therapy with the non-selective inhibitors is particularly unsuitable for patients considered unable to adhere to the strict dietary requirements necessary for safe usage. (For contra-indication in children, see under Precautions, above).

Phenelzine is given orally as the sulfate although doses are expressed in terms of the base. Phenelzine sulfate 25.8 mg is equivalent to about 15 mg of phenelzine. The usual initial dose is equivalent to phenelzine 15 mg three times daily; if no response has been obtained after 2 weeks the dosage may be increased to 15 mg four times daily; severely depressed patients in hospital may be given up to 30 mg three times daily. Once a response has been obtained the dosage may be gradually reduced for maintenance therapy; some patients may continue to respond to 15 mg on alternate days.

Phenelzine should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Anxiety disorders. MAOIs have been used in the treatment of anxiety disorders. MAOIs appear to be effective in *panic disorder* (p.952). They also appear to be effective in *social anxiety disorder* (see under Phobic Disorders, p.953) and can improve anticipatory anxiety and functional disability. The main treatment for *post-traumatic stress disorder* (p.953) is psychotherapy but MAOIs are one of the alternatives that can help to reduce traumatic recollections and nightmares, and to repress flashbacks.

References.

1. Buigues J, Vallejo J. Therapeutic response to phenelzine in patients with panic disorder and agoraphobia with panic attacks. *J Clin Psychiatry* 1987; **48:** 55–9.
2. Frank JB, *et al.* A randomized clinical trial of phenelzine and imipramine for posttraumatic stress disorder. *Am J Psychiatry* 1988; **145:** 1289–91.
3. Heimberg RG, *et al.* Cognitive behavioural group therapy vs phenelzine therapy for social phobia: 12 week outcome. *Arch Gen Psychiatry* 1998; **55:** 1133–41.
4. Aarre TF. Phenelzine efficacy in refractory social anxiety disorder: a case series. *Nord J Psychiatry* 2003; **57:** 313–15.

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 effects. MAOIs are rarely used as first-choice antidepressants because of the dangers of dietary and drug interactions. Even in depressed patients with atypical, hypochondriacal, hysterical, or phobic features, for which MAOIs are particularly effective, it is often recommended that another antidepressant type should be tried first. Reversible inhibitors of monoamine oxidase type A (RIMAs) offer an alternative to the MAOIs and less strict dietary restrictions are necessary. They may be effective in a wide range of depressive disorders, although their relative efficacy in atypical depression remains to be established.

Combination therapy with differing classes of antidepressants, including the MAOIs, has been used in the treatment of drug-resistant depression. However, such therapy may result in enhanced adverse reactions or interactions and is considered unsuitable or controversial by some. For further details, see Antidepressants under Interactions, above.

Hyperactivity. When drug therapy is required for attention deficit hyperactivity disorder (p.2148), initial treatment is usually with a central stimulant. MAOIs have been used successfully but problems with dietary restriction and potential drug interactions have limited their use.

Migraine. A number of drugs have been used for the prophylaxis of migraine (p.616), although propranolol is generally preferred. Antidepressants such as the tricyclics can be useful alternatives when these drugs are ineffective or unsuitable. MAOIs are best reserved for severe cases refractory to other forms of prophylactic treatment.

Preparations

BP 2008: Phenelzine Tablets;
USP 31: Phenelzine Sulfate Tablets.

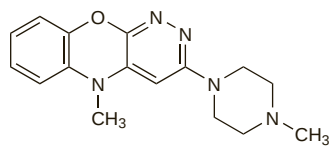
Proprietary Preparations (details are given in Part 3)
Austral.: Nardil; ***Belg.:*** Nardelzine; ***Canad.:*** Nardil; ***Irl.:*** Nardil; ***NZ:*** Nardil; ***UK:*** Nardil; ***USA:*** Nardil.

Pipofezine Hydrochloride *(rINNM)*

Hidrocloruro de pipofezina; Pipofézine, Chlorhydrate de; Pipofezine Dihydrochloride; Pipofezini Hydrochloridum. 5-Methyl-3-(4-methyl-1-piperazinyl)-5*H*-pyridazino[3,4-*b*][1,4]benzoxazine dihydrochloride.

Пипофезина Гидрохлорид

$C_{16}H_{19}N_5O,2HCl$ = 370.3.
CAS — 24886-52-0 (pipofezine); 24853-80-3 (pipofezine hydrochloride).



(pipofezine)

Profile

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

In the treatment of depression (p.373) pipofezine is usually given orally as the hydrochloride although doses are expressed in terms of the base; pipofezine hydrochloride 31.1 mg is equivalent to about 25 mg of pipofezine. An initial dose is 25 mg given four times daily, increased to an optimum total daily dose of 150 to 200 mg; if necessary up to a maximum of 500 mg may be given daily in divided doses. For maintenance a modified-release preparation providing pipofezine 150 mg may be given once or twice daily.

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

Preparations

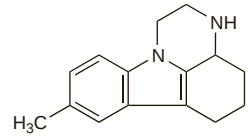
Proprietary Preparations (details are given in Part 3)
Rus.: Azaphen (Азафен).

Pirlindole *(rINN)*

Pirlindol; Pirlindolum. 2,3,3a,4,5,6-Hexahydro-8-methyl-1*H*-pyrazino[3,2,1-*jk*]carbazole.

Пирлиндол

$C_{15}H_{18}N_2$ = 226.3.
CAS — 60762-57-4.



Profile

Pirlindole has been given by mouth in the treatment of depression.

Preparations

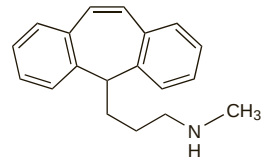
Proprietary Preparations (details are given in Part 3)
Port.: Implementor; ***Rus.:*** Pyrazidol (Пиразидол).

Protriptyline Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de protriptilina; MK-240; Protriptyline, chlorhydrate de; Protriptylini hydrochloridum. 3-(5*H*-Dibenzo[*a,d*]cyclohept-5-enyl)propyl(methyl)amine hydrochloride.

Протриптилина Гидрохлорид

$C_{19}H_{21}N,HCl$ = 299.8.
CAS — 438-60-8 (protriptyline); 1225-55-4 (protriptyline hydrochloride).
ATC — N06AA11.
ATC Vet — QN06AA11.



(protriptyline)

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

BP 2008 (Protriptyline Hydrochloride). A white to yellowish-white, odourless or almost odourless, powder. Freely soluble in water, in alcohol, and in chloroform; practically insoluble in ether. A 1% solution in water has a pH of 5.0 to 6.5.

USP 31 (Protriptyline Hydrochloride). A white to yellowish powder. Is odourless or has not more than a slight odour. Soluble 1 in 2 of water, 1 in 3.5 of alcohol, and 1 in 2.5 of chloroform; practically insoluble in ether. pH of a 1% solution in water is between 5.0 and 6.5.

Adverse Effects, Treatment, and Precautions

As for tricyclic antidepressants in general (see Amitriptyline, p.376).

Since protriptyline may have some stimulant properties anxiety and agitation can occur more frequently; cardiovascular effects such as tachycardia and orthostatic hypotension may also be more frequent than with other tricyclics. Photosensitivity rashes have been noted more often with protriptyline than with other tricyclic antidepressants and patients taking it should avoid direct sunlight.

Interactions

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

Pharmacokinetics

Protriptyline is well but slowly absorbed after oral doses: licensed drug information states that peak plasma concentrations are achieved only after 8 to 12 hours.

Paths of metabolism of protriptyline include *N*-oxidation and hydroxylation. Protriptyline is excreted in the urine, mainly in the form of its metabolites, either free or in conjugated form.

Protriptyline is widely distributed throughout the body and extensively bound to plasma and tissue protein. Protriptyline has been estimated to have a very prolonged elimination half-life ranging from 55 to 198 hours, which may be further prolonged in overdosage.

Uses and Administration

Protriptyline is a dibenzocycloheptatriene tricyclic antidepressant with actions and uses similar to those of amitriptyline (p.381). It is considerably less sedative than other tricyclics and may have a stimulant effect, thus making it particularly suitable for apathetic and withdrawn patients; its antimuscarinic effects are moderate.

In the treatment of depression, protriptyline hydrochloride is given in oral doses of 5 to 10 mg three or four times daily. It has been suggested that, because of its potential stimulant activity, any dosage increases should be added to the morning dose first and if insomnia occurs the last dose should be given no later than mid-afternoon. Higher doses of up to 60 mg daily may be required in severely depressed patients. A suitable initial dose for adolescents and the elderly is 5 mg three times daily; close monitoring of the cardiovascular system has been recommended if the dose exceeds a total of 20 mg daily in elderly subjects.

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

Preparations

BP 2008: Protriptyline Tablets;
USP 31: Protriptyline Hydrochloride Tablets.

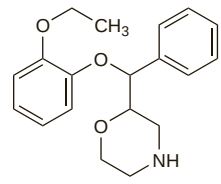
Proprietary Preparations (details are given in Part 3)
USA: Vivactil.

Reboxetine Mesilate *(BANM, rINNM)*

FCE-20124 (reboxetine or reboxetine mesilate); Mesilato de reboxetina; PNU-155950E; Réboxétine, Mésilate de; Reboxetine Mesylate *(USAN)*; Reboxetini Mesilas. (±)-(2*RS*)-2-[(α*RS*)-α-(2-Ethoxyphenoxy)benzyl]morpholine methanesulphonate.

Ребоксетина Мезилат

$C_{19}H_{23}NO_3,CH_4O_3S$ = 409.5.
CAS — 71620-89-8; 98769-81-4 (both reboxetine); 98769-82-5; 98769-84-7 (both reboxetine mesilate).
ATC — N06AX18.
ATC Vet — QN06AX18.



(reboxetine)

Adverse Effects

Adverse effects most commonly seen with reboxetine include insomnia, dry mouth, constipation, and increased sweating. Disturbance of visual accommodation, loss of appetite, vertigo, tachycardia, palpitations, vasodilatation, orthostatic hypotension, urinary hesitancy or retention (mainly in men), and erectile dysfunction including ejaculatory delay are also reported as being common adverse reactions. There have been reports of allergic dermatitis, convulsions, aggressive behaviour, cold extremities, and nausea and vomiting. Reduced plasma-potassium concentrations have been seen in elderly patients after prolonged use.