is 10 mg daily, gradually increasing to 30 to 50 mg daily. In the USA, daily doses of 25 to 50 mg are recommended for initial therapy in the elderly and adolescents, increasing to a maximum of 100 mg daily as required. Since imipramine has a prolonged half-life, once-daily dosage regimens may also be suitable, usually given at night.

Imipramine, as the hydrochloride, has also been given by intramuscular injection in the treatment of depression.

Imipramine is also used for the treatment of **nocturnal enuresis** in children in whom organic pathology has been excluded. However, drug therapy for nocturnal enuresis should be reserved for those in whom other methods have failed and should preferably only be given to cover periods away from home; tricyclic antidepressants are not recommended in children under 6 years of age (the *BNF* recommends that they should not be given until 7 years of age). Suggested doses of imipramine hydrochloride are:

- 25 mg for children aged 6 to 7 years (20 to 25 kg)
- 25 to 50 mg for children aged 8 to 11 years (25 to 35 kg)
- 50 to 75 mg for children over 11 years (35 to 54 kg)

The dose should be taken just before bedtime and treatment, including a period of gradual withdrawal, should not continue for longer than 3 months. A full physical examination is recommended before a further course.

Imipramine oxide hydrochloride (imipraminoxide hydrochloride) has also been used as an antidepressant and for nocturnal enuresis.

Imipramine should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Anxiety disorders. See under Clomipramine, p.387. In some countries, imipramine hydrochloride is licensed for the treatment of panic disorder in an initial oral dose of 10 mg daily; this dose may be increased as necessary to between 75 to 150 mg daily although doses of 200 mg daily may be needed in some patients.

Some references to the use of imipramine in anxiety disorders are given below.

1. Cross-National Collaborative Panic Study, Second Phase Investigators. Drug treatment of panic disorder: comparative efficacy of alprazolam, imipramine, and placebo. *Br J Psychiatry* 1992; **160:** 191–202.
2. Lepola UM, *et al*. Three-year follow-up of patients with panic disorder after short-term treatment with alprazolam and imipramine. *Int Clin Psychopharmacol* 1993; **8:** 115–18.
3. Rickels K, *et al*. Antidepressants for the treatment of generalised anxiety disorder: a placebo-controlled comparison of imipramine, trazodone, and diazepam. *Arch Gen Psychiatry* 1993; **50:** 884–95.
4. Clark DM, *et al*. A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder. *Br J Psychiatry* 1994; **164:** 759–69.
5. Barlow DH, *et al*. Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: a randomized controlled trial. *JAMA* 2000; **283:** 2529–36. Correction. *ibid.*; **284:** 2597.

Hyperactivity. Although not licensed in the UK for use in children with attention deficit hyperactivity disorder, the *BNFC* has suggested that imipramine hydrochloride may be given to those aged 6 years and over in an oral dose of 10 to 30 mg twice daily.

See also under Desipramine, p.388.

Pain. Antidepressants, usually amitriptyline or another tricyclic, are useful in alleviating some types of pain (see Choice of Analgesic, p.2). In some countries, imipramine hydrochloride is also available for the treatment of chronic pain; the usual recommended oral dose is 25 to 75 mg daily, although doses of up to 300 mg daily may be necessary.

Some references to the use of imipramine are given below.

1. Walsh TD. Controlled study of imipramine and morphine in chronic pain due to advanced cancer. *Proc Am Soc Clin Oncol* 1986; **5:** 237.
2. Sindrup SH, *et al*. Concentration-response relationship in imipramine treatment of diabetic neuropathy symptoms. *Clin Pharmacol Ther* 1990; **47:** 509–15.
3. Hummel T, *et al*. A comparison of the antinociceptive effects of imipramine, tramadol and anpirtoline. *Br J Clin Pharmacol* 1994; **37:** 325–33.
4. Cannon RO, *et al*. Imipramine in patients with chest pain despite normal coronary angiograms. *N Engl J Med* 1994; **330:** 1411–17.
5. Godfrey RG. A guide to the understanding and use of tricyclic antidepressants in the overall management of fibromyalgia and other chronic pain syndromes. *Arch Intern Med* 1996; **156:** 1047–52.
6. Minotti V, *et al*. Double-blind evaluation of short-term analgesic efficacy of orally administered diclofenac, diclofenac plus codeine, and diclofenac plus imipramine in chronic cancer pain. *Pain* 1998; **74:** 133–7.

Preparations

BP 2008: Imipramine Tablets;
USP 31: Imipramine Hydrochloride Injection; Imipramine Hydrochloride Tablets.

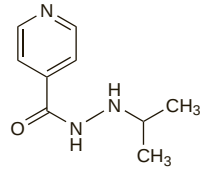
Proprietary Preparations (details are given in Part 3)
Arg.: Elepsin; Tofranil; ***Austral.:*** Melipramine; Tofranil; Tolerade; ***Austria:*** Tofranil; ***Belg.:*** Tofranil; ***Braz.:*** Depramina; Imipra; Praminan; Tofranil; Uni Imiprax; ***Canad.:*** Novo-Pramine; Tofranil; ***Cz.:*** Melipramin; ***Fr.:*** Tofranil; ***Ger.:*** Pryleugan; Tofranil; ***Hong Kong:*** Tofranil†; ***Hung.:*** Melipramin; ***India:*** Antidep; Depsonil; ***Indon.:*** Tofranil; ***Irl.:*** Tofranil; ***Israel:*** Primonil; Tofranil; ***Ital.:*** Tofranil; ***Mex.:*** Fixon; Talpramin; Tofranil; ***NZ:*** Tofranil; ***Philpp.:*** Tofranil; ***Port.:*** Tofranil; ***Rus.:*** Melipramin (Мелипрамин); ***S.Afr.:*** Ethipramine; Mipralin; Tofranil; ***Spain:*** Tofranil; ***Swed.:*** Tofranil†; ***Switz.:*** Tofranil; ***Thai.:*** Celamine; Sermonil; Topramine; ***Turk.:*** Tofranil; ***UK:*** Tofranil†; ***USA:*** Tofranil; ***Venez.:*** Tofranil.

Multi-ingredient: ***India:*** Depsonil-DZ.

Iproniazid Phosphate *(BANM, rINNM)*

Fosfato de iproniazida; Iproniazide, Phosphate d'; Iproniazidi Phosphas. 2′-Isopropylisonicotinohydrazide phosphate.

Ипрониазида Фосфат
$C_9H_{13}N_3O,H_3PO_4$ = 277.2.
CAS — 54-92-2 (iproniazid); 305-33-9 (iproniazid phosphate).
ATC — N06AF05.
ATC Vet — QN06AF05.



(iproniazid)

Profile

Iproniazid, a hydrazine derivative, is an irreversible inhibitor of both monoamine oxidase types A and B with actions and uses similar to those of phenelzine (p.419). It has been given orally in the treatment of depression.

Iproniazid is the isopropyl derivative of isoniazid (see p.288) and was developed for use in tuberculosis, but owing to its toxicity is no longer used for this purpose.

Effects on the liver. Of 91 cases of hepatitis due to antidepressant therapy, cytolytic reactions occurred in 11 treated with iproniazid.[1] Five patients died, 3 of them after involuntary rechallenge. High levels of antimitochondrial antibody were found in 5 patients.

1. Lefebure B, *et al*. Hépatites aux antidépresseurs. *Therapie* 1984; **39:** 509–16.

Porphyria. Iproniazid has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

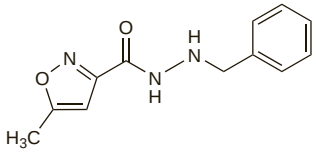
Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Marsilid†.

Isocarboxazid *(BAN, rINN)*

Isocarboxazida; Isocarboxazide; Isocarboxazidum; Isokarboksatsidi; Isokarboxazid; Ro-50831. 2′-Benzyl-5-methylisoxazole-3-carbohydrazide.

Изокарбоксазид
$C_{12}H_{13}N_3O_2$ = 231.3.
CAS — 59-63-2.
ATC — N06AF01.
ATC Vet — QN06AF01.



Pharmacopoeias. In *Chin.*

Adverse Effects, Treatment, and Precautions

As for MAOIs in general (see Phenelzine, p.415).

Interactions

For interactions associated with MAOIs, see Phenelzine, p.417.

Pharmacokinetics

Isocarboxazid is readily absorbed from the gastrointestinal tract reaching peak plasma concentrations 3 to 5 hours after ingestion. It is metabolised by the liver, and is excreted in the urine mainly in the form of metabolites.

Uses and Administration

Isocarboxazid, a hydrazine derivative, is an irreversible inhibitor of both monoamine oxidase types A and B with actions and uses similar to those of phenelzine (p.419).

Isocarboxazid is used in the treatment of depression but because of the risks associated with irreversible non-selective MAOIs (see p.373) usually other antidepressants are preferred. It is given in an initial oral dose of 30 mg daily in single or divided doses. If no improvement occurs after 4 weeks, doses of up to 60 mg daily can be tried for up to 4 to 6 weeks. Once a response has been obtained the dosage may be gradually reduced to a maintenance dose of 10 to 20 mg daily, although doses of up to 40 mg daily may be needed in some patients. Half the normal maintenance dose may be adequate in the elderly.

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

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Marplan†; ***Denm.:*** Marplan; ***USA:*** Marplan.

Lithium Carbonate *(USAN)*

CP-15467-61; Dilithium Carbonate; Ličio karbonatas; Lithii carbonas; Lithium Carb.; Lithium, carbonate de; Litio, carbonato de; Litiumkarbonaatti; Litiumkarbonat; Lítium-karbonát; Litu węglan; Litu weglan; Lityum Karbonat; NSC-16895; Uhličitan lithný. Carbonic acid, dilithium salt.
Li_2CO_3 = 73.89.
CAS — 554-13-2.
ATC — N05AN01.
ATC Vet — QN05AN01.

NOTE. Commercially available lithium materials have atomic weights ranging from 6.939 to 6.996. The molecular weight of lithium carbonate of 73.89 given above has been calculated using the lowest atomic weight; using the highest figure would give a molecular weight of 74.00. This difference does not affect the figure of 27 mmol of lithium being provided by 1 g of lithium carbonate and is unlikely to contribute noticeably to any variations in serum concentration. Nor should it affect the outcome of assays of serum-lithium concentrations given the limits of error of the assay methods.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Lithium Carbonate). A white or almost white powder. Slightly soluble in water; practically insoluble in alcohol.
USP 31 (Lithium Carbonate). A white odourless granular powder. Sparingly soluble in water, very slightly soluble in alcohol; dissolves, with effervescence, in dilute mineral acids.

Lithium Citrate

Citronan lithný tetrahydrát; Ličio citratas; Lithii citras; Lithii Citras Tetrahydricus; Lithium, citrate de; Litio, citrato de; Litiumcitrat; Lítium-citrát; Litiumsitraatti; Lityum Sitrat.
$C_6H_5Li_3O_7,4H_2O$ = 282.0.
CAS — 919-16-4 (anhydrous lithium citrate); 6080-58-6 (lithium citrate tetrahydrate).

NOTE. Commercially available lithium materials have atomic weights ranging from 6.939 to 6.996. The molecular weight of lithium citrate of 282.0 given above has been calculated using the lowest atomic weight; using the highest figure would give a molecular weight of 282.1. This difference does not affect the figure of 10.6 mmol of lithium being provided by 1 g of lithium citrate and is unlikely to contribute noticeably to any variations in serum concentration. Nor should it affect the outcome of assays of serum-lithium concentrations given the limits of error of the assay methods.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
US also includes lithium hydroxide.
Ph. Eur. 6.2 (Lithium Citrate). A white or almost white fine crystalline powder. Freely soluble in water; slightly soluble in alcohol.
USP 31 (Lithium Citrate). A white odourless deliquescent powder or granules. Freely soluble in water; slightly soluble in alcohol. pH of a 5% solution in water is between 7.0 and 10.0. Store in airtight containers.

Adverse Effects

Many of the adverse effects of lithium are dose-related and the margin between the therapeutic and toxic dose is narrow.

Initial adverse effects of lithium therapy include nausea, diarrhoea, vertigo, muscle weakness, and a dazed feeling; these effects often abate with continued therapy. Fine hand tremors, polyuria, and polydipsia may, however, persist. Other adverse effects that may occur at therapeutic serum-lithium concentrations include weight gain and oedema (which should not be treated with diuretics). Hypercalcaemia, hypermagnesaemia, and hyperparathyroidism have been reported. Skin dis-