unsuitable for the prolonged treatment that may be required in palliative care. See also under Interactions, above.

Preparations

BP 2008: Cyclizine Injection; Cyclizine Tablets; Dipipanone and Cyclizine Tablets;
USP 31: Cyclizine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Austria: Echnatol; ***Denm.:*** Marzine; ***Fin.:*** Marzine; ***Hong Kong:*** Marzine†; Valoid†; ***India:*** Medazine; ***Irl.:*** Valoid; ***Neth.:*** Kruidvat Reistabletten; ***Norw.:*** Marzine; ***NZ:*** Marzine; Nausicalm; Valoid; ***S.Afr.:*** Aculoid; Covamet; Emitex†; Medazine; Nauzine; Norizine†; Triazine; Valoid; ***Singapore:*** Marzine†; ***Swed.:*** Marzine†; ***Switz.:*** Marzine; ***UK:*** Valoid; ***USA:*** Bonine for Kids; Marezine.

Multi-ingredient: ***Austria:*** Echnatol B ; Migril; ***Fin.:*** Vertipam; ***Hong Kong:*** Migril†; Wellconal†; ***Irl.:*** Cyclimorph; Diconal†; Migril†; ***Neth.:*** Ercycof†; ***S.Afr.:*** Cyclimorph; Migril; Wellconal; ***UK:*** Cyclimorph; Diconal; Migril.

Cyproheptadine Hydrochloride

(BANM, rINNM)

Ciproheptadin-hidroklorid; Ciproheptadino hidrocloridas; Cyproheptadine, chlorhydrate de; Cyproheptadin-hydrochlorid seskvihydrát; Cyproheptadinhydroklorid; Cyproheptadini hydrochloridum; Cyproheptadini Hydrochloridum Sesquihydricum; Hidrocloruro de ciproheptadina; Siproheptadin Hidroklorür; Syproheptadiinihydrokloridi. 4-(5*H*-Dibenzo[*a,d*]cyclohepten-5-ylidene)-1-methylpiperidine hydrochloride sesquihydrate.

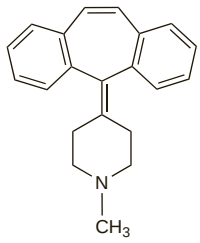
Ципрогептадина Гидрохлорид

$C_{21}H_{21}N,HCl,1/_2H_2O$ = 350.9.

CAS — 129-03-3 (cyproheptadine); 969-33-5 (anhydrous cyproheptadine hydrochloride); 41354-29-4 (cyproheptadine hydrochloride sesquihydrate).

ATC — R06AX02.

ATC Vet — QR06AX02.



(cyproheptadine)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cyproheptadine Hydrochloride). A white or slightly yellow, crystalline powder. Slightly soluble in water; sparingly soluble in alcohol; freely soluble in methyl alcohol. Protect from light.
USP 31 (Cyproheptadine Hydrochloride). A white to slightly yellow, odourless or practically odourless, crystalline powder. Soluble 1 in 275 of water, 1 in 35 of alcohol, 1 in 26 of chloroform, and 1 in 1.5 of methyl alcohol; practically insoluble in ether.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561. Increased appetite and weight gain may occur with cyproheptadine.

Abuse. Dependence developed in a patient who took about 180 mg of cyproheptadine daily by mouth for 5 years.[1]

1. Craven JL, Rodin GM. Cyproheptadine dependence associated with an atypical somatoform disorder. *Can J Psychiatry* 1987; **32:** 143–5.

Effects on the nervous system. Antimuscarinic toxicity manifest by hallucinations and agitation developed in a 9-year-old child taking cyproheptadine 4 mg twice daily for migraine prophylaxis.[1]

1. Watemberg NM, *et al*. Central anticholinergic syndrome on therapeutic doses of cyproheptadine. *Pediatrics* 1999; **103:** 158–60.

Interference with diagnostic tests. Cyproheptadine reduced hypoglycaemia-induced growth hormone secretion by between 5 and 97% in 8 healthy subjects.[1] It was suggested that if patients receiving cyproheptadine were given a pituitary function test that used growth hormone response to insulin-induced hypoglycaemia, then cyproheptadine therapy should be stopped before the test.

UK licensed product information states that cyproheptadine may cause a false positive test result for tricyclic antidepressants in urine.

1. Bivens CH, *et al*. Inhibition of hypoglycaemia-induced growth hormone secretion by the serotonin antagonists cyproheptadine and methysergide. *N Engl J Med* 1973; **289:** 236–9.

Interactions

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

Antidepressants. For reports suggesting that cyproheptadine can reduce the effectiveness of *SSRIs*, see under Fluoxetine, p.396.

Pharmacokinetics

After absorption from the gastrointestinal tract, cyproheptadine hydrochloride undergoes almost complete metabolism. Metabolites are excreted principally in the urine as conjugates, and also in the faeces.

Uses and Administration

Cyproheptadine, a piperidine derivative, is a sedating antihistamine with antimuscarinic, serotonin-antagonist, and calcium-channel blocking actions. It is used as the hydrochloride 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). Other uses include the management of migraine (p.564). Cyproheptadine hydrochloride is given as the sesquihydrate although doses are expressed in terms of the anhydrous substance. Anhydrous cyproheptadine hydrochloride 10 mg is equivalent to about 11 mg of cyproheptadine hydrochloride sesquihydrate.

For allergic conditions and pruritus the oral dose in adults is initially 4 mg three times daily, adjusted as necessary. The average dose requirement is 12 to 16 mg daily in three or four divided doses, but up to 32 mg daily may occasionally be necessary. The dose for children aged 2 to 6 years is 2 mg two or three times daily increasing to a maximum of 12 mg daily and for children aged 7 to 14 years, 4 mg two or three times daily up to a maximum of 16 mg daily. Cyproheptadine is not recommended in debilitated elderly patients.

A dose of 4 mg is used for both prophylaxis and treatment of migraine and other vascular headaches and may be repeated after 30 minutes; patients who respond usually obtain relief with 8 mg, and this dose should not be exceeded within a 4- to 6-hour period. A maintenance dose of 4 mg may be given every 4 to 6 hours.

Other cyproheptadine salts that have been given orally include the acetylaspartate, aspartate, cyclamate, orotate, acefyllinate (7-theophyllineacetate), and the pyridoxal phosphate salt (dihexazine).

Abdominal migraine. Cyproheptadine has been tried in the prophylactic treatment of children with abdominal migraine (see Pizotifen, p.624).

Angina pectoris. Cyproheptadine was used successfully to treat 2 patients with Prinzmetal's angina (p.1157) refractory to standard treatment with calcium-channel blockers and nitrates.[1] Serotonin is an important endocrine mediator of coronary vasospasm and the beneficial effects of cyproheptadine were attributed to its activity as a serotonin antagonist.

1. Schecter AD, *et al*. Refractory Prinzmetal angina treated with cyproheptadine. *Ann Intern Med* 1994; **121:** 113–14.

Appetite disorders. Cyproheptadine has been widely used as an appetite stimulant, including for anorexia nervosa and cachexia (see under Megestrol, p.2115), but in the long-term appears to have little value in producing weight gain and such use is no longer generally recommended. There has been concern that cyproheptadine was being promoted and used inappropriately as an appetite stimulant in some developing countries.[1]

1. Anonymous. Cyproheptadine: no longer promoted as an appetite stimulant. *WHO Drug Inf* 1994; **8:** 66.

Carcinoid syndrome. The management of carcinoid tumours (p.643) is largely symptomatic. Cyproheptadine hydrochloride, a serotonin antagonist, has had limited success in relieving symptoms such as diarrhoea but somatostatin analogues may now be preferred.[1] It has been used successfully with fenclonine, aprotinin, methylprednisolone, and antibacterials to prevent complications arising from release of tumour metabolites during hepatic embolisation, a procedure sometimes used to relieve the symptoms of carcinoid syndrome.[2] There have been a few reports of tumour regression, in addition to symptomatic control, after treatment of carcinoid tumours with cyproheptadine.[3,4]

1. Caplin ME, *et al*. Carcinoid tumour. *Lancet* 1998; **352:** 799–805.
2. Maton PN, *et al*. Role of hepatic arterial embolisation in the carcinoid syndrome. *BMJ* 1983; **287:** 932–5. Correction to dosage. ibid.; 1664.
3. Harris AL, Smith IE. Regression of carcinoid tumour with cyproheptadine. *BMJ* 1982; **285:** 475.
4. Leitner SP, *et al*. Partial remission of carcinoid tumor in response to cyproheptadine. *Ann Intern Med* 1989; **111:** 760–1.

Serotonin syndrome. Cyproheptadine has been successfully used to treat the serotonin syndrome (p.416) in patients who have developed the syndrome after overdoses involving serotonergic drugs or who have had their antidepressant therapy changed without an adequate wash-out period.[1,2]

1. Lappin RI, Auchincloss EL. Treatment of the serotonin syndrome with cyproheptadine. *N Engl J Med* 1994; **331:** 1021–2.
2. McDaniel WW. Serotonin syndrome: early management with cyproheptadine. *Ann Pharmacother* 2001; **35:** 870–3.

Sexual dysfunction. Cyproheptadine has been tried in the management of sexual dysfunction induced by SSRIs (see Effects on Sexual Function under Fluoxetine, p.393) but may possibly reduce the effectiveness of the SSRI.

Preparations

BP 2008: Cyproheptadine Tablets;
USP 31: Cyproheptadine Hydrochloride Syrup; Cyproheptadine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Periactin; ***Austria:*** Periactin; ***Belg.:*** Periactin; ***Braz.:*** Periatin; Preptin†; ***Chile:*** Viternum; ***Cz.:*** Peritol; ***Denm.:*** Periactin†; ***Fr.:*** Periactine; ***Ger.:*** Peritol; ***Hong Kong:*** Cyprogin; ***Hung.:*** Peritol; ***India:*** Apenorm†; Ciplactin; Peritol; Practin; ***Indon.:*** Alphahist; Apeton; Cydifar; Cylat; Ennamax; Esprocy; Glocyp; Heptasan; Lexahist; Poncohist; Profut; Prohessen; Pronicy; Sinapdin; ***Irl.:*** Periactin; ***Ital.:*** Periactin; ***Mex.:*** Viternum; ***Neth.:*** Periactin; ***NZ:*** Periactin; ***Pol.:*** Peritol; ***Port.:*** Trimetabol†; Viternum; ***Rus.:*** Peritol (Перитол); ***S.Afr.:*** Cipla-Actin; Periactin; ***Singapore:*** Cyprotin; ***Spain:*** Klarivitina†; Periactin; Viternum; ***Swed.:*** Periactin; ***Switz.:*** Periactin†; ***Thai.:*** Cyheptine; Cyprogin; Cyprono; Cyprosian; Cyprotec; Hepdine; Periactin; Polytab; ***Turk.:*** Prakten; Sipraktin; ***UK:*** Periactin; ***Venez.:*** Cyprodin; Eptacor†; Periactin†.

Multi-ingredient: ***Arg.:*** Apeplus; Apetitol Forte; Ciprocort; Ciprovit Calcio; Ciprovit Energizante; Ciprovit Magnesico; Mikesan; Nipiol†; Potencil; Sudevil Vita; ***Braz.:*** Apetivit BC; Apetiviton BC; Apevitin BC; Apmed; Bonapetit†; Cobactin; Cobaglobal; Cobavit; Cobavital; Polivitam†; Trimetabol; ***Chile:*** Apetrol; Grisetin Con Carnitina†; Orodina; Peracon; Revil; Rodepan; Viternum Vitaminado; ***Hong Kong:*** Petina Compound; Tres Orix Forte; ***Ital.:*** Carpantin†; ***Mex.:*** Cipro-Dexol†; Ciprolisina; Pangavit Pediatrico; Rocavit; ***Spain:*** Anti Anorex Triple; Childrevit†; Covitasa B12; Desarrol; Enoton; Glotone; Medenorex; Pantobamin; Pranzo; Stolina; Tonico Juventus; Tres Orix Forte†; Trimetabol; Troforex Pepsico; Vita Menal; ***Venez.:*** Cipromet†; Cyprodex.

Deptropine Citrate *(BANM, rINNM)*

Citrato de deptropina; Deptropiinisitraatti; Deptropincitrat; Deptropin-citrát; Deptropine, citrate de; Deptropini citras; Deptropino citratas; Dibenzheptropine Citrate. (1*R*,3*r*,5*S*)-3-(10,11-Dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-yloxy)tropane dihydrogen citrate.

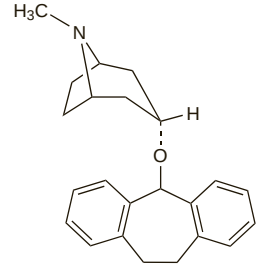
Дептропина Цитрат

$C_{23}H_{27}NO,C_6H_8O_7$ = 525.6.

CAS — 604-51-3 (deptropine); 2169-75-7 (deptropine citrate).

ATC — R06AX16.

ATC Vet — QR06AX16.



(deptropine)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Deptropine Citrate). A white or almost white, microcrystalline powder. Very slightly soluble in water and in dehydrated alcohol; practically insoluble in dichloromethane. A saturated solution in water has a pH of 3.7 to 4.5. Protect from light.

Profile

Deptropine citrate is a sedating antihistamine (p.561) with a marked antimuscarinic action. It was given by mouth mainly in the treatment of respiratory-tract disorders.