atic and the danger of an interaction between the drugs should also be borne in mind (see under Interactions, above).

1. Leucht S, *et al*. Lithium for schizophrenia revisited: a systematic review and meta-analysis of randomized controlled trials. *J Clin Psychiatry* 2004; **65:** 177–86.

Skin disorders. Some salts or derivatives of lithium (notably lithium succinate, p.1604, but also lithium gluconate) have been applied topically in preparations for seborrhoeic dermatitis.

References.

1. Dreno B, *et al*. Lithium gluconate 8% vs ketoconazole 2% in the treatment of seborrhoeic dermatitis: a multicentre, randomized study. *Br J Dermatol* 2003; **148:** 1230–6.

Preparations

BP 2008: Lithium Carbonate Tablets; Lithium Citrate Oral Solution; Prolonged-release Lithium Carbonate Tablets;
USP 31: Lithium Carbonate Capsules; Lithium Carbonate Extended-release Tablets; Lithium Carbonate Tablets; Lithium Citrate Syrup.

Proprietary Preparations (details are given in Part 3)
Arg.: Ceglution; Eskalit; Karlit; Lithiun; ***Austral.:*** Lithicarb; Quilonum; ***Austria:*** Neurolepsin; Quilonorm; ***Belg.:*** Camcolit; Maniprex; Priadel; ***Braz.:*** Carbolim; Carbolitium; Litiocar†; Neurolithium; ***Canad.:*** Carbolith; Duralith; Lithane; ***Chile:*** Cabalex†; Cade L; Carbolit; Carboron; Psicolit; ***Cz.:*** Contemnol†; ***Denm.:*** Litarex; ***Fin.:*** Lito; ***Fr.:*** Lithioderm; Neurolithium; Teralithe; ***Ger.:*** Hypnorex; leukominerase†; Li 450†; Quilonum; ***Gr.:*** Lithiofor; Milithin; ***Hong Kong:*** Camcolit; Lithicarb; Lithiofor; ***Hung.:*** Liticarb; ***India:*** Licab; Staleth; ***Indon.:*** Frimania; ***Irl.:*** Camcolit; Priadel; ***Israel:*** Licarbium; ***Ital.:*** Carbolithium; ***Jpn:*** Limas; ***Malaysia:*** Priadel†; ***Mex.:*** Carbolit; Litheum; ***Neth.:*** Camcolit; Litarex; Priadel; ***Norw.:*** Lithionit; ***NZ:*** Lithicarb; Priadel; ***Philipp.:*** Quilonium-R; ***Port.:*** Priadel; ***S.Afr.:*** Camcolit; Lentolith; Quilonum; ***Singapore:*** Camcolit; Priadel†; ***Spain:*** Plenur; ***Swed.:*** Lithionit; ***Switz.:*** Litarex; Lithiofor; Neurolithium; Priadel; Quilonorm; ***Thai.:*** Licarb; Limed; Lit-300; Phanate; ***Turk.:*** Kilonum; Lithunil; ***UK:*** Camcolit; Li-Liquid; Liskonum; Lithonate; Priadel; ***USA:*** Eskalith†; Lithobid.

Multi-ingredient: ***Austral.:*** Caprilate; ***Ger.:*** NeyDop N (Revitorgan-Dilutionen N Nr 97)†; Togal Classic; ***Spain:*** Citinoides.

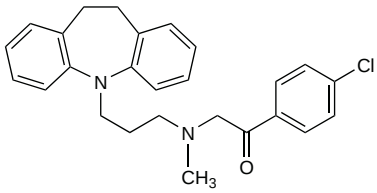
Lofepramine Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de lofepramina; Leo-640; Lofépramine, Chlorhydrate de; Lofepramini Hydrochloridum; Lopramine Hydrochloride; WHR-2908A. 5-{3-[*N*-(Chlorophenacyl)-*N*-methylamino]propyl}-10,11-5*H*-dihydrodibenz[*b,f*]azepine hydrochloride.

Лофепрамина Гидрохлорид

$C_{26}H_{27}ClN_2O,HCl$ = 455.4.

CAS — 23047-25-8 (lofepramine); 26786-32-3 (lofepramine hydrochloride).
ATC — N06AA07.
ATC Vet — QN06AA07.



(lofepramine)

Pharmacopoeias. In *Br.*
BP 2008 (Lofepramine Hydrochloride). A fine, yellowish-white to green-yellow powder with a faint characteristic odour. It exhibits polymorphism. Very slightly soluble in alcohol and in methyl alcohol; slightly soluble in acetone. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for tricyclic antidepressants in general (see Amitriptyline, p.376) although it has a lower incidence of antimuscarinic adverse effects. Lofepramine should be avoided in patients with severe hepatic or severe renal impairment.

Effects on the liver. See under Amitriptyline, p.377.

Overdosage. Lofepramine may be less toxic in overdosage than earlier tricyclics.[1] An analysis of data from the Office of National Statistics in England and Wales has also shown that the risk of death after an overdose with lofepramine was not significantly different from that associated with the SSRIs which, as a group, are considered to be safer in overdose than the tricyclics.[2]

1. Reid F, Henry JA. Lofepramine overdosage. *Pharmacopsychiatry* 1990; **23:** 23–27.
2. Mason J, *et al*. Fatal toxicity associated with antidepressant use in primary care. *Br J Gen Pract* 2000; **50:** 366–70.

Interactions

For interactions associated with tricyclic antidepressants, see Amitriptyline, p.379.

Pharmacokinetics

Lofepramine is readily absorbed from the gastrointestinal tract; peak plasma concentrations occur within 1 hour of oral doses. Since lofepramine slows gastrointestinal transit time absorption can, however, be delayed, particularly in overdosage. It is extensively demethylated by first-pass metabolism in the liver to its active, primary metabolite, desipramine (p.387). Paths of metabolism also include *N*-oxidation and hydroxylation. The plasma half-life is about 5 hours. Lofepramine is mainly excreted in the urine, chiefly in the form of its metabolites. Up to 99% of lofepramine is bound to plasma proteins. Lofepramine is distributed into breast milk.

Uses and Administration

Lofepramine is a dibenzazepine tricyclic antidepressant with actions and uses similar to those of amitriptyline (p.381). One of its metabolites is desipramine (p.387). Lofepramine is one of the less sedating tricyclics.

In the treatment of depression (p.373) lofepramine is given orally as the hydrochloride although doses are expressed in terms of the base. Lofepramine hydrochloride 76.1 mg is equivalent to about 70 mg of lofepramine. The usual dose is the equivalent of 70 mg two or three times daily.

Lofepramine should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Administration in the elderly. UK licensed drug information suggests that some elderly patients may respond to lower than usual doses of lofepramine, but in a study[1] involving 46 elderly patients with various grades of depression lofepramine 70 mg once daily was no more effective than placebo at the end of 28 days of treatment.

1. Tan RSH, *et al*. The effect of low dose lofepramine in depressed elderly patients in general medical wards. *Br J Clin Pharmacol* 1994; **37:** 321–4.

Preparations

BP 2008: Lofepramine Tablets.

Proprietary Preparations (details are given in Part 3)
Cz.: Tymelyt†; ***Denm.:*** Tymelyt†; ***Ger.:*** Gamonil†; ***Irl.:*** Gamanil; ***Port.:*** Deprimil†; ***S.Afr.:*** Emdalen; ***Spain:*** Deftan†; ***Swed.:*** Tymelyt†; ***Switz.:*** Gamonil†; ***UK:*** Feprapax†; Gamanil†; Lomont.

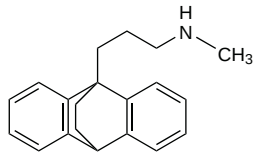
Maprotiline *(BAN, USAN, rINN)*

Maprotiliini; Maprotilin; Maprotilina; Maprotilinum. 3-(9,10-Dihydro-9,10-ethanoanthracen-9-yl)propyl(methyl)amine; *N*-Methyl-9,10-ethanoanthracene-9(10*H*)-propylamine.

Мапротилин

$C_{20}H_{23}N$ = 277.4.

CAS — 10262-69-8.
ATC — N06AA21.
ATC Vet — QN06AA21.



Maprotiline Hydrochloride *(BANM, rINNM)*

Ba-34276; Hidrocloruro de maprotilina; Maprotiliinihydrokloridi; Maprotilin Hidroklorür; Maprotiline, chlorhydrate de; Maprotilinhidroklorid; Maprotilin-hydrochlorid; Maprotilinhydroklorid; Maprotilini hydrochloridum; Maprotilino hidrochloridas.

Мапротилина Гидрохлорид

$C_{20}H_{23}N,HCl$ = 313.9.

CAS — 10347-81-6.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn,* and *US.*
Ph. Eur. 6.2 (Maprotiline Hydrochloride). A white or almost white crystalline powder. It shows polymorphism. Slightly soluble in water; soluble in alcohol; very slightly soluble in acetone; sparingly soluble in dichloromethane; freely soluble in methyl alcohol.
USP 31 (Maprotiline Hydrochloride). A fine white to off-white, practically odourless, crystalline powder. Slightly soluble in water; freely soluble in chloroform and in methyl alcohol; practically insoluble in isooctane. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

Adverse effects with maprotiline, a tetracyclic antidepressant, are broadly similar to those with tricyclic antidepressants (see Amitriptyline, p.376) but antimuscarinic effects are less frequent.

Skin rashes seem more common with maprotiline than with tricyclic antidepressants. Seizures have occurred in patients with no prior history of such disorders as well as in those with a history of epilepsy and the risk is increased if high doses of maprotiline are given. It should not be used in patients with epilepsy or a lowered seizure threshold.

Incidence of adverse effects. By March 1985 the UK CSM[1] had received reports of the following adverse reactions associated with maprotiline from a cumulative total of 2.5 million prescriptions: convulsions (124), hepatic reactions (4), and haematological reactions (8). There had also been 454 reports of skin rashes.

1. CSM. Dangers of newer antidepressants. *Current Problems 15* 1985. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024422&RevisionSelectionMethod=LatestReleased (accessed 05/08/08)

Effects on the skin. In addition to many recorded instances of skin rashes with maprotiline (see Incidence of Adverse Effects, above) cutaneous vasculitis, which resolved on stopping therapy, has also been seen.[1]

1. Oakley AMM, Hodge L. Cutaneous vasculitis from maprotiline. *Aust N Z J Med* 1985; **15:** 256–7.

Epileptogenic effect. In a retrospective review of 186 psychiatric patients with no history of seizures, 5 of 32 patients taking maprotiline developed generalised tonic-clonic seizures, compared with 1 of 45 receiving a tricyclic antidepressant.[1] There were no seizures in the remaining patients who received other medications, or no drug treatment. Two of the 5 patients having seizures with maprotiline were taking doses of 75 to 150 mg daily, 2 were taking daily doses of 200 to 300 mg, and one patient had partial complex seizures with a daily dose of 150 mg and generalised tonic-clonic seizures after increasing the daily dose to 300 mg.

1. Jabbari B, *et al*. Incidence of seizures with tricyclic and tetracyclic antidepressants. *Arch Neurol* 1985; **42:** 480–1.

Overdosage. Apart from seizures being more common with maprotiline, features of overdosage are similar to those experienced with tricyclic antidepressant poisonings (see Adverse Effects of Amitriptyline, p.376).

For a discussion of choice of antidepressant with respect to toxicity in overdosage, see under Depression, p.373.

References.

1. Crome P, Newman B. Poisoning with maprotiline and mianserin. *BMJ* 1977; **2:** 260.
2. Curtis RA, *et al*. Fatal maprotiline intoxication. *Drug Intell Clin Pharm* 1984; **18:** 716–20.
3. Knudsen K, Heath A. Effects of self poisoning with maprotiline. *BMJ* 1984; **288:** 601–3.
4. Crome P, Ali C. Clinical features and management of self-poisoning with newer antidepressants. *Med Toxicol* 1986; **1:** 411–20.

Porphyria. Maprotiline hydrochloride is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

Interactions associated with maprotiline are similar to those associated with tricyclic antidepressants (see Amitriptyline, p.379).

Pharmacokinetics

Maprotiline is slowly but completely absorbed from the gastrointestinal tract. Peak plasma concentrations are reached within 8 hours of an oral dose. It is widely distributed throughout the body and plasma protein binding is about 88 to 89%.

Maprotiline is extensively demethylated in the liver to its principal active metabolite, desmethylmaprotiline; paths of metabolism of both maprotiline and desmethylmaprotiline include *N*-oxidation, aliphatic and aromatic hydroxylation, and the formation of aromatic methoxy derivatives. In addition to desmethylmaprotiline, maprotiline-*N*-oxide is also reported to be pharmacologically active. The average elimination half-life of maprotiline is reported to be about 43 hours and that of its active metabolite even longer (range 60 to 90 hours). Maprotiline is excreted in the urine, mainly in the form of its metabolites, either in free or in conjugated form; appreciable amounts are also excreted in the faeces.

Maprotiline is distributed into breast milk (see Breast Feeding under Precautions of Amitriptyline, p.378).

◊ References.

1. Maguire KP, *et al*. An evaluation of maprotiline: intravenous kinetics and comparison of two oral doses. *Eur J Clin Pharmacol* 1980; **18:** 249–54.
2. Alkalay D, *et al*. Bioavailability and kinetics of maprotiline. *Clin Pharmacol Ther* 1980; **27:** 697–703.
3. Firkusny L, Gleiter H. Maprotiline metabolism appears to cosegregate with the genetically-determined CYP2D6 polymorphic hydroxylation of debrisoquine. *Br J Clin Pharmacol* 1994; **37:** 383–8.

Uses and Administration

Maprotiline is a tetracyclic antidepressant with actions and uses similar to those of tricyclic antidepressants (see Amitriptyline, p.381). It is one of the more sedating antidepressants but antimuscarinic effects are less marked. Like the tricyclics, maprotiline is an inhibitor of the reuptake of noradrenaline; it also has weak affinity for central adrenergic (α_1) receptors.

Maprotiline is usually given orally as the hydrochloride but it has also been given by injection as the mesilate and in oral drops as the resinate.

In the treatment of depression (p.373) maprotiline hydrochloride is given in oral doses of 25 to 75 mg daily in divided doses, gradually increased to 150 mg daily if necessary; up to 225 mg daily may be required in severely depressed patients in hospital. The dosage should be adjusted after 2 weeks according to response. Because of the prolonged half-life of maprotiline the total daily dose may also be given as a single dose. A suggested initial dose for elderly patients is 25 mg daily gradually increased according to response to 50 to 75 mg daily.

Maprotiline should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Preparations

USP 31: Maprotiline Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Austria: Ludiomil; ***Belg.:*** Ludiomil; ***Braz.:*** Ludiomil; ***Canad.:*** Ludiomil†; ***Chile:*** Mapromil; ***Cz.:*** Ludiomil; Maprotibene; ***Denm.:*** Ludiomil; Maludil; ***Fr.:*** Ludiomil; ***Ger.:*** Deprilept; Ludiomil; Maprolu; ***Gr.:*** Aprotilin†; Ludiomil; ***Hong Kong:*** Ludiomil†; ***Hung.:*** Ludiomil; Maprolu†; ***Indon.:*** Ludiomil; Ludios; Sandepril; Tilsan; ***Israel:*** Melodil; ***Ital.:*** Ludiomil; ***Malaysia:*** Ludiomil; ***Mex.:*** Ludiomil; ***Neth.:*** Ludiomil; ***NZ:*** Ludiomil; ***Pol.:*** Ludiomil; ***Port.:*** Ludiomil; ***Rus.:*** Ludiomil (Людиомил); ***S.Afr.:*** Ludiomil; ***Singapore:*** Ludiomil†; ***Spain:*** Ludiomil; ***Swed.:*** Ludiomil; ***Switz.:*** Ludiomil; ***Thai.:*** Ludiomil; ***Turk.:*** Ludiomil; Maprotil; ***UK:*** Ludiomil†; ***Venez.:*** Ludiomil.

Melitracen Hydrochloride *(USAN, rINNM)*

Hidrocloruro de melitraceno; Mélitracène, Chlorhydrate de; Melitraceni Hydrochloridum; N-7001; U-24973A. 3-(9,10-Dihydro-10,10-dimethyl-9-anthrylidene)propyldimethylamine hydrochloride.

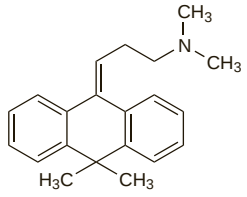
Мелитрацена Гидрохлорид

$C_{21}H_{25}N,HCl$ = 327.9.

CAS — 5118-29-6 (melitracen); 10563-70-9 (melitracen hydrochloride).

ATC — N06AA14.

ATC Vet — QN06AA14.



(melitracen)

Profile

Melitracen is a tricyclic antidepressant (see Amitriptyline, p.376).

In the treatment of depression (p.373) melitracen is given orally as the hydrochloride although doses are expressed in terms of the base; melitracen hydrochloride 28.1 mg is equivalent to about 25 mg of melitracen. The recommended initial dose is the equivalent of 25 mg two or three times daily gradually increased to a total of 225 mg daily if necessary. Elderly patients should generally be given reduced doses of 25 or 30 mg daily initially. Melitracen may also be given in lower doses with flupentixol (p.997) in the management of depression with anxiety. A combination of melitracen 10 mg and flupentixol 500 micrograms is given orally in the morning and at midday. In severe cases the morning dose may be doubled. The total daily dose should not exceed melitracen 40 mg and flupentixol 2 mg. Elderly patients may be given melitracen 10 mg with flupentixol 500 micrograms in the morning; in severe cases this dose may be given in the morning and at midday.

Melitracen should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Dixeran; ***Belg.:*** Dixeran†.

Multi-ingredient: ***Austria:*** Deanxit; ***Belg.:*** Deanxit; ***Hong Kong:*** Anfree; Deanxit; ***Ital.:*** Deanxit†; ***Singapore:*** Deanxit; ***Spain:*** Deanxit; ***Switz.:*** Deanxit; ***Thai.:*** Deanxit.

Mianserin Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de mianserina; Mianseriinihydrokloridi; Mianserin Hidroklorür; Miansérine, chlorhydrate de; Mianserin-hydrochlorid; Mianserinhydroklorid; Mianserini hydrochloridum; Mianserino hidrochloridas; Mianseryny chlorowodorek; Mianszerin-hidroklorid; Org-GB-94. 1,2,3,4,10,14b-Hexahydro-2-methyldibenzo[*c,f*]pyrazino[1,2-*a*]azepine hydrochloride.

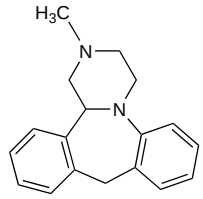
Миансерина Гидрохлорид

$C_{18}H_{20}N_2,HCl$ = 300.8.

CAS — 24219-97-4 (mianserin); 21535-47-7 (mianserin hydrochloride).

ATC — N06AX03.

ATC Vet — QN06AX03.



(mianserin)

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Mianserin Hydrochloride). A white or almost white crystalline powder or crystals. Sparingly soluble in water; slightly soluble in alcohol; soluble in dichloromethane. A 1% solution in water has a pH of 4.0 to 5.5. Protect from light.

Adverse Effects

Antimuscarinic and cardiac adverse effects are fewer and milder with mianserin, a tetracyclic antidepressant, than with tricyclic antidepressants but effects are otherwise broadly similar (see Amitriptyline, p.376); mianserin may be associated with a lower risk of cardiotoxicity in overdosage.

The most common adverse effect associated with mianserin is drowsiness. Mianserin also causes bone-marrow depression usually presenting as leucopenia, granulocytopenia, or agranulocytosis; aplastic anaemia has been reported. These adverse haematological reactions generally occur during the first few weeks of therapy and especially in the elderly.

Other adverse effects reported include disturbances of liver function and jaundice, breast disorders (gynaecomastia, nipple tenderness, and non-puerperal lactation), and polyarthropathy.

Effects on the blood. Between 1976 and the end of 1988 the UK CSM had received 239 reports of adverse haematological reactions associated with mianserin use.[1] The reports included 68 of agranulocytosis and 84 of granulocytopenia or leucopenia where mianserin was considered to be the probable or possible cause; there had been 17 fatalities. Allowing for the pattern of prescribing there was a greater number of reports of white blood cell disorders in patients over 65 years of age but there was no sex difference. The data also indicated that the adverse reactions were most likely to develop during the first 3 months of therapy. By the end of 1992 the number of reports of mianserin-induced agranulocytosis or neutropenia received by the CSM[2] had risen to 79 and 105, respectively.

A case of fatal aplastic anaemia associated with mianserin use has also been reported.[3]

Proposed mechanisms of mianserin haematotoxicity have included a direct toxicity[4] and an immunologically-mediated mechanism.[5] There is evidence from studies *in vitro* of a significant correlation between the desmethyl metabolite and cytotoxicity. Mianserin is given as a racemic preparation and the formation of metabolites was greater with the *R*(−)-enantiomer than with the *S*(+)-enantiomer.[6]

1. CSM. Mianserin and white blood cell disorders in the elderly. *Current Problems 25* 1989. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024441&RevisionSelectionMethod=LatestReleased (accessed 05/08/08)
2. CSM/MCA. Drug-induced neutropenia and agranulocytosis. *Current Problems* 1993; **19:** 10–11. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024456&RevisionSelectionMethod=LatestReleased (accessed 05/08/08)
3. Durrant S, Read D. Fatal aplastic anaemia associated with mianserin. *BMJ* 1982; **285:** 437.
4. O'Donnell JL, *et al.* Possible mechanism for mianserin induced neutropenia associated with saturable elimination kinetics. *BMJ* 1985; **291:** 1375–6.
5. Stricker BHC, *et al.* Thrombocytopenia and leucopenia with mianserin-dependent antibodies. *Br J Clin Pharmacol* 1985; **19:** 102–4.
6. Riley RJ, *et al.* A stereochemical investigation of the cytotoxicity of mianserin metabolites in vitro. *Br J Clin Pharmacol* 1989; **27:** 823–30.

Effects on the cardiovascular system. Although mianserin is considered to be less cardiotoxic than the tricyclic antidepressants adverse effects have been noted in individual patients. Two elderly patients developed signs of disturbed cardiac function (cardiac failure, atrial and ventricular fibrillation, bradycardia, and frequent ventricular ectopic beats) which resolved after the drug was stopped.[1] One of the patients also developed hypokalaemia which was possibly caused by mianserin. It was suggested that persons most likely to experience problems were the elderly with a history of cardiovascular disorders. Further reports of mianserin-induced cardiac effects include recurrent ventricular fibrillation in a 61-year-old man after an overdose of mianserin[2] and bradycardia in a 50-year-old woman after a therapeutic dose.[3]

1. Whiteford H, *et al.* Disturbed cardiac function possibly associated with mianserin therapy. *Med J Aust* 1984; **140:** 166–7.
2. Haefeli WE, *et al.* Recurrent ventricular fibrillation in mianserin intoxication. *BMJ* 1991; **302:** 415–16.
3. Carcone B, *et al.* Symptomatic bradycardia caused by mianserin at therapeutic doses. *Hum Exp Toxicol* 1991; **10:** 383–4.

Effects on the liver. By March 1985 the UK CSM had received 57 reports of hepatic reactions associated with mianserin use from a total of 5 million prescriptions. Reactions had included jaundice and other abnormalities of liver function, but no fatalities had been reported.[1]

Case reports have also been published concerning jaundice;[2-5] liver function returned to normal after stopping mianserin or lowering the dose.

1. CSM. Dangers of newer antidepressants. *Current Problems 15* 1985. http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024422&RevisionSelectionMethod=LatestReleased (accessed 14/08/08)
2. Adverse Drug Reactions Advisory Committee. Mianserin: a possible cause of neutropenia and agranulocytosis. *Med J Aust* 1980; **2:** 673–4.
3. Goldstraw PW, *et al.* Mianserin and jaundice. *N Z Med J* 1983; **96:** 985.
4. Zarski J-P, *et al.* Toxicité hépatique des nouveaux anti-dépresseurs: a propos d'une observation. *Gastroenterol Clin Biol* 1983; **7:** 220–1.
5. Otani K, *et al.* Hepatic injury caused by mianserin. *BMJ* 1989; **299:** 519.

Effects on the musculoskeletal system. A patient developed an acute polyarthritis affecting the hands and feet 6 days after starting therapy with mianserin;[1] at that time the UK CSM had received 19 reports of arthritis and arthralgia associated with mianserin. For the suggestion that effects at serotonin receptors may be involved in such adverse effects see under Mirtazapine, p.410.

1. Hughes A, Coote J. Arthropathy associated with treatment with mianserin. *BMJ* 1986; **292:** 1050.

Effects on the skin. Reports of adverse dermatological reactions in individual patients related to mianserin therapy have included toxic epidermal necrolysis[1] and erythema multiforme.[2,3]

1. Randell P. Tolvon and toxic epidermal necrolysis. *Med J Aust* 1979; **2:** 653.
2. Quraishy E. Erythema multiforme during treatment with mianserin—a case report. *Br J Dermatol* 1981; **104:** 481.
3. Cox NH. Erythema multiforme due to mianserin—a case against generic prescribing. *Br J Clin Pract* 1985; **39:** 293–4.

Effects on the tongue. Glossitis associated with mianserin therapy was reported in 2 patients.[1] Additionally, glossitis accompanied by severe facial oedema has been noted in another patient.[2] In all cases symptoms resolved after withdrawal of mianserin.

1. de la Fuente JR, Berlanga C. Glossitis associated with mianserin. *Lancet* 1984; **i:** 233.
2. Leibovitch G, *et al.* Severe facial oedema and glossitis associated with mianserin. *Lancet* 1989; **ii:** 871–2.

Epileptogenic effect. By March 1985 the UK CSM had received 64 reports of convulsions associated with mianserin use from a total of 5 million prescriptions.[1] In a previous review[2] concerning 40 of these cases it was considered that a causal connection could be established only in a minority. It was suggested that mianserin is no more epileptogenic than tricyclic antidepressants, an opinion that was also shared by other reviewers.[3]

1. CSM. Dangers of newer antidepressants. *Current Problems 15* 1985. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024422&RevisionSelectionMethod=LatestReleased (accessed 05/08/08)
2. Edwards JG, Glen-Bott M. Mianserin and convulsive seizures. *Br J Clin Pharmacol* 1983; **15:** 299S–311S.
3. Richens A, *et al.* Antidepressant drugs, convulsions and epilepsy. *Br J Clin Pharmacol* 1983; **15:** 295S–298S.

Overdosage. Experience with 100 consecutive cases of intoxication with mianserin[1] revealed that when it was the only drug ingested symptoms were mild and neither deep coma nor convulsions occurred. More serious symptoms and 2 fatalities were seen in patients who had taken multiple drug overdoses. The results suggested that after an acute overdose mianserin is less toxic than the tricyclic antidepressants. This conclusion was also supported by a large follow-up study[2] comparing the outcome of suicide attempts among patients who had taken mianserin in overdose with those who had taken amitriptyline.

1. Chand S, *et al.* One hundred cases of acute intoxication with mianserin hydrochloride. *Pharmakopsychiatrie* 1981; **14:** 15–17.
2. Inman WHW. Blood disorders and suicide in patients taking mianserin or amitriptyline. *Lancet* 1988; **ii:** 90–2.

Precautions

As for tricyclic antidepressants in general (see Amitriptyline, p.378). Although mianserin is less cardiotoxic than the tricyclic antidepressants, it still should be used with caution in patients with cardiovascular disorders, such as heart block, or after recent myocardial infarction. Similarly, patients with angle-closure glaucoma or prostatic hyperplasia should be monitored even though antimuscarinic effects are rare. Mianserin should be used with caution in patients with diabetes mellitus, epilepsy, and hepatic or renal impairment; it should be avoided in severe hepatic disease.

Patients should be carefully monitored during early antidepressant therapy until significant improvement in depression is observed because suicide is an inherent risk in depressed patients. For further details, see under Depression, p.373. Suicidal thoughts and behaviour may also develop during early treatment with antidepressants for other disorders; the same precautions observed when treating patients with depression should therefore be observed when treating patients with other disorders.