Pain. Antidepressants, usually amitriptyline or another tricyclic, are useful in alleviating some types of pain (see Choice of Analgesic, p.2). Nortriptyline has also been tried and may produce fewer adverse effects than amitriptyline. An initial oral dose of 10 to 25 mg at night has been suggested by the *BNF* for the management of **neuropathic pain**.

References to the use of nortriptyline.

1. Atkinson JH, *et al.* A placebo-controlled randomized clinical trial of nortriptyline for chronic low back pain. *Pain* 1998; **76:** 287–96.
2. Watson CP, *et al.* Nortriptyline versus amitriptyline in postherpetic neuralgia: a randomized trial. *Neurology* 1998; **51:** 1166–71.

Smoking cessation. For reference to the use of nortriptyline in management of smoking cessation, see under Amitriptyline, p.382.

Preparations

BP 2008: Nortriptyline Capsules; Nortriptyline Tablets;
USP 31: Nortriptyline Hydrochloride Capsules; Nortriptyline Hydrochloride Oral Solution.

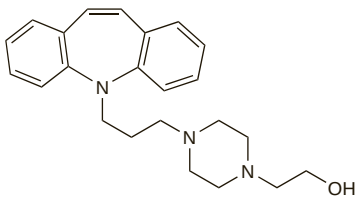
Proprietary Preparations (details are given in Part 3)
Arg.: Ateben†; ***Austral.:*** Allegron; ***Austria:*** Nortrilen; ***Belg.:*** Nortrilen; ***Braz.:*** Nortrip; Pamelor; ***Canad.:*** Aventyl; Norventyl†; ***Cz.:*** Nortrilen; ***Denm.:*** Noritren; ***Fin.:*** Noritren; ***Ger.:*** Nortrilen; ***Gr.:*** Nortrilen; ***Hong Kong:*** Nortrilen; ***India:*** Sensival; ***Israel:*** Nortylin; ***Ital.:*** Noritren; ***Neth.:*** Nortrilen; ***Norw.:*** Noritren; ***NZ:*** Norpress; ***Port.:*** Norterol; ***Spain:*** Norfenazin; Paxtibi; ***Swed.:*** Sensaval; ***Switz.:*** Nortrilen; ***Thai.:*** Norline; Nortrilen; Nortyline; Ortrip; ***UK:*** Allegron; ***USA:*** Aventyl; Pamelor.

Multi-ingredient: ***Arg.:*** Karile; ***Chile:*** Motitrel; ***Indon.:*** Motival; ***Irl.:*** Motival; ***Ital.:*** Dominans; ***Mex.:*** Motival; ***S.Afr.:*** Motival; ***Spain:*** Tropargal; ***Thai.:*** Cetavol; ***UK:*** Motival†.

Opipramol Hydrochloride *(BANM, USAN, rINNM)*

G-33040; Hidrocloruro de opipramol; Opipramol, Chlorhydrate d'; Opipramol Hidroklorür; Opipramoli Dihydrochloridum; Opipramoli Hydrochloridum; Opipramolu dichlorowodorek. 2-[4-(3-5*H*-Dibenz[*b,f*]azepin-5-ylpropyl)piperazin-1-yl]ethanol dihydrochloride.

Опипрамола Гидрохлорид
$C_{23}H_{29}N_3O,2HCl$ = 436.4.
CAS — 315-72-0 (opipramol); 909-39-7 (opipramol dihydrochloride).
ATC — N06AA05.
ATC Vet — QN06AA05.



(opipramol)

Pharmacopoeias. In *Pol.*

Profile

Opipramol hydrochloride is a dibenzazepine tricyclic antidepressant (see Amitriptyline, p.376) given in oral doses of 50 to 300 mg daily in the treatment of depression.

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

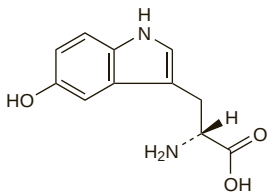
Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Insidon; ***Ger.:*** Insidon; ***Israel:*** Oprimol; ***Pol.:*** Pramolan; ***Switz.:*** Insidon; ***Turk.:*** Deprenil; Insidon; Insomin; Inzeton; Opridon; Oprimol.

Oxitriptan *(rINN)*

5-HTP; L-5-Hydroxytryptophan; Oxitriptán; Oxitriptanum; Ro-0783/B. L-2-Amino-3-(5-hydroxy-1*H*-indol-3-yl)propionic acid.

Окситриптан
$C_{11}H_{12}N_2O_3$ = 220.2.
CAS — 4350-09-8 (oxitriptan); 56-69-9 (DL-5-hydroxytryptophan).
ATC — N06AX01.
ATC Vet — QN06AX01.



Profile

Oxitriptan is the L form of 5-hydroxytryptophan, a precursor of serotonin. Like tryptophan (p.427) it is used in the treatment of depression; it is given in oral doses of up to 600 mg daily.

Oxitriptan is also used in doses of up to 1 g daily in myoclonic disorders, especially posthypoxic myoclonus (p.470). It has also been used in neurological conditions including migraine, pain syndromes, and sleep disorders, and as an adjunct in epilepsy and parkinsonism.

DL-Oxitriptan has also been used as an antidepressant.

Preparations

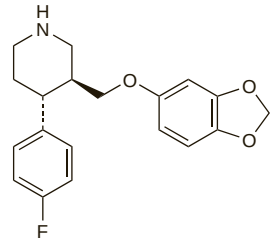
Proprietary Preparations (details are given in Part 3)
Cz.: Tript-OH; ***Fr.:*** Levotonine; ***Ger.:*** Levothym†; ***Ital.:*** Tript-OH; ***Port.:*** Cincofarm; ***Spain:*** Cincofarm; ***Switz.:*** Tript-OH.

Multi-ingredient: ***Indon.:*** Deprex; Menose.

Paroxetine *(BAN, USAN, rINN)*

BRL-29060; FG-7051; Paroksetiini; Paroxetin; Paroxetina; Paroxétine; Paroxetinum. (−)-*trans*-5-(4-*p*-Fluorophenyl-3-piperidylmethoxy)-1,3-benzodioxole.

Пароксетин
$C_{19}H_{20}FNO_3$ = 329.4.
CAS — 61869-08-7.
ATC — N06AB05.
ATC Vet — QN06AB05.



Paroxetine Hydrochloride *(BANM, rINNM)*

BRL-29060A; Hidrocloruro de paroxetina; Paroksetiinihydrokloridihemihydraatti; Paroksetin Hidroklorür; Paroksetino hidrochloridas hemihidratas; Paroksetyny chlorowodorek; Paroxetin hydrochlorid; Paroxétine, chlorhydrate de; Paroxétine (chlorhydrate de) hémihydraté; Paroxetine Hydrochloride Hemihydrate; Paroxetinhydrokloridhemihydrat; Paroxetini hydrochloridum; Paroxetini hydrochloridum hemihydricum.

Пароксетина Гидрохлорид
$C_{19}H_{20}FNO_3,HCl, ½H_2O$ = 374.8.
CAS — 78246-49-8 (anhydrous paroxetine hydrochloride); 110429-35-1 (paroxetine hydrochloride hemihydrate).

Pharmacopoeias. In *Eur.* (see p.vii) and *US*, which permit the anhydrous and hemihydrate forms.
Ph. Eur. 6.2 (Paroxetine Hydrochloride, Anhydrous). A white or almost white, hygroscopic, crystalline powder. It exhibits polymorphism. Slightly soluble in water; sparingly soluble in dehydrated alcohol and in dichloromethane; freely soluble in methyl alcohol. Store in airtight containers at a temperature not exceeding 25°.
Ph. Eur. 6.2 (Paroxetine Hydrochloride Hemihydrate). A white or almost white, crystalline powder. It exhibits pseudopolymorphism. Slightly soluble in water; sparingly soluble in alcohol and in dichloromethane; freely soluble in methyl alcohol. Protect from light.
USP 31 (Paroxetine Hydrochloride). It is anhydrous or contains one-half molecule of water of hydration. A white to off-white solid. Slightly soluble in water; soluble in alcohol and in methyl alcohol. Store the anhydrous form in airtight containers.

Paroxetine Mesilate *(BANM, rINNM)*

Mesilato de paroxetina; Paroxétine, Mésilate de; Paroxetine Mesylate *(USAN)*; Paroxetini Mesilas.

Пароксетина Мезилат
$C_{19}H_{20}FNO_3,CH_4O_3S$ = 425.5.
CAS — 217797-14-3.
ATC — N06AB05.
ATC Vet — QN06AB05.

Adverse Effects, Treatment, and Precautions

As for SSRIs in general (see Fluoxetine, p.391).

Extrapyramidal reactions (including orofacial dystonias) and withdrawal symptoms associated with paroxetine have been reported to the UK CSM more commonly than with other SSRIs. For further details, see Extrapyramidal Effects under Adverse Effects of Fluoxetine, p.393 and Withdrawal under Precautions, p.396.

Breast feeding. For comments on the use of SSRIs in breast feeding patients, see under Precautions for Fluoxetine, p.394.

Children. SSRIs are associated with an increased risk of potentially suicidal behaviour when used for the treatment of depression in children and adolescents under 18 years old; for further details, see under Effects on Mental State in Fluoxetine, p.392.

Pregnancy. For discussion of the risks of SSRIs during pregnancy, and whether paroxetine is associated with a greater teratogenic risk than other SSRIs, see under Fluoxetine, p.395.

Interactions

For interactions associated with SSRIs, see Fluoxetine, p.396.

Pharmacokinetics

Paroxetine is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring within about 5 hours of ingestion. It undergoes extensive first-pass metabolism in the liver. The main metabolic pathway is oxidation followed by methylation and formation of glucuronide and sulfate conjugates. The cytochrome P450 isoenzyme CYP2D6 is partly responsible for the metabolism of paroxetine. Paroxetine is widely distributed throughout body tissues and is about 95% bound to plasma proteins. The elimination half-life of paroxetine is reported to be about 21 hours. Excretion is via the urine (about 64%) and the faeces (about 36%), mainly as metabolites in both cases. Paroxetine is distributed into breast milk (see Breast Feeding under Precautions in Fluoxetine, p.394).

◊ References.

1. Dalhoff K, *et al.* Pharmacokinetics of paroxetine in patients with cirrhosis. *Eur J Clin Pharmacol* 1991; **41:** 351–4.
2. Hiemke C, Härtter S. Pharmacokinetics of selective serotonin reuptake inhibitors. *Pharmacol Ther* 2000; **85:** 11–28.

Uses and Administration

Paroxetine, a phenylpiperidine derivative, is an SSRI with actions and uses similar to those of fluoxetine (p.397). It is given orally usually as paroxetine hydrochloride, as a single dose in the morning; it is also given as the mesilate. Doses are expressed in terms of the base; paroxetine hydrochloride 22.8 mg or paroxetine mesilate 25.8 mg are each equivalent to about 20 mg of paroxetine. The doses given below refer to preparations containing paroxetine hydrochloride; similar doses are also used when paroxetine is given as the mesilate.

In the treatment of **depression**, the usual dose of paroxetine is 20 mg daily, increased gradually, if necessary, in weekly increments of 10 mg to a maximum of 50 mg daily (but see Administration, below).

In the treatment of **generalised anxiety disorder**, the initial dose is 20 mg daily; further increases in increments of 10 mg at intervals of at least one week to a maximum of 50 mg have been given (but see Administration, below).

The initial dose in **obsessive-compulsive disorder** is 20 mg daily increased weekly in 10-mg increments to a usual maintenance dose of 40 mg daily; some patients may require up to 60 mg daily (but see Administration, below).

In the treatment of **panic disorder** with or without agoraphobia, the initial dose is 10 mg daily increased weekly in 10-mg increments according to response; the usual recommended maintenance dose is 40 mg daily, although some patients may benefit from 60 mg daily (but see Administration, below).

The recommended starting dose for the treatment of **post-traumatic stress disorder** is 20 mg daily. If necessary this may be increased in increments of 10 mg at intervals of at least one week to a maximum of 50 mg daily (but see Administration, below).

The initial dose for the treatment of **social anxiety disorder** is 20 mg daily increased after several weeks, if necessary, by increments of 10 mg to a maximum of 50 or 60 mg daily (but see Administration, below).

A suggested maximum daily dose in elderly or debilitated patients is 40 mg; US licensed product information also recommends a starting dose of 10 mg daily in such patients. Reduced doses should be given to patients with hepatic or renal impairment, see below.

A modified-release preparation (as the hydrochloride) is also available in the USA for the treatment of depression, panic disorder, and social anxiety disorder; the maximum doses with this preparation may be slightly greater than those recommended with the immediate-release preparation. The modified-release preparation may also be used in the treatment of **premenstrual dysphoric disorder**. The initial dose is 12.5 mg once daily, usually in the morning, which may be increased to 25 mg once daily, if necessary, after an interval of at least one week. Treatment may be given throughout the menstrual cycle or limited to the luteal phase.

Paroxetine should be withdrawn gradually to reduce the risk of withdrawal symptoms. For further details, see Withdrawal under Precautions of Fluoxetine, p.396.

◊ Reviews.

1. Wagstaff AJ, *et al.* Paroxetine: an update of its use in psychiatric disorders in adults. *Drugs* 2002; **62:** 655–703. Correction. *ibid.*; 1461.

Administration. Although paroxetine is licensed in the UK at higher doses the UK CSM considers that there is a lack of evidence from clinical trials of additional efficacy with paroxetine when given above the following daily doses:

- depression, generalised anxiety disorder, social anxiety disorder, post-traumatic stress disorder: 20 mg
- obsessive-compulsive disorder, panic disorder: 40 mg

1. CSM/MCA Paroxetine prescribing advice. *Current Problems* 2004; **30:** 3. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007448&RevisionSelectionMethod= LatestReleased (accessed 14/08/08)

Administration in hepatic or renal impairment. In the USA the recommended initial oral dose of paroxetine in patients with severe renal or hepatic impairment is the equivalent of 10 mg daily, increased to a maximum of 40 mg daily as necessary. UK licensed drug information recommends that doses in such patients are limited to the lower end of the range.

Anxiety disorders. Paroxetine is used in anxiety disorders including generalised anxiety disorder (p.952), obsessive-compulsive disorder (p.952), panic disorder (p.952), post-traumatic stress disorder (p.953), and social anxiety disorder (see under Phobic Disorders, p.953). It has also been tried for adult night terrors (see under Sleep-associated Movement Disorders, p.958).

References.

1. Oehrberg S, *et al.* Paroxetine in the treatment of panic disorder: a randomised, double-blind, placebo-controlled study. *Br J Psychiatry* 1995; **167:** 374–9.
2. Zohar J, *et al.* Paroxetine versus clomipramine in the treatment of obsessive-compulsive disorder. *Br J Psychiatry* 1996; **169:** 468–74.
3. Lecrubier Y, *et al.* Long-term evaluation of paroxetine, clomipramine and placebo in panic disorder. *Acta Psychiatr Scand* 1997; **95:** 153–60.
4. Wilson SJ, *et al.* Adult night terrors and paroxetine. *Lancet* 1997; **350:** 185.
5. Stein MB, *et al.* Paroxetine treatment of generalized social phobia (social anxiety disorder). *JAMA* 1998; **280:** 708–13.
6. Baldwin D, *et al.* Paroxetine in social phobia/social anxiety disorder: randomised, double-blind, placebo-controlled study. *Br J Psychiatry* 1999; **175:** 120–6.
7. Baldwin DS. Clinical experience with paroxetine in social anxiety disorder. *Int Clin Psychopharmacol* 2000; **15** (suppl): S19–24.
8. Marshall RD, *et al.* Efficacy and safety of paroxetine treatment for chronic PTSD: a fixed-dose, placebo-controlled study. *Am J Psychiatry* 2001; **158:** 1982–8.
9. Tucker P, *et al.* Paroxetine in the treatment of chronic posttraumatic stress disorder: results of a placebo-controlled, flexible-dosage trial. *J Clin Psychiatry* 2001; **62:** 860–8.
10. Liebowitz MR, *et al.* A randomized, double-blind, fixed-dose comparison of paroxetine and placebo in the treatment of generalized social anxiety disorder. *J Clin Psychiatry* 2002; **63:** 66–74.
11. Stein DJ, *et al.* Efficacy of paroxetine for relapse prevention in social anxiety disorder: a 24-week study. *Arch Gen Psychiatry* 2002; **59:** 1111–18.
12. Stocchi F, *et al.* Efficacy and tolerability of paroxetine for the long-term treatment of generalized anxiety disorder. *J Clin Psychiatry* 2003; **64:** 250–8.
13. Hollander E, *et al.* Acute and long-term treatment and prevention of relapse of obsessive-compulsive disorder with paroxetine. *J Clin Psychiatry* 2003; **64:** 1113–21.
14. Lepola U, *et al.* Controlled-release paroxetine in the treatment of patients with social anxiety disorder. *J Clin Psychiatry* 2004; **65:** 222–9.
15. Sheehan DV, *et al.* Efficacy and tolerability of controlled-release paroxetine in the treatment of panic disorder. *J Clin Psychiatry* 2005; **66:** 34–40.
16. Rickels K, *et al.* Remission of generalized anxiety disorder: a review of the paroxetine clinical trials database. *J Clin Psychiatry* 2006; **67:** 41–7.

Depression. As discussed on p.373, there is very little difference in efficacy between the different groups of antidepressant drugs, and choice is often made on the basis of adverse effect profile. SSRIs such as paroxetine are widely used as an alternative to the older tricyclics as they have fewer adverse effects and are safer in overdosage.

References.

1. Leyman S, *et al.* Paroxetine: post-marketing experience on 4024 depressed patients in Belgium. *Eur J Clin Res* 1995; **7:** 287–96.
2. Rodríguez-Ramos P, *et al.* Effects of paroxetine in depressed adolescents. *Eur J Clin Res* 1996; **8:** 49–61.
3. Franchini L, *et al.* Dose-response efficacy of paroxetine in preventing depressive recurrences: a randomized, double-blind study. *J Clin Psychiatry* 1998; **59:** 229–32.
4. Williams JW, *et al.* Treatment of dysthymia and minor depression in primary care: a randomized controlled trial in older adults. *JAMA* 2000; **284:** 1519–26.
5. Golden RN, *et al.* Efficacy and tolerability of controlled-release and immediate-release paroxetine in the treatment of depression. *J Clin Psychiatry* 2002; **63:** 577–84.
6. Rapaport MH, *et al.* Efficacy of controlled-release paroxetine in the treatment of late-life depression. *J Clin Psychiatry* 2003; **64:** 1065–74.
7. Misri S, *et al.* The use of paroxetine and cognitive-behavioral therapy in postpartum depression and anxiety: a randomized controlled trial. *J Clin Psychiatry* 2004; **65:** 1236–41.
8. Trivedi MH, *et al.* Effectiveness of low doses of paroxetine controlled release in the treatment of major depressive disorder. *J Clin Psychiatry* 2004; **65:** 1356–64.
9. Dunner DL, *et al.* Efficacy and tolerability of controlled-release paroxetine in the treatment of severe depression: post hoc analysis of pooled data from a subset of subjects in four double-blind clinical trials. *Clin Ther* 2005; **27:** 1901–11.

Hot flushes. Some SSRIs, including paroxetine, have been tried in the treatment of hot flushes; for further details see under Fluoxetine, p.398.

Hypochondriasis. For mention of the use of SSRIs, including paroxetine, in hypochondriasis, see under Fluoxetine, p.398.

Premenstrual syndrome. Paroxetine (as a modified-release preparation) is used to control both the psychological and somatic symptoms of premenstrual syndrome (p.2099).

References.

1. Cohen LS, *et al.* Paroxetine controlled release for premenstrual dysphoric disorder: a double-blind, placebo-controlled trial. *Psychosom Med* 2004; **66:** 707–13.

Pruritus. Paroxetine has produced some benefit in the relief of non-dermatological pruritus.[1]

1. Zylicz Z, *et al.* Paroxetine in the treatment of severe non-dermatological pruritus: a randomized, controlled trial. *J Pain Symptom Manage* 2003; **26:** 1105–12.

Sexual dysfunction. Impotence or ejaculatory problems have been reported as adverse effects of SSRIs; for the potential use of these effects in the management of premature ejaculation see Fluoxetine, p.399.

Preparations

BP 2008: Paroxetine Tablets;
USP 31: Paroxetine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Afenexil; Aropax; Datevan; Meplar; Neurotrox; Olane; Pamoxet; Paxil; Psicoasten; Sicopax; Sicotral; Sostel; Tiarix; Xilanic; ***Austral.:*** Aropax; Extine; Oxetine; Paxtine; ***Austria:*** Allenopar; Aparo†; Ennos; Glaxopar; Paluxetil†; Parocetan; Paroglax; Paroxat; Seroxat; ***Belg.:*** Aropax; Seroxat; ***Braz.:*** Aropax; Benepax; Cebrilin; Parox; Paxtrat; Pondera; Roxetin; ***Canad.:*** Paxil; ***Chile:*** Aroxat; Bectam; Pamax; Posivyl; Seretran; Traviata; ***Cz.:*** Apo-Parox; Arketis; Parolex; Remood; Seroxat; ***Denm.:*** Oxetine†; Serodur; Seroxat; ***Fin.:*** Optipar; Seroxat; ***Fr.:*** Deroxat; Divarius; ***Ger.:*** Euplix; Oxet†; ParoLich; Paroxat; Paroxedura; Seroxat; Tagonis; ***Gr.:*** Noprilex; Seroxat; Taberil; ***Hong Kong:*** Seroxat; ***Hung.:*** Apodepi; Paretin; Parogen; Paroxat; Rexetin; Seroxat; ***India:*** Pari; Parotin; Xet; ***Indon.:*** Seroxat; ***Irl.:*** Meloxat; Paroser; Parox; Paxt; Seroxat; ***Israel:*** Paxxet; Seroxat; ***Ital.:*** Daparox; Dropaxin; Eutimil; Serestill; Sereupin; Seroxat; Stiliden; ***Jpn:*** Paxil; ***Malaysia:*** Seroxat; ***Mex.:*** Apo-Oxpar; Aropax; Paxil; ***Neth.:*** Seroxat; ***Norw.:*** Seroxat; ***NZ:*** Aropax; Loxamine; ***Philipp.:*** Seroxat; ***Pol.:*** Deprozel; Paromerck; Paxeratio; Paxtin; Rexetin; Seroxat; Xetanor; ***Port.:*** Denerval; Oxepar†; Paxetil; Seroxat; ***Rus.:*** Paxil (Паксил); Rexetin (Рексетин); ***S.Afr.:*** Aropax; Deparoc; Parax; Paxil; Sedarin; Serrapress; Xet; ***Singapore:*** Seroxat; ***Spain:*** Casbol; Frosinor; Motivan; Paratonina; Paroturt; Seroxat; Xetin; ***Swed.:*** Euplix†; Paroxiflex; Seroxat; ***Switz.:*** Deroxat; Dexantol; Parexat; Paronex; Paroxetop; ***Thai.:*** Seroxat; ***Turk.:*** Paxil; Seroxat; ***UK:*** Seroxat; ***USA:*** Paxil; Pexeva; ***Venez.:*** Paxil.

Phenelzine Sulfate *(pINNM)*

Phénelzine, Sulfate de; Phenelzine Sulphate *(BANM)*; Phenelzini Sulfas; Sulfato de fenelzina. Phenethylhydrazine hydrogen sulphate.

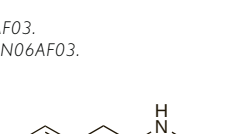
Фенельзина Сульфат

$C_8H_{12}N_2,H_2SO_4$ = 234.3.

CAS — 51-71-8 (phenelzine); 156-51-4 (phenelzine sulfate).

ATC — N06AF03.

ATC Vet — QN06AF03.



(phenelzine)

Pharmacopoeias. In *Br.* and *US.*

BP 2008 (Phenelzine Sulphate). A white powder or pearly platelets with a pungent odour. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether. Protect from light.

USP 31 (Phenelzine Sulfate). A white to yellowish-white powder having a characteristic odour. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether. pH of a 1% solution in water is between 1.4 and 1.9. Store in airtight containers. Protect from heat and light.

Adverse Effects

Adverse effects commonly associated with phenelzine and other MAOIs include orthostatic hypotension and attacks of dizziness. Other common adverse effects include headache, dry mouth, constipation and other gastrointestinal disturbances (including nausea and vomiting), and oedema. Drowsiness, weakness, and fatigue are reported frequently although CNS stimulation may also occur and symptoms include agitation, nervousness, euphoria, restlessness, insomnia, and convulsions. Psychotic episodes, with hypomania or mania, confusion, hallucinations, or toxic delirium, may be induced in susceptible persons.

Sweating and muscle tremors, twitching, or hyperreflexia may occur, which in overdosage may present as extreme hyperpyrexia and neuromuscular irritability. Other reported reactions include blurred vision, nystagmus, urinary retention or difficulty in micturition, arrhythmias, skin rashes, leucopenia, sexual disturbances, and weight gain with inappropriate appetite. Jaundice has been reported with hydrazine MAOIs and, on rare occasions, fatal progressive hepatocellular necrosis. Peripheral neuropathies associated with the hydrazine derivatives may be caused by pyridoxine deficiency. Hyponatraemia, possibly due to inappropriate secretion of antidiuretic hormone, has been associated with the use of antidepressants, particularly in the elderly.

Symptoms of **overdosage** may be minor at first and progress over the ensuing 24 to 48 hours. After mild overdosage and symptomatic and supportive therapy, recovery may occur in 3 to 4 days, but after massive overdosage symptoms may persist for up to 2 weeks. CNS depression and drowsiness have been observed with overdosage, but CNS stimulation is more common, with irritability, hyperactivity, agitation, hallucinations, or convulsions. Respiratory depression and coma may ultimately occur. Cardiovascular effects include hypertension, sometimes with severe headache, although hypotension is more frequently observed; cardiac arrhythmias and peripheral collapse can also develop. Profuse sweating, hyperpyrexia, and neuromuscular excitation with hyperreflexia are also prominent features of overdosage.

MAOIs have been the most commonly implicated drugs in the serotonin syndrome (see below). A severe hypertensive crisis, sometimes fatal, may occur if an MAOI is taken with some other drugs or certain foods (see Interactions, below). These reactions are characterised by severe headache and a rapid and sometimes prolonged rise in blood pressure followed by intracranial haemorrhage or acute cardiac failure.

For the adverse effects of reversible inhibitors of monoamine oxidase type A (RIMAs), see Moclobemide, p.411.

Incidence of adverse effects. A suspicion that the reported adverse effects of MAOIs were both exaggerated and overemphasised prompted a comparative study in patients receiving phenelzine or imipramine.[1] The report noted that the dosages of phenelzine used were at the upper end of the usual therapeutic range (mean 77 mg daily) while those of imipramine were in the middle of the usual therapeutic range (mean 139 mg daily). A very similar profile of adverse effects in the two groups was observed. With the exception of significantly increased incidence of drowsiness in the phenelzine-treated group, the 2 groups did not differ in the frequency of autonomic, CNS, cardiovascular, or psychological adverse effects. However, a significantly greater number of phenelzine-treated patients had to stop their treatment because of the severity of the adverse effects. Nonetheless it was considered that phenelzine was reasonably well-tolerated when compared with imipramine.