet* 1985; **10:** 477–97.
3. Yasuda SU, *et al.* The roles of CYP2D6 and stereoselectivity in the clinical pharmacokinetics of chlorpheniramine. *Br J Clin Pharmacol* 2002; **53:** 519–25.


### Uses and Administration

Chlorphenamine maleate, an alkylamine derivative, is a sedating antihistamine that causes a moderate degree of sedation; it also has antimuscarinic activity.

Chlorphenamine is a racemic mixture; the dextrorotatory isomer, dexchlorpheniramine, has about twice the activity of chlorphenamine by weight.

Chlorphenamine maleate and dexchlorpheniramine maleate are used for the symptomatic relief of allergic conditions including urticaria and angioedema (p.565), rhinitis (p.565), and conjunctivitis (p.564), and in pruritic skin disorders (p.565). They are common ingredients of compound preparations for symptomatic treatment of coughs and the common cold (p.564). However, such preparations should be used with caution in children, and generally avoided in those under 2 years of age (see p.562). Chlorphenamine may be given intravenously as an adjunct in the emergency treatment of anaphylactic shock (p.563).

*Chlorphenamine maleate* is given in oral doses of 4 mg every 4 to 6 hours up to a maximum of 24 mg daily. Doses for children, according to age, are: 1 to 2 years, 1 mg twice daily; 2 to 5 years, 1 mg every 4 to 6 hours (maximum 6 mg daily); 6 to 12 years, 2 mg every 4 to 6 hours (maximum 12 mg daily). Although not licensed in the UK, the *BNFC* suggests that children aged 1 month and over may be given 1 mg twice daily.

Chlorphenamine maleate may be given by intramuscular, by subcutaneous, or by slow intravenous injection over a period of 1 minute. The usual dose is 10 to 20 mg and the total dose given by these routes in 24 hours should not normally exceed 40 mg. For children, doses of 87.5 micrograms/kg subcutaneously four times daily have been suggested. The following parenteral doses may also be used in children: the usual dose in those aged 1 month to 1 year is 250 micrograms/kg; those aged 1 to 5 years may be given a dose of 2.5 to 5 mg and those aged 6 to 12 years, 5 to 10 mg. Alternatively, children and adolescents aged 1 to 18 years may be given a dose of 200 micrograms/kg. The *BNFC* suggests that doses for children may be repeated if necessary up to 4 times in 24 hours.

*Dexchlorpheniramine maleate* is given in oral doses of 2 mg every 4 to 6 hours up to a maximum of 12 mg daily. Children aged 2 to 5 years may be given 0.5 mg every 4 to 6 hours (maximum 3 mg daily), and those aged 6 to 12 years, 1 mg every 4 to 6 hours (maximum 6 mg daily).

*Modified-release* oral preparations of chlorphenamine maleate or dexchlorpheniramine maleate are available in some countries; dosage is specific to a particular formulation.

Dexchlorpheniramine maleate has been applied topically in some countries, although as with other antihistamines there is a risk of sensitisation. Chlorphenamine polistirex (a sulfonated diethenylbenzene-ethenylbenzene copolymer complex), chlorphenamine tannate, and dexchlorpheniramine tannate are given orally and are used similarly to the maleate.

**Malaria.** Chlorphenamine may be tried in patients with malaria who have chloroquine-induced pruritus (see Effects on the Skin, p.600), but additionally it has been shown to have some promise as an adjunct in the treatment of chloroquine-resistant malaria itself. Early studies indicated that chlorphenamine was only one of a number of drugs that reversed chloroquine resistance *in vitro* in isolates of *Plasmodium falciparum*. Later clinical studies in children in Nigeria showed enhanced efficacy when chlorphenamine was given with chloroquine.[1-5] The overall management of malaria is discussed on p.594.


1. Sowunmi A, *et al.* Enhanced efficacy of chloroquine-chlorpheniramine combination in acute uncomplicated falciparum malaria in children. *Trans R Soc Trop Med Hyg* 1997; **91:** 63–7.
2. Sowunmi A, Oduola AMJ. Comparative efficacy of chloroquine/chlorpheniramine combination and mefloquine for the treatment of chloroquine-resistant Plasmodium falciparum malaria in Nigerian children. *Trans R Soc Trop Med Hyg* 1997; **91:** 689–93.
3. Sowunmi A, *et al.* Comparative efficacy of chloroquine plus chlorpheniramine and pyrimethamine/sulfadoxine in acute uncomplicated falciparum malaria in Nigerian children. *Trans R Soc Trop Med Hyg* 1998; **92:** 77–81.
4. Sowunmi A, *et al.* Comparative efficacy of chloroquine plus chlorpheniramine and halofantrine in acute uncomplicated falciparum malaria in Nigerian children. *Trans R Soc Trop Med Hyg* 1998; **92:** 441–5.
5. Okonkwo CA, *et al.* Effect of chlorpheniramine on the pharmacokinetics of and response to chloroquine of Nigerian children with falciparum malaria. *Trans R Soc Trop Med Hyg* 1999; **93:** 306–11.


### Preparations

***BP 2008:*** Chlorphenamine Injection; Chlorphenamine Oral Solution; Chlorphenamine Tablets;
***USP 31:*** Acetaminophen, Chlorpheniramine Maleate, and Dextromethorphan Hydrobromide Tablets; Chlorpheniramine Maleate and Phenylpropanolamine Hydrochloride Extended-release Capsules; Chlorpheniramine Maleate and Phenylpropanolamine Hydrochloride Extended-release Tablets; Chlorpheniramine Maleate and Pseudoephedrine Hydrochloride Extended-release Capsules; Chlorpheniramine Maleate and Pseudoephedrine Hydrochloride Oral Solution; Chlorpheniramine Maleate Extended-release Capsules; Chlorpheniramine Maleate Injection; Chlorpheniramine Maleate Syrup; Chlorpheniramine Maleate Tablets; Dexchlorpheniramine Maleate Syrup; Dexchlorpheniramine Maleate Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Afeme; Alergidryl†; Alergitrat; Isomerine†; Qura Plus; ***Austral.:*** Polaramine; ***Austria:*** Polaramin; ***Belg.:*** Polaramine†; ***Braz.:*** Alergonil; Alergovalle†; Alergyo; Alermine†; Deflux†; Dexclor†; Dexlerg; Dexmin†; Expectamin F; Histamin; Hystin; Polamin†; Polaramine; Polaren; Polaryn; ***Canad.:*** Chlor-Tripolon; Novo-Pheniram; ***Chile:*** Asafen Nueva Formula†; Clorprimeton; Nipolen; Prodel; Scadan; ***Denm.:*** Polaramin; ***Fr.:*** Polaramine; ***Ger.:*** Polaronil; ***Gr.:*** Istamex; Polaramine†; ***Hong Kong:*** Allermin; Apomin; Chlorpyrimine; Dapriton; Kenyamine; Medifen†; Pirimat; Piriton†; Polaramine; Rhiniramine; Sprinsol†; Synchloramin; Uni-Ramine; ***India:*** Cofton; ***Indon.:*** Chlorphenon; Cohistan; CTM; Orphen; Pehachlor; Polamec; Polaramine; Polarist; Polofar; ***Irl.:*** Piriton; ***Israel:*** Ahiston; Anaphyl†; ***Ital.:*** Polaramin; Trimeton; ***Malaysia:*** Chloramine†; Chlormine; Chlorpyrimine; D-Antihist†; Dex-Antihist†; Dexchloramine; Polamine†; Polaramine; Somin; ***Mex.:*** Alerdil; Antadex-H; Blendox; Cloro-Trimeton; Cronal; Docsi; Hierbal; Histadryl; Polaramine†; ***Neth.:*** Polaramine; ***Norw.:*** Phenamin; Polaramin; ***NZ:*** Histafen; Polaramine; ***Philipp.:*** Antamin; Baromini; Chlor-Trimeton; Valemine; Virgomine; ***Port.:*** Trenelone; ***S.Afr.:*** Allergex; Chlor-Trimeton†; Chlorhist†; Polaramine†; Rhineton; ***Singapore:*** Allerphen†; Chloramine; Chlorpyrimine; Dexchloramine; Dextramine; Piriton; Polaramine; Rhiniramine; Somin; ***Spain:*** Antihistaminico; Polaramine; ***Swed.:*** Polaramin; ***Switz.:*** Polaramine; ***Thai.:*** Allergin†; Chlorleate; Chlorpheno; Chlorpyrimine; Cohistan; Histatab; Histatapp; Icolid Plus; Kloramin; Nasamine†; Piriton†; ***UAE:*** Chlorohistol; ***UK:*** Allercalm; Allergy Relief; Allerief; Calimal; Hayleve; Piriton; Pollenase Antihistamine; ***USA:*** Aller-Chlor; Allergy; Allergy Relief; Chlo-Amine; Chlor-Pro; Chlor-Trimeton; ChlorTan; Ed-Chlor-Tan; Efidac 24 Chlorpheniramine; PediaCare Allergy Formula; Pediatan; Pediox-S; QDALL AR; TanaHist PD; Teldrin; ***Venez.:*** Clorotrimeton; Inquiramin†; Liramin.

**Multi-ingredient:** numerous preparations are listed in Part 3.

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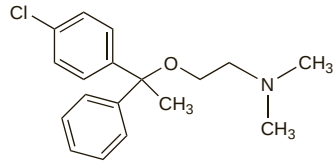
## Chlorphenoxamine Hydrochloride *(BANM, rINNM)*

Chlorphénoxamine, Chlorhydrate de; Chlorphenoxamini Hydrochloridum; Hidrocloruro de clorfenoxamina; Klorfenoksamin Hidroklorür. 2-(4-Chloro-α-methylbenzhydryloxy)-*NN*-dimethylethylamine hydrochloride.

Хлорфеноксамина Гидрохлорид

$C_{18}H_{22}ClNO,HCl$ = 340.3.
*CAS — 77-38-3 (chlorphenoxamine); 562-09-4 (chlorphenoxamine hydrochloride).*
*ATC — D04AA34; R06AA06.*
*ATC Vet — QD04AA34; QR06AA06.*



*(chlorphenoxamine)*