

it should be given at least 30 minutes before travelling), and in the treatment of vertigo of various causes (p.565). Diphenhydramine is used for its antimuscarinic properties in the control of parkinsonism (p.791) and drug-induced extrapyramidal disorders (p.971) (although the possibility that diphenhydramine itself may cause extrapyramidal symptoms should be remembered). Diphenhydramine has pronounced central sedative properties and may be used as a hypnotic in the short-term management of insomnia (p.564). It is a common ingredient 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). It may also be given in combination preparations containing analgesics, particularly paracetamol. Diphenhydramine may be used parenterally as an adjunct in the emergency treatment of anaphylactic shock (p.563) or when oral therapy is not feasible.

For most indications, diphenhydramine hydrochloride is given in usual oral doses of 25 to 50 mg three or four times daily. The dose for children is 6.25 to 25 mg three or four times daily, or a total daily dose of 5 mg/kg may be given in divided doses. The maximum dose in adults and children is about 300 mg daily. A dose of 20 to 50 mg may be used as a hypnotic in adults and children over 12 years old.

When oral therapy is not feasible, diphenhydramine hydrochloride may be given by deep intramuscular injection or by intravenous injection using concentrations of 1% or 5%. Usual doses are 10 to 50 mg, although doses of 100 mg have been given. No more than 400 mg should be given in 24 hours. Children may be given 5 mg/kg daily in divided doses to a maximum of 300 mg in 24 hours. Diphenhydramine hydrochloride is applied topically, usually in preparations containing 1 to 2% although, as with other antihistamines, there is a risk of sensitisation.

Diphenhydramine citrate is given orally in a dose of 76 mg at night in combination preparations for its hypnotic action. Diphenhydramine di(acefyllinate) is given as an antiemetic for the prevention and treatment of motion sickness. The usual oral dose is 90 to 135 mg, which may be repeated if necessary at intervals of at least 6 hours, to a maximum of 540 mg daily. Other diphenhydramine salts that have been used include the polistirex, the salicylate, and the tannate by mouth, the methylbromide rectally, and the metilsulfate applied topically.

Dimenhydrinate (p.576) is diphenhydramine teoclate and mefenidramium metilsulfate is diphenhydramine methylsulfomethylate.

Preparations

BP 2008: Diphenhydramine Oral Solution;

USP 31: Acetaminophen and Diphenhydramine Citrate Tablets; Acetaminophen, Diphenhydramine Hydrochloride, and Pseudoephedrine Hydrochloride Tablets; Diphenhydramine and Pseudoephedrine Capsules; Diphenhydramine Hydrochloride Capsules; Diphenhydramine Hydrochloride Elixir; Diphenhydramine Hydrochloride Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Almerina; Amodyn; Benadryl; Benadryl Antiallergico; Caladryl D; Drepattil; Fabologer; Histalor; Klonadryl; Mudantos H; **Austral.:** Snuzaid; Unison; **Austria:** Calmaben; Dermodyn; Dibondrin; Histaxin; Noctor; Sleepat; **Belg.:** Azaron; Benlyl; Diphamine; Nuicalm; Nustasium; R Calm; **Braz.:** Difendrin; **Canada:** Aller-Aide; Allerdy; Allergy Caplets; Allergy Elixir; Allergy Formula; Allernix; Benadryl; Calmax; Children's Allergy Formula; Dormex; Dormphen; Isomnal; Jack & Jill Bedtime; Jack & Jill Thin Strips Cough & Cold; Neo Citran Nighttime Cough; Nyctol; Simply Sleep; Sleep Aid; Sleep-Eze D; Somnax; Triaminic Thin Strips Nighttime Cough & Runny Nose; Unison; **Chile:** Jaquedryl; Pasient; Somol; **Cz.:** Benadryl N; Psilo-Balsam; **Fr.:** Butix; Nautamine; **Ger.:** Benadryl N; Betadorm D; Dolestan; Dormult N; Emesax; Halbmund; Hevert-Dorm; Moradorm; nervo OPT N; ratioAllerg; S8; Sedativum-Hevert; Sediat; Sedopretten; Sleepat; Vivinox Sleep; **Gr.:** Sleepat; **Hong Kong:** Benadryl; Calox; Hydramine Cream; Unison; **Hung.:** Psilo-Balsam; **India:** Benadryl; Cofryl; Diminil; **Indon.:** Arcodyl; Benadryl; Oteda; Paradyl; Recodyl; Sidiadryl; **Israel:** Nyctol; **Ital.:** Aliserin; Allergan; Nyctol; **Mex.:** Benadryl; Bionaryl; Bonanot; Drafen; Glcodril; Histadryl; Indumir; Lurispain; Nyctol; Tzoali; **Ulcoid.:** Unison; **NZ:** Unison; **Philipp.:** Allerin AH; Benadryl Antihistamine; Benaxil; Dramelin; **Port.:** Benaderma; Benergina; Codleryl; Nyctol; **Rus.:** Psilo-Balsam (Псило-Бальзам); **S.Afr.:** Betasleep; Sleep-eze-PM; **Singapore:** Benocent; Paxidorm; **Spain:** Benadryl; Neosayonol; Nyctol; Sonodor; **Swed.:** Desentol; **Switz.:** Bedorma; Benocent; Comprimes somniferes "S"; Dobacent; **Thai.:** Benadryl; **Turk.:** Allenik; Allerjin; Benison; Fenotral; **UAE:** Amydramine II; **UK:** Adult Chesty Cough; Child Chesty Cough; Dreemon; Histergan; Mandaly Paediatric; Nightcalm; Nyctol; Paxi-

dorm; Sleep Aid; Sleep-eze; **USA:** 40 Winks; Aler-Dryl; AllerMax; Altaryl Childrens Allergy; Banophen Allergy; Ben-Tann; Benadryl; Benadryl Allergy; Benadryl Childrens Allergy; Benadryl Itch; Childrens PediaCare Nighttime Cough; Compoz Night-time Sleep Aid; Dermamycin; Diphen AF; Diphenhist; Dormin; Dyant; Dyuss; Genahist; Maximum Strength Sleepgels; Maximum Strength Unison SleepGels; Miles Nervine; MouthKote P/R; Nyctol; Scot-Tussin Allergy; Siladryl; Silphen; Simply Sleep; Sleep-Ettes D; Sleepwell 2-nite; Snooze Fast; Somnax; Triaminic Cough & Runny Nose; Tusstat; Twi-lite; **Venez.:** Benadryl; Di-Fedril; Ystajl.

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

Diphenylpyraline Hydrochloride (BANM, rINNM)

Diphenylpyraline, Chlorhydrate de; Diphenylpyralini Hydrochloridum; Hidrocloruro de difenilpiralina. 4-Benzhydryloxy-1-methylpiperidine hydrochloride.

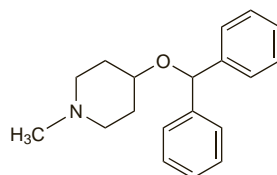
Дифенилпиралина Гидрохлорид

$C_{15}H_{23}NO \cdot HCl = 317.9$.

CAS — 147-20-6 (diphenylpyraline); 132-18-3 (diphenylpyraline hydrochloride).

ATC — R06AA07.

ATC Vet — QR06AA07.



(diphenylpyraline)

Pharmacopoeias. In Br.

BP 2008 (Diphenylpyraline Hydrochloride). A white or almost white, odourless or almost odourless powder. Freely soluble in water, in alcohol, and in chloroform; practically insoluble in ether.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561.

Interactions

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

Pharmacokinetics

◇ References.

- Graham G, Bolt AG. Half-life of diphenylpyraline in man. *J Pharmacokin Biopharm* 1974; **2**: 191–5 (ranged from 24 to 40 hours).

Uses and Administration

Diphenylpyraline hydrochloride, a piperidine derivative, is a sedating antihistamine with antimuscarinic and significant sedative properties.

It has been given for the symptomatic relief of allergic conditions including rhinitis (p.565), and in pruritic skin disorders (p.565). It has also been used in compound preparations for the symptomatic treatment of coughs and the common cold (p.564).

Diphenylpyraline hydrochloride has been given in an oral dose of up to 6 mg daily in 3 or 4 divided doses. Diphenylpyraline and diphenylpyraline hydrochloride have been applied topically although, as with other antihistamines, there is a risk of sensitisation.

Diphenylpyraline teoclate is piprinhydrinate (p.588).

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Arbid N†.

Multi-ingredient: **Austria:** Arbid; Astronautal; Eucillin; Prurimix; Tropoderm; **Belg.:** Bicol; Rhini-San; **Braz.:** Ornatrol†; **Canada:** Creo-Rectal; Vito Bronches†; **Cz.:** Proctospre†; Prurimix†; **Ger.:** Perdiphen†; Proctospre†; Tempil N; **Hong Kong:** Phenahist; **India:** Eskold Expectorant†; Eskold†; **Mex.:** Flumil; **S.Afr.:** Actophlem; Eskomade; Solphylex; Theophen Comp; **Switz.:** Arbid.

Doxylamine Succinate (BANM, rINNM)

Doksilamin Süksinat; Doksilamino-vandenilio süksinatas; Doksylamiinivetyuksinaatti; Doksilamin-hidrogén-szukcinát; Doxylamine Hydrogen Succinate; Doxylamine, hydrogenosuccinate de; Doxylamine, Succinate de; Doxylamin-hydrogen-sukcinát; Doxylamini hydrogenosuccinas; Doxylamini Succinas; Doxylaminium Succinate; Doxylaminvatesuccinat; Histadoxylamine Succinate; Succinato de doxilamina. NN-Dimethyl-2-[α-methyl-α-(2-pyridyl)benzyloxy]ethylamine hydrogen succinate.

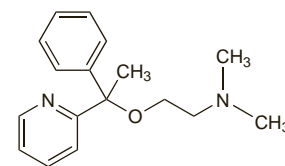
Доксиламин Суксинат

$C_{17}H_{22}N_2O_4 \cdot C_4H_6O_4 = 388.5$.

CAS — 469-21-6 (doxylamine); 562-10-7 (doxylamine succinate).

ATC — R06AA09.

ATC Vet — QR06AA09.



(doxylamine)

Pharmacopoeias. In Eur. (see p.vii) and US.

Ph. Eur. 6.2 (Doxylamine Hydrogen Succinate; Doxylamine Succinate BP 2008). A white or almost white powder. Very soluble in water; freely soluble in alcohol.

USP 31 (Doxylamine Succinate). A white or creamy-white powder having a characteristic odour. Soluble 1 in 1 of water, 1 in 2 of alcohol and of chloroform, and 1 in 370 of ether; very slightly soluble in benzene. Protect from light.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561. The controversy surrounding the use in pregnancy of combination products of doxylamine is discussed on p.563.

Overdose. In an evaluation of 109 cases of intoxication with doxylamine,¹ no correlation was found between the amount ingested or plasma concentration and the frequency or extent of symptoms. The most common symptom was impaired consciousness. Psychotic behaviour, seizures, and antimuscarinic symptoms such as tachycardia and mydriasis were also observed. Rhabdomyolysis occurred in one patient and was accompanied by transient impairment of renal function. The same group commented² that rhabdomyolysis had been noted in 7 of 442 cases of doxylamine overdose, with an associated rise in plasma creatine kinase and myoglobinuria, and suggested that doxylamine has a direct toxic effect on striated muscle.

- Köppel C, et al. Poisoning with over-the-counter doxylamine preparations: an evaluation of 109 cases. *Hum Toxicol* 1987; **6**: 355–9.
- Köppel C, et al. Rhabdomyolysis in doxylamine overdose. *Lancet* 1987; **i**: 442–3.

Interactions

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

Pharmacokinetics

After oral doses of doxylamine succinate peak plasma concentrations occur after 2 to 3 hours. An elimination half-life of about 10 hours has been reported.

◇ References.

- Friedman H, et al. Clearance of the antihistamine doxylamine: reduced in elderly men but not in elderly women. *Clin Pharmacokin* 1989; **16**: 312–16.

Uses and Administration

Doxylamine succinate, a monoethanolamine derivative, is a sedating antihistamine with antimuscarinic and pronounced sedative effects.

Doxylamine succinate is given for the symptomatic relief of hypersensitivity reactions, in pruritic skin disorders (p.565), as a hypnotic in the short-term treatment of insomnia (p.564), and as an ingredient of compound preparations for symptomatic treatment of coughs and the common cold (p.564).

In general it is no longer used in the management of nausea and vomiting of early pregnancy (see p.563 for the controversy that has surrounded the use in pregnancy of combination products of doxylamine).

Oral doses of up to 25 mg of doxylamine succinate have been given every 4 to 6 hours to a maximum of 150 mg daily. The usual hypnotic dose is 25 mg orally at night.

Preparations

USP 31: Acetaminophen, Dextromethorphan Hydrobromide, Doxylamine Succinate, and Pseudoephedrine Hydrochloride Oral Solution; Doxylamine Succinate Syrup; Doxylamine Succinate Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Dozile; Restavit; **Canada:** Unison-2; **Chile:** Calmax; Dorminotil; Nocpaz; Trimetapaz; Zarcop; **Cz.:** Hoggar N†; **Fr.:** Donormyl; Lidene; Nocyt; **Ger.:** Gittalun; Hewedormir; doxyl intens†; Hoggar Night; Mereprine; Munlett†; SchlafTabs; Sedaplus; **India:** Rest-Aid; **Israel:** Sleep Aid; Unison; **NZ:** Dozile; **Philipp.:** Unison; **Port.:** Dormidina; **S.Afr.:** Equi-Sleep†; Restwel; **Spain:** Dormidina; **Switz.:** Sanalepsi N; **Turk.:** Unison; **USA:** Aldex AN; Unison Sleep Tabs.

Multi-ingredient: **Austral.:** Analgesic/Calmative; Codalgil Plus; Dimetapp Cold, Cough & Flu; Dolased Analgesic Calmative; Dolased Day/Night Pain Relief; Fiorinal; Mersyndol; Ordov Migradol†; Panadeine Plus; Panalgesc; **Austria:** Wick Erkaltungs-Saft für die Nacht; Wick Husten-saft; **Belg.:** Pholco-Mereprine; **Braz.:** Broncolex†; EMS Expectorante; Hytos Plus; Revenil; Revenil Dospan; Revenil Expectorante; Silencium; Silomat Plus†; **Canada:** Dalmacol; Diclectin; Mersyndol with Codeine; Neo Citran Cold & Flu†; Nighttime; Nighttime Cold & Flu; Nyquil Sinus; NyQuil†; ratio-Calmadone; Regular Strength Sinus Medication; Tylenol Sinus (Nighttime Relief); Vicks Nyquil Cold & Flu; **Cz.:** Wick Medinait†; **Fr.:** DolirhumePro; **Ger.:** Paedisup; Wick Medinait†; **India:** Doxinate; Vornate; **Indon.:** Dexamolex; Siladex; **Ir.:** Syndol; **Ital.:** Vicks Medinait; **NZ:** Dimetapp Cold, Cough & Flu Day & Night†; Mersyndol; Pryndette†; **Pol.:** Tabcin Impact†; **Port.:** Nauseflex; **S.Afr.:** Abflex; Acurate; Adco-Dol; Adco-Dol; Betapain; Cepacol; Codoxol; Doxsyn; Forpyn†; Lenapain; Nethaprin Dospan; Nethaprin Expectorant; Nomopain; Paxidal; Pyncler†; Pynstop; Sedapain; Sedi-