Pharmacokinetics

Trazodone is readily absorbed from the gastrointestinal tract although absorption is affected by food. When trazodone is taken shortly after a meal there may be an increase in the amount absorbed, a decrease in the maximum concentration, and a lengthening in the time to maximum concentration compared with the fasting state; peak plasma concentrations occur about one hour after a dose when taken on an empty stomach and after about 2 hours when taken with food. Protein binding is reported to be about 89 to 95%.

Trazodone is extensively metabolised in the liver and paths of metabolism include *N*-oxidation and hydroxylation. It is metabolised to its active metabolite *m*-chlorophenylpiperazine via the cytochrome P450 isoenzyme CYP3A4. Trazodone is excreted mainly in the urine almost entirely in the form of its metabolites, either in free or in conjugated form: some is excreted in the faeces via biliary elimination. The elimination of trazodone from the plasma is biphasic, with a terminal elimination half-life of 5 to 9 hours.

Small amounts of trazodone are distributed into breast milk.

◊ References.

1. Bayer AJ, *et al*. Pharmacokinetic and pharmacodynamic characteristics of trazodone in the elderly. *Br J Clin Pharmacol* 1983; **16:** 371–6.
2. Nilsen OG, Dale O. Single dose pharmacokinetics of trazodone in healthy subjects. *Pharmacol Toxicol* 1992; **71:** 150–3.
3. Nilsen OG, *et al*. Pharmacokinetics of trazodone during multiple dosing to psychiatric patients. *Pharmacol Toxicol* 1993; **72:** 286–9.

Uses and Administration

Trazodone is a triazolopyridine antidepressant chemically unrelated to other classes of antidepressants. It blocks the reuptake of serotonin at presynaptic neurones and has an action at 5-HT_1 receptors. Trazodone is also an antagonist at 5-$HT_{2A/2C}$ receptors. Unlike the tricyclic antidepressants, trazodone does not inhibit the peripheral reuptake of noradrenaline, although it may indirectly facilitate neuronal release. Trazodone blocks central α_1-adrenoceptors and appears to have no effect on the central reuptake of dopamine. It does not appear to have very significant antimuscarinic properties, but has a marked sedative action.

For the treatment of **depression** trazodone hydrochloride is given in oral doses of 150 mg daily initially; total daily dosage may be increased by 50 mg every 3 or 4 days up to 300 to 400 mg daily if necessary. The daily dosage may be divided throughout the day after food or be given as a single dose at night. Divided daily dosages of up to 600 mg may be given in severe depression in hospitalised patients. A suggested initial dose in elderly and other susceptible patients is 100 mg daily, and total daily doses above 300 mg are unlikely to be needed in these patients.

In the treatment of **anxiety** (p.952), trazodone hydrochloride is given in an initial oral dose of 75 mg daily increasing to 300 mg daily if necessary.

As with other antidepressants, trazodone should be withdrawn gradually.

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. Trazodone has a different biochemical profile from both the tricyclics and the SSRIs.

References.

1. Weisler RH, *et al*. Comparison of bupropion and trazodone for the treatment of major depression. *J Clin Psychopharmacol* 1994; **14:** 170–9.

Disturbed behaviour. Trazodone has produced beneficial results[1-3] when tried in various disorders for the control of symptoms such as agitation, aggression, and disruptive behaviour (see p.954). Some[4] also consider that, in the management of dementia, trazodone might be worth trying in nonpsychotic patients with disturbed behaviour, especially those with mild symptoms or those intolerant of or unresponsive to antipsychotics. However, the evidence for such use is poor; a systematic review on the use of trazodone in the treatment of behavioural and psychological symptoms of dementia found that the evidence from randomised, placebo-controlled studies was insufficient for any recommendations to be made.[5] The risk of adverse effects such as sedation and orthostatic hypotension, which may be particularly problematic in the elderly, should also be considered.[4]

1. Pasion RC, Kirby SG. Trazodone for screaming. *Lancet* 1993; **341:** 970.
2. Lebert F, *et al*. Behavioral effects of trazodone in Alzheimer's disease. *J Clin Psychiatry* 1994; **55:** 536–8.
3. Sultzer DL, *et al*. A double-blind comparison of trazodone and haloperidol for treatment of agitation in patients with dementia. *Am J Geriatr Psychiatry* 1997; **5:** 60–9.
4. Rabins PV, *et al*. APA Work Group on Alzheimer's Disease and other Dementias. Steering Committee on Practice Guidelines. American Psychiatric Association practice guideline for the treatment of patients with Alzheimer's disease and other dementias. Second edition. *Am J Psychiatry* 2007; **164** (12 suppl): 5–56. Also available at: http://www.psychiatryonline.com/pracGuide/loadGuidelinePdf.aspx?file=AlzPG101007 (accessed 23/07/08)
5. Martinon-Torres G, *et al*. Trazodone for agitation in dementia. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2004 (accessed 24/11/05).

Sexual dysfunction. Priapism can occur as an adverse effect of trazodone (see Effects on Sexual Function in Adverse Effects, above) and this has led to trials of oral trazodone for the treatment of erectile dysfunction (p.2179). Positive responses have been reported, both with yohimbine[1] and alone.[2] However, there appear to have been few controlled studies and a systematic review[3] considered some of these to be either small, brief, or methodologically weak. Meta-analysis[3] of data from 6 studies did not find trazodone to be superior to placebo but subgroup analysis possibly suggested a better outcome in patients with psychogenic erectile dysfunction and in those given doses of 150 to 200 mg daily.

1. Montorsi F, *et al*. Effect of yohimbine-trazodone on psychogenic impotence: a randomized, double-blind, placebo-controlled study. *Urology* 1994; **44:** 732–6.
2. Lance R, *et al*. Oral trazodone as empirical therapy for erectile dysfunction: a retrospective review. *Urology* 1995; **46:** 117–20.
3. Fink HA, *et al*. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003; **92:** 441–6.

Substance dependence. The antidepressant, anxiolytic, and sedative properties of trazodone have been reported to have been useful when tried in patients having withdrawal syndromes from a variety of substances including alcohol (p.1626),[1] cocaine (p.1860),[2] and benzodiazepines (p.987).[3-5]

1. Le Bon O, *et al*. Double-blind, placebo-controlled study of the efficacy of trazodone in alcohol post-withdrawal syndrome: polysomnographic and clinical evaluations. *J Clin Psychopharmacol* 2003; **23:** 377–83.
2. Small GW, Purcell JJ. Trazodone and cocaine abuse. *Arch Gen Psychiatry* 1985; **42:** 524.
3. Ansseau M, De Roeck J. Trazodone in benzodiazepine dependence. *J Clin Psychiatry* 1993; **54:** 189–91.
4. Rickels K, *et al*. Trazodone and valproate in patients discontinuing long-term benzodiazepine therapy: effects on withdrawal symptoms and taper outcome. *Psychopharmacology (Berl)* 1999; **141:** 1–5.
5. Petrovic M, *et al*. A programme for short-term withdrawal from benzodiazepines in geriatric hospital inpatients: success rate and effect on subjective sleep quality. *Int J Geriatr Psychiatry* 1999; **14:** 754–60.

Preparations

USP 31: Trazodone Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Taxagon; ***Austria:*** Trittico; ***Belg.:*** Nestrolan; Trazolan; ***Braz.:*** Donaren; ***Canad.:*** Desyrel; Trazorel†; ***Chile:*** Diapresan; Trant; Trittico; Tronsalan; ***Cz.:*** Trittico AC; ***Fin.:*** Azona; ***Ger.:*** Thombran; ***Gr.:*** Trittico; ***Hong Kong:*** Trittico; ***Hung.:*** Depsan†; Trittico; ***Irl.:*** Molipaxin; ***Israel:*** Depyrel†; Trazodil; Trittico; ***Ital.:*** Trittico; ***Mex.:*** Sideril; ***Neth.:*** Trazolan; ***Pol.:*** Trittico; ***Port.:*** Trazone; Triticum; ***Rus.:*** Trittico (Триттико); ***S.Afr.:*** Molipaxin; ***Singapore:*** Trittico; ***Spain:*** Deprax; ***Switz.:*** Trittico; ***Thai.:*** Desirel; Trazo; ***Turk.:*** Desyrel; ***UK:*** Molipaxin; ***USA:*** Desyrel†; ***Venez.:*** Trittico.

Trimipramine *(BAN, USAN, rINN)*

IL-6001; 7162-RP; Trimeprimine; Trimipramiini; Trimipramin; Trimipramina; Trimipraminum. Dimethyl{3-(10,11-dihydro-5*H*-dibenz[*b*,*f*]azepin-5-yl-2-methyl)propyl}amine.

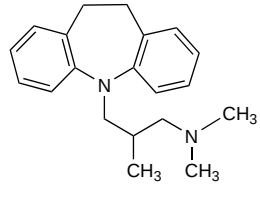
Тримипрамин

$C_{20}H_{26}N_2$ = 294.4.

CAS — 739-71-9.

ATC — N06AA06.

ATC Vet — QN06AA06.



Trimipramine Maleate *(BANM, USAN, rINNM)*

Maleato de trimipramina; Trimipramiinimaleaatti; Trimipramin maleinát; Trimipramine Hydrogen Maleate; Trimipramine, maléate de; Trimipramini maleas; Trimipraminmaleat; Trimipramin-maleát; Trimipramino maleatas.

Тримипрамина Малеат

$C_{20}H_{26}N_2,C_4H_4O_4$ = 410.5.

CAS — 521-78-8.

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

Ph. Eur. 6.2 (Trimipramine Maleate). A white or almost white crystalline powder. Slightly soluble in water and in alcohol. Protect from light.

USP 31 (Trimipramine Maleate). A white to almost white crystalline powder. Slightly soluble in water and in alcohol. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

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

Porphyria. Trimipramine is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

Interactions

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

Pharmacokinetics

Trimipramine is readily absorbed after oral doses, peak plasma concentrations being obtained in 2 hours. It is metabolised in the liver to its major metabolite desmethyltrimipramine, which is active. Trimipramine is excreted in the urine mainly in the form of its metabolites. It is about 95% bound to plasma proteins. The plasma elimination half-life is reported to be about 23 hours.

◊ References.

1. Maurer H. Metabolism of trimipramine in man. *Arzneimittelforschung* 1989; **39:** 101–3.
2. Musa MN. Nonlinear kinetics of trimipramine in depressed patients. *J Clin Pharmacol* 1989; **29:** 746–7.

Uses and Administration

Trimipramine is a dibenzazepine tricyclic antidepressant with actions and uses similar to those of amitriptyline (p.381). It has marked antimuscarinic and sedative properties.

Trimipramine is given orally as the maleate although doses are expressed in terms of the base. Trimipramine maleate 34.9 mg is equivalent to about 25 mg of trimipramine. In the treatment of depression, the usual initial dose is the equivalent of trimipramine 50 to 75 mg daily, gradually increased as necessary to 150 to 300 mg daily. The recommended initial dose for the elderly in the UK is 30 to 75 mg daily, gradually increased as necessary. In the USA, the elderly and adolescents may be given 50 mg daily initially followed by gradual increments as necessary up to a maximum of 100 mg daily. Trimipramine may be given in divided doses during the day, but since it has a prolonged half-life, once-daily dosage regimens are also suitable and usually given at night.

Trimipramine has also been given orally as the hydrochloride and the mesilate; the mesilate has also been given intramuscularly.

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

Preparations

BP 2008: Trimipramine Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Surmontil; ***Canad.:*** Apo-Trimip; Novo-Tripramine†; Rhotrimine; Surmontil†; ***Denm.:*** Surmontil; ***Fin.:*** Surmontil; ***Fr.:*** Surmontil; ***Ger.:*** Eldoral†; Herphonal; Stangyl; Trimidura; Trimineurin; ***Hong Kong:*** Surmontil; ***Hung.:*** Sapilent; ***India:*** Surmontil†; ***Irl.:*** Surmontil; ***Israel:*** Surmontil; ***Ital.:*** Surmontil; ***Neth.:*** Surmontil†; ***Norw.:*** Surmontil; ***NZ:*** Surmontil; Tripress; ***Philipp.:*** Surmontil; ***Port.:*** Surmontil; ***S.Afr.:*** Surmontil; Tydamine; ***Spain:*** Surmontil; ***Swed.:*** Surmontil; ***Switz.:*** Surmontil; Trimine; ***UK:*** Surmontil; ***USA:*** Surmontil; ***Venez.:*** Surmontil†.

Tryptophan *(USAN, rINN)*

Triptofán; Triptofanas; Triptófano; Tryptofaani; Tryptofan; L-Tryptophan; Tryptophane; Tryptophanum; W. L-2-Amino-3-(indol-3-yl)propionic acid.

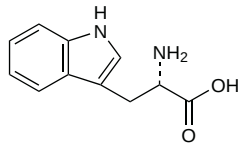
Триптофан

$C_{11}H_{12}N_2O_2$ = 204.2.

CAS — 73-22-3.

ATC — N06AX02.

ATC Vet — QN06AX02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.

Ph. Eur. 6.2 (Tryptophan). A white or almost white crystalline or amorphous powder. Sparingly soluble in water; slightly soluble in alcohol; dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Tryptophan). White to slightly yellowish-white crystals or crystalline powder. Soluble in hot alcohol and in dilute hydrochloric acid. pH of a 1% solution in water is between 5.5 and 7.0.

Adverse Effects

Tryptophan-containing products have been associated with the eosinophilia-myalgia syndrome; for further details, see below.

Other adverse effects that have been reported include nausea, headache, lightheadedness, and drowsiness.

An increased incidence of bladder tumours has been reported in *mice* given L-tryptophan orally as well as in cholesterol pellets embedded in the bladder lumen. However, there was no increase in tumour incidence when only high-dose, oral tryptophan was given.

Eosinophilia-myalgia syndrome. In late 1989 the first notification linking the eosinophilia-myalgia syndrome with the use of tryptophan-containing products was made in the USA.[1] There followed a number of similar published case reports from the USA, Europe, and Japan. Reviews of tryptophan-associated eosinophilia-myalgia syndrome have noted that by early 1990 over 1500 cases were known in the USA.[2,3]

In early 1990 the CDC in the USA summarised the features and known reports concerning the syndrome.[4] As the name implies the characteristic features are an intense eosinophilia together with disabling fatigue and muscle pain, although multisystem organ involvement and inflammatory disorders affecting the joints, skin, connective tissue, lungs, heart, and liver have also been recorded. Symptoms have generally developed over several weeks and the syndrome has occurred in patients who had been receiving tryptophan for many years previously with no untoward effect. In most patients slow and gradual improvement in the degree of eosinophilia and other clinical manifestations has followed the withdrawal of tryptophan, but in some patients the disease has progressed despite withdrawal and there have been fatalities.[5-7] The inflammatory condition has necessitated the use of corticosteroids in some patients.

The eosinophilia-myalgia syndrome has been reported in patients taking both tryptophan-containing prescription products for depression and non-prescription dietary supplements for a number of disorders including insomnia, the premenstrual syndrome, and stress; it does not appear to have occurred in patients receiving amino-acid preparations containing tryptophan as part of total parenteral nutrition regimens. The recognition of this syndrome led to the withdrawal of tryptophan-containing products or severe restrictions being imposed upon their use in many countries during 1990.

Various theories were proposed as to the reason for the association of tryptophan with this syndrome. Confusion existed because the reports implicated a very wide range of products from different manufacturers. However, later evidence appeared to have confirmed that contaminated tryptophan had originated from a single manufacturer in Japan.[8-10] Bulk tryptophan was imported from Japan for manufacture into finished pharmaceutical dosage forms and it was noted in one of these reports[9] that a single product was often found to contain two or more lots of powdered tryptophan that were blended together during the production of tablets or capsules. Many trace contaminants have been found in batches of tryptophan associated with the syndrome.[11] One contaminant has been identified as 1,1′-ethylidenebis(tryptophan).[12] Its inclusion in bulk tryptophan powder appeared to coincide with alterations in the manufacturing conditions that involved a change in the strain of *Bacillus amyloliquefaciens* used in the fermentation process and a reduction in the amount of charcoal used for purification.[9] Other investigations indicated the presence of bacitracin-like peptides in batches of the contaminated tryptophan.[13] However, further work[14] has provided only weak support for an association between the syndrome and any one particular contaminant and the causative agent remains to be confirmed. Nonetheless, since the syndrome only appeared to be associated with tryptophan from one manufacturer, tryptophan preparations were reintroduced in the UK in 1994 for restricted use under carefully monitored conditions.[15] In January 2005, the UK requirement for patient registration and monitoring was removed.

1. Anonymous. Eosinophilia-myalgia syndrome—New Mexico. *MMWR* 1989; **38:** 765–7.
2. Troy JL. Eosinophilia-myalgia syndrome. *Mayo Clin Proc* 1991; **66:** 535–8.
3. Milburn DS, Myers CW. Tryptophan toxicity: a pharmacoepidemiologic review of eosinophilia-myalgia syndrome. *DICP Ann Pharmacother* 1991; **25:** 1259–62.
4. Kilbourne EM, *et al.* Interim guidance on the eosinophilia-myalgia syndrome. *Ann Intern Med* 1990; **112:** 85–6.
5. Anonymous. Eosinophilia-myalgia syndrome associated with ingestion of -tryptophan—United States, through August 24, 1990. *JAMA* 1990; **264:** 1655.
6. Kaufman LD, *et al.* Clinical follow-up and immunogenetic studies of 32 patients with eosinophilia-myalgia syndrome. *Lancet* 1991; **337:** 1071–4.
7. Hertzman PA, *et al.* The eosinophilia-myalgia syndrome: status of 205 patients and results of treatment 2 years after onset. *Ann Intern Med* 1995; **122:** 851–5.
8. Slutsker L, *et al.* Eosinophilia-myalgia syndrome associated with exposure to tryptophan from a single manufacturer. *JAMA* 1990; **264:** 213–17.
9. Belongia EA, *et al.* An investigation of the cause of the eosinophilia-myalgia syndrome associated with tryptophan use. *N Engl J Med* 1990; **323:** 357–65.
10. Varga J, *et al.* The cause and pathogenesis of the eosinophilia-myalgia syndrome. *Ann Intern Med* 1992; **116**: 140–7.
11. Hill RH, *et al.* Contaminants in L-tryptophan associated with eosinophilia myalgia syndrome. *Arch Environ Contam Toxicol* 1993; **25:** 134–42.
12. Mayeno AN, *et al.* Characterization of "peak E", a novel amino acid associated with eosinophilia-myalgia syndrome. *Science* 1990; **250:** 1707–8.
13. Barnhart ER, *et al.* Bacitracin-associated peptides and contaminated -tryptophan. *Lancet* 1990; **336:** 742.
14. Philen RM, *et al.* Tryptophan contaminants associated with eosinophilia-myalgia syndrome. *Am J Epidemiol* 1993; **138:** 154–9.
15. CSM/MCA. L-Tryptophan (Optimax): limited availability for resistant depression. *Current Problems* 1994; **20:** 2. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024457&RevisionSelectionMethod=LatestReleased (accessed 05/08/08)

Precautions

Tryptophan has been associated with eosinophilia-myalgia syndrome (see above); caution is advised in patients receiving the drug who develop some, but not all, of the symptoms of this syndrome. It should not be used in those with a history of eosinophilia-myalgia syndrome associated with tryptophan treatment.

Patients taking tryptophan may experience drowsiness and, if affected, they should not drive or operate machinery. For further details of the effects of antidepressant therapy on driving see under Amitriptyline, p.379.

Abnormal metabolism of tryptophan may occur in patients with pyridoxine deficiency and tryptophan is thus sometimes given with pyridoxine supplements.

Interactions

Although tryptophan has been given to patients receiving MAOIs in the belief that clinical efficacy may be improved, it should be noted that the adverse effects may also be potentiated. For further details, see Antidepressants under Interactions of Phenelzine, p.418.

Use of tryptophan with drugs that inhibit the reuptake of serotonin may exacerbate the adverse effects of the latter and precipitate the serotonin syndrome (p.416).

There have been occasional reports of sexual disinhibition in patients taking tryptophan with phenothiazines or benzodiazepines.

For a report of tryptophan reducing blood concentrations of levodopa, see Nutritional Agents under Interactions of Levodopa, p.808.

Pharmacokinetics

Tryptophan is readily absorbed from the gastrointestinal tract. Tryptophan is extensively bound to plasma albumin. It is metabolised in the liver by tryptophan pyrrolase and tryptophan hydroxylase. Metabolites include hydroxytryptophan, which is then converted to serotonin, and kynurenine derivatives. Some tryptophan is converted to nicotinic acid and nicotinamide. Pyridoxine and ascorbic acid are cofactors in the decarboxylation and hydroxylation, respectively, of tryptophan; pyridoxine apparently prevents the accumulation of the kynurenine metabolites.

◊ References.

1. Green AR, *et al.* The pharmacokinetics of -tryptophan following its intravenous and oral administration. *Br J Clin Pharmacol* 1985; **20:** 317–21.

Uses and Administration

Tryptophan is an amino acid that is an essential constituent of the diet. Tryptophan and DL-tryptophan have been used as dietary supplements.

Tryptophan is a precursor of serotonin. Because CNS depletion of serotonin is considered to be involved in depression, tryptophan has been used in its treatment. Although it has been given alone, evidence of effectiveness is scant and tryptophan has generally been used as adjunctive therapy in depression. It has sometimes been given with pyridoxine and ascorbic acid, which are involved in its metabolism to serotonin (see Pharmacokinetics, above).

In many countries preparations containing tryptophan have either been withdrawn from the market or their availability severely restricted or limited because of its association with the eosinophilia-myalgia syndrome. In the UK, tryptophan is restricted to use as an adjunct to other antidepressant medication or in patients who have failed to respond to an adequate trial of standard antidepressant drug treatment. Therapy should be started by hospital specialists; thereafter tryptophan may be prescribed in the community.

In the treatment of depression the usual oral dose of tryptophan is 1 g given three times daily, but some patients may require up to 6 g daily in divided doses. Lower doses may be required in the elderly especially those with renal or hepatic impairment.

Depression. Evidence of benefit for tryptophan when given alone for depression (p.373) is lacking, though there is some suggestion of a weak antidepressant effect.[1] It has therefore mainly been used with other antidepressants in the belief that it would potentiate their effects. Although beneficial effects have been reported in some patients given tryptophan with SSRIs, tricyclic antidepressants, or MAOIs, either alone or with lithium, evidence of efficacy is mainly limited to case reports and small controlled studies.[2-4]

After the publication of reports linking the use of tryptophan with the eosinophilia-myalgia syndrome (see under Adverse Effects, above) preparations containing tryptophan for depression were withdrawn from the market or their use restricted. For details of UK restrictions see Uses and Administration, above.

1. Shaw K, *et al.* Tryptophan and 5-hydroxytryptophan for depression. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 24/11/05).
2. Barker WA, *et al.* The Newcastle chronic depression study: results of a treatment regime. *Int Clin Psychopharmacol* 1987; **2:** 261–72.
3. Smith S. Tryptophan in the treatment of resistant depression—a review. *Pharm J* 1998; **261:** 819–21.
4. Levitan RD, *et al.* Preliminary randomized double-blind placebo-controlled trial of tryptophan combined with fluoxetine to treat major depressive disorder: antidepressant and hypnotic effects. *J Psychiatry Neurosci* 2000; **25:** 337–46.

Dietary supplementation. The use of tryptophan as a dietary supplement has been reviewed.[1] However, because of its association with the eosinophilia-myalgia syndrome (see under Adverse Effects, above), the addition of tryptophan to food intended for human consumption is prohibited in some countries.

1. Li Wan Po A, Maguire T. Tryptophan: useful dietary supplement or a health hazard? *Pharm J* 1990; **244:** 484–5.

Insomnia. Tryptophan, sometimes in the form of dietary supplements, has enjoyed some popularity for the treatment of insomnia (p.957). However, in comparison with other hypnotics such as the benzodiazepines, the effects of tryptophan have been difficult to substantiate, and enthusiasm for tryptophan has waned considerably amongst sleep researchers.[1] It should also be noted that since the publication of reports linking the use of tryptophan with the eosinophilia-myalgia syndrome (see under Adverse Effects, above) preparations indicated for insomnia have been withdrawn from the market in many countries.

1. Lahmeyer HW. Tryptophan for insomnia. *JAMA* 1989; **262:** 2748.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Kalma; ***Canad.:*** Tryptan; ***Ger.:*** Ardeydorm; Ardeytropin; Kalma; ***UK:*** Optimax.

Multi-ingredient: ***Fr.:*** Vita-Dermacide; ***Ital.:*** Brioplus; Fisioreve; ***USA:*** PDP Liquid Protein.

Venlafaxine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de venlafaxina; Venlafaxine, chlorhydrate de; Venlafaxin-hydrochlorid; Venlafaxini hydrochloridum; Venlafaxinum hydrochloridum; Wenlafaksyny chlorowodorek; Wy-45030. (*RS*)-1-(2-Dimethylamino-1-*p*-methoxyphenylethyl)cyclohexanol hydrochloride.

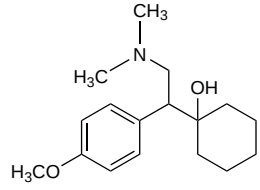
Венлафаксина Гидрохлорид

$C_{17}H_{27}NO_2$,HCl = 313.9.

CAS — 93413-69-5 (venlafaxine); 99300-78-4 (venlafaxine hydrochloride).

ATC — N06AX16.

ATC Vet — QN06AX16.



(venlafaxine)