reference nutrient intake (RNI) is 1.3 mg daily and 1.1 mg daily for adult males and females respectively; the estimated average requirement (EAR) is 1.0 mg daily and 0.9 mg daily respectively. In the USA the RDAs for adult males and females are 1.3 and 1.1 mg daily respectively.

1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41*. London: HMSO, 1991.
2. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for thiamin, riboflavin, niacin, vitamin B , folate, vitamin B , pantothenic acid, biotin, and choline*. Washington, DC: National Academy Press, 2000. Also available at: http://www.nap.edu/openbook.php?isbn=0309065542 (accessed 21/07/08)

Uses and Administration

Riboflavin, a water-soluble vitamin, is essential for the utilisation of energy from food. The active, phosphorylated forms, flavine mononucleotide (FMN) and flavine adenine dinucleotide (FAD), are involved as coenzymes in oxidative/reductive metabolic reactions. Riboflavin is also necessary for the functioning of pyridoxine and nicotinic acid.

Riboflavin deficiency develops when the dietary intake is inadequate. Deficiency leads to the development of a well-defined syndrome known as ariboflavinosis, characterised by cheilosis, angular stomatitis, glossitis, keratitis, surface lesions of the genitalia, and seborrhoeic dermatitis. There may also be normocytic anaemia and ocular symptoms including itching and burning of the eyes, and corneal vascularisation. Some of these symptoms may, in fact, be due to other vitamins such as pyridoxine or nicotinic acid which do not function correctly in the absence of riboflavin. Riboflavin deficiency may also occur with other vitamin B-complex deficiency states such as pellagra.

Riboflavin is used in the treatment and prevention of riboflavin deficiency. It is usually given in oral doses of 1 or 2 mg for prophylaxis; up to 30 mg daily in divided doses is used for treatment. Riboflavin, as the sodium phosphate, is also a component of intramuscular or intravenous vitamins B and C injections; riboflavin sodium phosphate 1.27 g is equivalent to about 1 g of riboflavin.

Riboflavin tetrabutyrate has also been used.

Riboflavin is also used as a colouring agent for food.

Glutaric aciduria. Milder forms of glutaric aciduria type II (p.1451) may respond to riboflavin.[1] Treatment with riboflavin 50 mg daily resulted in progressive improvement in a 4-year-old boy, with full recovery after 1 year. His brother, who had sustained permanent brain damage after epileptic seizures, showed moderate clinical improvement with riboflavin therapy.[2] In an adult patient with a history of recurrent pancreatitis and exercise intolerance, treatment with riboflavin 120 mg daily and levocarnitine resulted in no further episodes, although abnormal concentrations of amino acids were still apparent in her urine.[3]

1. Gregersen N, *et al*. Riboflavin responsive glutaric aciduria type II. *Prog Clin Biol Res* 1990; **321:** 477–94.
2. Uziel G, *et al*. Riboflavin-responsive glutaric aciduria type II presenting as a leukodystrophy. *Pediatr Neurol* 1995; **13:** 333–5.
3. Liang W-C, *et al*. Riboflavin-responsive glutaric aciduria type II with recurrent pancreatitis. *Pediatr Neurol* 2004; **31:** 218–21.

Migraine. Results from open studies[1,2] and a placebo-controlled trial[3] have suggested that riboflavin in high doses (400 mg daily) might be of some benefit in the prophylaxis of migraine attacks (p.616).

1. Schoenen J, *et al*. High-dose riboflavin as a prophylactic treatment of migraine: results of an open pilot study. *Cephalalgia* 1994; **14:** 328–9.
2. Boehnke C, *et al*. High-dose riboflavin treatment is efficacious in migraine prophylaxis: an open study in a tertiary care centre. *Eur J Neurol* 2004; **11:** 475–7.
3. Schoenen J, *et al*. Effectiveness of high-dose riboflavin in migraine prophylaxis: a randomized controlled trial. *Neurology* 1998; **50:** 466–70.

Preparations

BP 2008: Vitamins B and C Injection;
BPC 1973: Compound Vitamin B Tablets; Strong Compound Vitamin B Tablets;
USP 31: Riboflavin Injection; Riboflavin Tablets.

Proprietary Preparations (details are given in Part 3)
Belg.: Berivine; Ribon; ***Fin.:*** Vita-B2; ***Fr.:*** Beflavine; ***Ger.:*** B2-ASmedic; ***Hong Kong:*** FAD Ophthalmic Soln; Hibon; ***Indon.:*** Alinamin; ***Thai.:*** Boflavin.

Multi-ingredient: ***Austral.:*** Antioxidant Forte Tablets; Antioxidant Tablets; Extralife Eye-Care; Liv-Detox†; ***Austria:*** Beneuran Vit B-Komplex†; ***Braz.:*** Sulfatofer†; ***Ger.:*** Kwim†; ***Hong Kong:*** Alinamin-F; ***India:*** Hepa-Merz; ***Indon.:*** Matase; ***Ital.:*** Emazian B12†; Emoantitossina†; Facovit; Fosforilasi; Neuroftal†; ***Jpn:*** Neurovitan†; ***Mex.:*** Pangavit Pediatrico; ***Philipp.:*** Godex; ***Pol.:*** Biovision; ***Singapore:*** Alinamin-F; ***Spain:*** Aftasone B C; ***Thai.:*** Alinamin-F; B-100 Complex; ***Turk.:*** Neuvitan; ***UK:*** Quiet Life; Se-Power; ***USA:*** Cerefolin.

Vitamin B_6 Substances

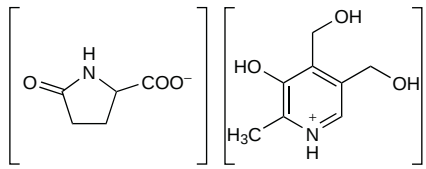
Vitamina B_6.

Vitamin B_6 is usually available as pyridoxine but the term is also used to refer to the related compounds, pyridoxal and pyridoxamine.

Metadoxine

Metadoxina; Pyridoxine Pidolate. Pyridoxine *l*-5-oxopyrrolidine-2-carboxylate.

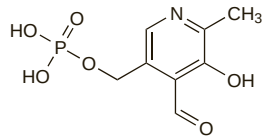
$C_8H_{11}NO_3$, $C_5H_7NO_3$ = 298.3.
CAS — 74536-44-0.



Pyridoxal Phosphate

Codecarboxylase; MC-l; Piridoxal, fosfato de; Pyridoxal 5-Phosphate. 3-Hydroxy-5-hydroxymethyl-2-methylpyridine-4-carboxaldehyde 5′-phosphate.

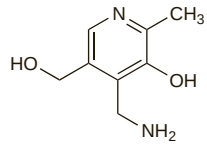
$C_8H_{10}NO_6P$ = 247.1.
CAS — 54-47-7.
ATC — A11HA06.
ATC Vet — QA11HA06.



Pyridoxamine Hydrochloride

Piridoxamina, hidrocloruro de; Pyridoxamine Dihydrochloride. 4-Aminomethyl-5-hydroxy-6-methyl-3-pyridinemethanol hydrochloride.

$C_8H_{12}N_2O_2$,2HCl = 241.1.
CAS — 524-36-7.



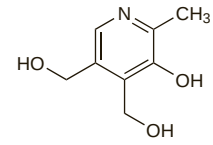
(pyridoxamine)

Pyridoxine Hydrochloride *(BANM, rINNM)*

Adermine Hydrochloride; Hidrocloruro de piridoxina; Piridoksin Hidroklorür; Piridoksino hidrochloridas; Piridossina Cloridrato; Piridoxin-hidroklorid; Pirydoksyny chlorowodorek; Pyridoksiini-hydrokloridi; Pyridoxine, chlorhydrate de; Pyridoxin-hydrochlorid; Pyridoxinhydroklorid; Pyridoxini hydrochloridum; Pyridoxinii Chloridum; Pyridoxinium Chloride; Pyridoxol Hydrochloride; Vitamin B_6. 3-Hydroxy-4,5-bis(hydroxymethyl)-2-picoline hydrochloride.

Пиридоксина Гидрохлорид

$C_8H_{11}NO_3$,HCl = 205.6.
CAS — 65-23-6 (pyridoxine); 58-56-0 (pyridoxine hydrochloride).
ATC — A11HA02.
ATC Vet — QA11HA02.



(pyridoxine)

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

Ph. Eur. 6.2 (Pyridoxine Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water; slightly soluble in alcohol. A 5% solution in water has a pH of 2.4 to 3.0. Protect from light.

USP 31 (Pyridoxine Hydrochloride). White or practically white crystals or crystalline powder. Soluble 1 in 5 of water and 1 in 115 of alcohol; insoluble in ether. Its solutions in water have a pH of about 3. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

Long-term use of large doses of pyridoxine is associated with the development of severe peripheral neuropathies; the dose at which these occur is controversial (see below).

Breast feeding. Vitamin B_6 is excreted into breast milk.[1,2] While some have expressed concern over the inhibition of breast milk secretion by pyridoxine,[3] others have cautioned that pyridoxine deficiency may cause seizures in the neonate.[4] The American Academy of Pediatrics considers the use of pyridoxine to be usually compatible with breast feeding.[5]

1. West KD, Kirksey A. Influence of vitamin B intake on the content of the vitamin in human milk. *Am J Clin Nutr* 1976; **29:** 961–9.
2. Roepke JLB, Kirksey A. Vitamin B nutriture during pregnancy and lactation: 1. Vitamin B intake, levels of the vitamin in biological fluids, and condition of the infant at birth. *Am J Clin Nutr* 1979; **32:** 2249–56.
3. Greentree LB. Dangers of vitamin B in nursing mothers. *N Engl J Med* 1979; **300:** 141–2.
4. Lande NI. More on dangers of vitamin B in nursing mothers. *N Engl J Med* 1979; **300:** 926–7.
5. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 09/01/06)

Effects on the nervous system. Severe sensory neuropathy has been described in patients receiving large doses of pyridoxine (2 to 6 g daily) for periods of 2 to 40 months.[1] There has, however, been debate as to whether smaller doses can produce such effects. Some contend that amounts of pyridoxine below this level are unlikely to produce toxic effects.[2,3] However, there have been some case reports[4,5] with amounts up to about 500 mg daily and prolonged use of even lower doses (about 200 mg daily or less) may also cause sensory peripheral neuropathy.[6] After a review of the possible toxicity associated with lower doses of pyridoxine, proposals were put forward in the UK to limit the dose freely available in dietary supplements to 10 mg daily; products supplying up to 50 mg daily would continue to be available from pharmacies and higher doses would only be available on prescription.[7] These proposals were heavily contested.[7,8] An upper limit of 100 mg daily has been suggested in the USA.[8]

1. Schaumburg H, *et al*. Sensory neuropathy from pyridoxine abuse: a new megavitamin syndrome. *N Engl J Med* 1983; **309:** 445–8.
2. Pauling L. Sensory neuropathy from pyridoxine abuse. *N Engl J Med* 1984; **310:** 197.
3. Baker H, Frank O. Sensory neuropathy from pyridoxine abuse. *N Engl J Med* 1984; **310:** 197.
4. Berger A, Schaumburg HH. More on neuropathy from pyridoxine abuse. *N Engl J Med* 1984; **311:** 986.
5. Waterston JA, Gilligan BS. Pyridoxine neuropathy. *Med J Aust* 1987; **146:** 640–2.
6. Dordain G, Deffond D. Neuropathies à la pyridoxine: revue de la littérature. *Therapie* 1994; **49:** 333–7.
7. Collier J. Vitamin B-6: food or medicine? *BMJ* 1998; **317:** 92–3.
8. Anonymous. Still time for rational debate about vitamin B . *Lancet* 1998; **351:** 1523.

Interactions

Pyridoxine reduces the effects of levodopa (see p.808), but this does not occur if a dopa decarboxylase inhibitor is also given. Pyridoxine reduces the activity of altretamine. It has also been reported to decrease serum concentrations of phenobarbital (p.494) and phenytoin (p.500). Many drugs may increase the requirements for pyridoxine; such drugs include hydralazine, isoniazid, penicillamine, and oral contraceptives.

Pharmacokinetics

Pyridoxine, pyridoxal, and pyridoxamine are readily absorbed from the gastrointestinal tract after oral doses

and are converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is oxidation to 4-pyridoxic acid and other inactive metabolites which are excreted in the urine. As the dose increases, proportionally greater amounts are excreted unchanged in the urine. Pyridoxal crosses the placenta and is distributed into breast milk.

Human Requirements

For adults, the daily requirement of pyridoxine is probably about 1.5 to 2 mg and this amount is present in most normal diets. The requirement tends to increase as protein intake increases due to the role of the vitamin in amino acid metabolism. Meats, especially chicken, kidney, and liver, cereals, eggs, fish, and certain vegetables and fruits are good sources of pyridoxine.

UK and US recommended dietary intake. In the UK[1] dietary reference values (see p.1925) have been published for vitamin B_6 and similarly in the USA recommended dietary allowances (RDAs) have been set.[2] Differing amounts are recommended for infants and children of varying ages, for adult males and females, and during pregnancy and lactation. In the UK the reference nutrient intake (RNI) is 15 micrograms per g of protein daily for adult males and females and the estimated average requirement (EAR) is 13 micrograms per g of protein daily for the same group. In the USA the RDA for adult men ranges from 1.3 to 1.7 mg daily and that for adult women ranges from 1.3 to 1.5 mg daily.[2] The tolerable upper intake level is 100 mg daily.[2] The Expert Group on Vitamins and Minerals[3] have established a safe upper level (SUL) for vitamin B_6 of 170 micrograms/kg daily.

1. DoH. Dietary reference values for food energy and nutrients for the United Kingdom: report of the panel on dietary reference values of the committee on medical aspects of food policy. *Report on health and social subjects 41*. London: HMSO, 1991.
2. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board. *Dietary Reference Intakes for thiamin, riboflavin, niacin, vitamin B , folate, vitamin B , pantothenic acid, biotin, and choline*. Washington, DC: National Academy Press, 2000. Also available at: http://www.nap.edu/openbook.php?isbn=0309065542 (accessed 21/07/08)
3. Expert Group on Vitamins and Minerals. Safe Upper Levels for vitamins and minerals (May 2003). Available at: http://www.food.gov.uk/multimedia/pdfs/vitmin2003.pdf (accessed 09/01/06)

Uses and Administration

Pyridoxine, a water-soluble vitamin, is involved mainly in amino acid metabolism, but is also involved in carbohydrate and fat metabolism. It is also required for the formation of haemoglobin.

Deficiency of pyridoxine is rare in humans because of its widespread distribution in foods. Pyridoxine deficiency may however be drug-induced and can occur, for instance, during isoniazid therapy. Inadequate utilisation of pyridoxine may result from certain inborn errors of metabolism. Pyridoxine deficiency may lead to anaemia, dermatitis, cheilosis, and neurological symptoms such as peripheral neuritis, and convulsions.

Pyridoxine is used in the treatment and prevention of pyridoxine deficiency states. It is usually given orally, the preferred route, but may also be given by the subcutaneous, intramuscular, or intravenous routes. Doses of pyridoxine hydrochloride up to 150 mg daily are used in general deficiency states; higher doses of up to 400 mg daily are used in the treatment of sideroblastic anaemias (see below); and similar high doses have been used to treat certain metabolic disorders such as homocystinuria (see Amino Acid Metabolic Disorders, below) or primary hyperoxaluria (below). Pyridoxine has also been used to treat seizures due to hereditary syndromes of pyridoxine deficiency or dependency in infants.

Pyridoxine has also been tried in the treatment of many other disorders, including depression and other symptoms associated with the premenstrual syndrome (see below) and the use of oral contraceptives, although its efficacy has been questioned.

Pyridoxine is usually given as the hydrochloride although other salts such as the citrate, oxoglurate, phosphate, and phosphoserinate, have also been used. Metadoxine, the pidolate, has been investigated in alcoholism (see below).

For the use of pyridoxine in the prophylaxis of isoniazid-induced peripheral neuritis and for the treatment of acute isoniazid toxicity, see Treatment of Adverse Effects, under Isoniazid, p.289.

Pyridoxal phosphate may be used to treat vitamin B_6 deficiency. Pyridoxamine has also been given.

◊ Reviews.

1. Bender DA. Non-nutritional uses of vitamin B . *Br J Nutr* 1999; **81:** 7–20.
2. Lheureux P, *et al.* Pyridoxine in clinical toxicology: a review. *Eur J Emerg Med* 2005; **12:** 78–85.

Alcoholism and alcohol poisoning. Pyridoxine and its pidolate, known as metadoxine, have been tried in the treatment of alcohol poisoning and alcoholism.[1] One study showed pyridoxine to be ineffective in acute alcohol poisoning[2] but another[3] suggested that the pidolate might be of benefit as an adjunct in the management of alcohol withdrawal (p.1626). In patients treated for alcoholic fatty liver, liver function returned to normal more quickly with metadoxine, even in patients who did not completely abstain from alcohol.[4]

1. Addolorato G, *et al.* Metadoxine in the treatment of acute and chronic alcoholism: a review. *Int J Immunopathol Pharmacol* 2003; **16:** 207–14.
2. Mardel S, *et al.* Intravenous pyridoxine in acute ethanol intoxication. *Hum Exp Toxicol* 1994; **13:** 321–3.
3. Rizzo A, *et al.* Uso terapeutico della metadoxina nell'alcolismo cronico: studio clinico in doppio cieco su pazienti ricoverati in un reparto di medicina generale. *Clin Ter* 1993; **142:** 243–50.
4. Caballería J, *et al.* Metadoxine accelerates fatty liver recovery in alcoholic patients: results of a randomized double-blind, placebo-control trial. *J Hepatol* 1998; **28:** 54–60.

Amino acid metabolic disorders. Pyridoxine has been used in various inborn errors of amino acid metabolism, such as homocystinuria (p.1922), with or without cobalamins and folate. Relatively high doses may need to be given (see above). For children with metabolic disorders such as homocystinuria and cystathioninuria, the *BNFC* suggests pyridoxine in an oral dose of 50 to 100 mg once or twice daily for neonates, and 50 to 250 mg once or twice daily in patients aged 1 month to 18 years. For the use of pyridoxine in primary hyperoxaluria, another inherited metabolic disorder, see below.

Anaemias. Some patients with acquired or hereditary sideroblastic anaemia (p.1044) that is severe enough to require treatment will respond to high doses (up to 400 mg daily) of pyridoxine, and a trial is considered worthwhile in all patients.

Cardiovascular disease. For mention of the possible link between vitamin B_6, hyperhomocysteinaemia, and cardiovascular disease, see under Folic Acid, p.1941. Pyridoxal phosphate is thought to prevent cellular calcium overload in ischaemia-reperfusion injury, but a large multicentre study[1] investigating doses of 250 mg daily orally given 3 to 10 hours before coronary artery bypass graft surgery in intermediate- to high-risk patients, and for a further 30 days after the procedure, found it did not reduce the incidence of cardiovascular death or non-fatal myocardial infarction.

1. Alexander JH, *et al.* MEND-CABG II Investigators. Efficacy and safety of pyridoxal 5′-phosphate (MC-1) in high-risk patients undergoing coronary artery bypass graft surgery: the MEND-CABG II randomized clinical trial. *JAMA* 2008; **299:** 1777–87.

Carpal tunnel syndrome. Pyridoxine has been advocated by some[1] for patients with carpal tunnel syndrome (see Soft-tissue Rheumatism, p.13), but evidence of efficacy is considered to be limited.[2] In most studies reporting improvement with pyridoxine, doses have ranged from 50 to 300 mg daily for 12 weeks; a review concluded that treatment should be stopped if there is no apparent response after this period.[3]

1. Lewis PJ. Pyridoxine supplements may help patients with carpal tunnel syndrome. *BMJ* 1995; **310:** 1534.
2. O'Connor D, *et al.* Non-surgical treatment (other than steroid injection) for carpal tunnel syndrome. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 09/01/06).
3. Aufiero E, *et al.* Pyridoxine hydrochloride treatment of carpal tunnel syndrome; a review. *Nutr Rev* 2004; **62:** 96–104.

Epilepsy. Pyridoxine-dependent epilepsy is an autosomal recessive disorder associated with decreased central γ-aminobutyric acid (GABA) concentrations and elevated cerebral glutamate concentrations. Untreated patients suffer from progressive encephalopathy, mental retardation, and intractable epilepsy; lifelong supplementation with pyridoxine can control epileptic symptoms but mental retardation may still develop. An epidemiological study[1] defined cases as those children with recurrent seizures that ceased within 7 days of oral pyridoxine at a usual dose of 30 mg/kg daily (minimum dose 15 mg/kg daily; maximum dose 1000 mg/kg daily), or within 30 minutes of intravenous pyridoxine (usual dose 100 mg; minimum dose 50 mg), that recurred when supplementation was withdrawn, and ceased again upon dosage as before. The study found that, despite their rarity, pyridoxine-dependent seizures frequently present atypically, and the author suggested that pyridoxine be given to all children with intractable seizures beginning before 3 years of age, including neonates with suspected hypoxic-ischaemic encephalopathy.

Test doses of pyridoxine intravenously, repeated at intervals of 10 minutes up to a total of 500 mg if necessary, have been suggested in the diagnosis of pyridoxine-dependent epilepsy; if the patient responds then a daily oral dose of 5 mg/kg is suggested although there is no real consensus on the appropriate dosage.[2] The *BNFC* suggests an intravenous test dose of 50 to 100 mg; in those who respond, oral doses of 50 to 100 mg once daily in neonates or 20 to 50 mg once or twice daily in older children, are suggested, adjusted as required. Alternatively, in patients with recurrent seizures refractory to conventional anticonvulsant therapy, oral pyridoxine supplementation of 15 mg/kg daily should lead to resolution of clinical seizures within a week in those with the condition; however, in some patients the daily dose required may be lower.[3]

A study in one patient[4] found that although pyridoxine 5 mg/kg reduced glutamate concentrations in CSF from the untreated value of 200 times normal limits, it did so only to 10 times the normal value, despite remission of symptoms. Doses of 10 mg/kg daily were required to normalise CSF glutamate, and it was suggested that this was a more appropriate target for therapy. In some children, pyridoxal phosphate has been suggested to be more effective than pyridoxine in controlling seizures.[5]

1. Baxter P. Epidemiology of pyridoxine dependent and pyridoxine responsive seizures in the UK. *Arch Dis Child* 1999; **81:** 431–3.
2. Gospe SM. Current perspectives on pyridoxine-dependent seizures. *J Pediatr* 1998; **132:** 919–23.
3. Gospe SM. Pyridoxine-dependent seizures: findings from recent studies pose new questions. *Pediatr Neurol* 2002; **26:** 181–5.
4. Baumeister FAM, *et al.* Glutamate in pyridoxine-dependent epilepsy: neurotoxic glutamate concentration in the cerebrospinal fluid and its normalization by pyridoxine. *Pediatrics* 1994; **94:** 318–21.
5. Wang H-S, *et al.* Pyridoxal phosphate is better than pyridoxine for controlling idiopathic intractable epilepsy. *Arch Dis Child* 2005; **90:** 512–15.

Palmar-plantar erythrodysesthesia syndrome. Pyridoxine, in doses of 100 to 300 mg daily, has been used successfully[1] for treating and preventing palmar-plantar erythrodysesthesia syndrome associated with antineoplastic therapy (see p.639).

1. Nagore E, *et al.* Antineoplastic therapy-induced palmar plantar erythrodysesthesia ('hand-foot') syndrome: incidence, recognition and management. *Am J Clin Dermatol* 2000; **1:** 225–34.

Premenstrual syndrome. Pyridoxine has been widely used in the premenstrual syndrome (p.2099) despite controversy over its effectiveness. Some consider that depressive symptoms may be provoked by pyridoxine deficiency because of its role as a coenzyme in the production of certain neurotransmitters, but it is difficult to attribute any of the other symptoms of the premenstrual syndrome to pyridoxine deficiency and doses of 50 mg are no more effective than a placebo.[1] A systematic review found that although treatment with pyridoxine was more effective than placebo, there was insufficient high-quality evidence to recommend its routine use in premenstrual syndrome.[2] If pyridoxine is used, the dosage should be restricted (see Effects on the Nervous System, above) because of concerns about neurotoxicity.[3]

1. West CP. The premenstrual syndrome. *Prescribers' J* 1987; **27** (2): 9–15.
2. Wyatt KM, *et al.* Efficacy of vitamin B-6 in the treatment of premenstrual syndrome: systematic review. *BMJ* 1999; **318:** 1375–81.
3. Severino SK, Moline ML. Premenstrual syndrome: identification and management. *Drugs* 1995; **49:** 71–82.

Primary hyperoxaluria. Primary hyperoxaluria (as distinct from the various forms secondary to other disorders) is a genetic disorder characterised by excessive synthesis and urinary excretion of oxalic acid. Two forms are known, type I (hyperglycolic aciduria) and type II (L-glyceric aciduria), associated with different enzyme defects. They are marked by recurrent calcium oxalate kidney stones, or nephrocalcinosis, leading to renal failure, together with extrarenal deposition of calcium oxalate and frequently severe peripheral vascular insufficiency. Treatment with high doses of pyridoxine may help decrease oxalate excretion particularly in type I disease,[1,2] although response is variable.[3] A few patients may respond to lower (physiological) doses.[4] Such treatment can be used with an oral orthophosphate supplement, which helps reduce renal deposition of calcium oxalate, and the combination appears to preserve renal function.[5] Therapy with magnesium salts, potassium citrate, and thiazide diuretics has also been suggested.[2] In patients in whom renal failure develops, the results of kidney transplantation have been disappointing, due to deposition of calcium oxalate in the new kidney, although transplanting the liver as well can correct the enzyme defect.[1,6] Pre-emptive liver transplantation, performed before renal failure or systemic oxalosis has occurred, may be an option.[2]

1. Cochat P, Basmaison O. Current approaches to the management of primary hyperoxaluria. *Arch Dis Child* 2000; **82:** 470–3.
2. Marangella M, *et al.* The primary hyperoxalurias. *Contrib Nephrol* 2001; **136:** 11–32.
3. Toussaint C. Pyridoxine-responsive PH1: treatment. *J Nephrol* 1998; **11** (suppl 1): 49–50.
4. Yendt ER, Cohanim M. Response to a physiologic dose of pyridoxine in type I primary hyperoxaluria. *N Engl J Med* 1985; **312:** 953–7.
5. Milliner DS, *et al.* Results of long-term treatment with orthophosphate and pyridoxine in patients with primary hyperoxaluria. *N Engl J Med* 1994; **331:** 1553–8.
6. Watts RWE, *et al.* Combined hepatic and renal transplantation in primary hyperoxaluria type I: clinical report of nine cases. *Am J Med* 1991; **90:** 179–88.

Tardive dyskinesia. In a double-blind, controlled, crossover study,[1] daily oral doses of vitamin B_6 1.2 g effectively reduced the symptoms of tardive dyskinesia (see Extrapyramidal Disorders, p.971).

1. Lerner V, *et al*. Vitamin B treatment for tardive dyskinesia: a randomized, double-blind, placebo-controlled, crossover study. *J Clin Psychiatry* 2007; **68:** 1648–54.

Preparations

BP 2008: Pyridoxine Tablets; Vitamins B and C Injection;
BPC 1973: Strong Compound Vitamin B Tablets;
USP 31: Pyridoxine Hydrochloride Injection; Pyridoxine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Benadon; ***Austral.:*** Pyroxin; ***Austria:*** Diclo-B; ***Belg.:*** Bedoxine; ***Braz.:*** Dimedril†; Fonto-Vit B6; Neuri B6; Seis-B; ***Canad.:*** Carthamex; ***Chile:*** Metadoxil†; Vitabe; ***Fin.:*** Heksavit; Vita-B6; ***Fr.:*** Becilan; Dermo 6; ***Ger.:*** B6-ASmedic; B Vicotrat; Bonasanit; Hexobion; ***Gr.:*** Besix; ***Hung.:*** Beres B6; Metadoxil; ***India:*** Pyricontin; ***Indon.:*** Liconam; Stopmun; ***Irl.:*** Complument Continus; ***Israel:*** Anacrodyne; B-Six; ***Ital.:*** Benadon; Memosprint†; Metadoxil; Xanturenasi; ***Mex.:*** Abrixone; Fortical; Metasin; Valparina; ***Philipp.:*** Drexabion; Hybutin; Jaga; Lixtress; Meganerv; Nervafil; Nervilan; Neuro-B's; Neurobexol; Neurobion; Neurolink; Polynerv; Supraneuron; Vineuron; ***Port.:*** Benadon; Metadoxil†; ***Rus.:*** Metadoxil (Метадоксил); ***S.Afr.:*** Beesix; Lactosec; ***Spain:*** Benadon; Conductasa; Godabion B6†; ***Swed.:*** Benadon; ***Switz.:*** Benadon; Complument Continus†; ***Thai.:*** B-6; Metadoxil; ***Turk.:*** B Vigen; Libavit B ; Postadoxine; ***USA:*** Vitelle Nestrex†; ***Venez.:*** Benadon†; Beplus; Biprin; Clodoxin; Suprabion; Vibralen†.

Multi-ingredient: ***Arg.:*** 6 Copin; Algio Nervomax; Algio Nervomax Fuerte; Blastop; Butineuron; Cadencial Plus; Calcimax Magnesio; Centella Incaico; Cobenexol Forte; Cobenexol Fuerte; CVP B1 B6 B12†; Dexabion; Dolo Nervobion; Dolo Nervobion 10000; Dorixina B1 B6 B12; Flexicamin B12; Flogiatrin B12; Holomagnesio B6; KLB6 Fruit Diet; Klosidol B1 B6 B12; Lohp; Magnebe; Megacistin; Megaplus; Nervobion Fuerte; Nervomax TB12; Neuronal Vascular†; Plenovit Melatonina; Presterin; QX 10; Sindrolen†; Total Magnesiano B6; ***Austral.:*** Bio Magnesium; Extralife Flow-Care; Extralife Fluid-Care; Extralife PMS-Care; Extralife Uri-Care; Liv-Detox†; Mag-Oro; Medinat PMT-Eze†; Zinc Zenith; ***Austria:*** Arca-Be; Aslavital; Astronautal; Beneuran compositum; Beneuran Vit B-Komplex†; Contravert B ; Diclovit; Dolo-Neurobion; Echnatol B ; Neurobion; Neuromerck; Neuromultivit; Pronerv; Sigmalin B ; Sigmalin B forte; Sigmalin B ohne Coffein; Vertirosan Vitamin B ; ***Belg.:*** Betapyr; Neurobion; Vioneurin†; ***Braz.:*** Alergo Filinal; Aminocid†; Aminotox†; Anekron; Benistina†; Betaliver†; Bicavine; Biohepax; Bronquitos; Cianotrat-Dexa; Citoneurin; Dexa-Citoneurin; Dexa-Cronobe; Dexa-Neuriberi†; Dexacobal; Dexador; Dexadoze; Dexagil; Dexaneurin; Dexanevral†; Diagrin†; Doxal; Dramavit B6†; Dramin B-6; Dramin B-6 DL; Emetrol†; Enjool†; Epativan; Epocler; Estac†; Gabax; Hepacitron†; Hepatobe†; Hepatox; Hormo Hepatico†; Levordiol; Megestran†; Monotrean B6; Nausicalm; Nausilon B6; Necro B-6; Nicopaverina B6†; Pantevit; Plagon; Trirubin†; Vitatonus; Vominil†; Xantinon Complex; ***Canad.:*** Diclectin; Penta-3B; Penta-3B + C; ProstGard†; ***Chile:*** Activator†; Betonvit†; Dolotol 12; Ferro Vitaminico; Gamalate B6; Glutacyl Vitaminado; Hexalectol; Nefersil B; Neurobionta; Neurocam; Tol 12; Tol 12 Plus; ***Cz.:*** Magne-B ; Milgamma N; Neuromultivit; ***Fin.:*** Neurobion; Neurovitan; Wicnecarb; Wicnevit; ***Fr.:*** Arthrolib; Catarstat; Cysti-Z†; Cystine B ; Lyso-6; Magne-B ; Phakan†; Uvimag B ; ***Ger.:*** B-Komplex forte; Bevit Forte; Bramin-hepa†; Dolo-Neurobion forte†; Dolo-Neurobion N†; Hepagrisevit Forte-N†; Hewedolor neuro; Medivitan N; Medivitan N Neuro; Medyn; Milgamma; Milgamma N; Milgamma-NA; Milneuron NA; Neuralysan S†; Neuro; Neuro uno; Neuro-AS N†; neuro-B forte; Neuro-Effekton B; Neuro-Lichtenstein M; Neuro-Lichtenstein N; Neuro-ratiopharm N; Neuro-ratiopharm†; Neuro-Vibolex; Neurobion; Neurobion N; Neurotrat S; Nifurantin B 6; Novirell B Duo; Pleomix-B; Reisegold†; Telbibur N†; Vitaject†; Vitamin B duo; ***Gr.:*** Lyso-6; Neurobion; ***Hong Kong:*** 3B; C-Sik†; Milgamma; Navidoxine; Neuro B1-6-12†; Neurobion; Neuromin; Neurorubine; Nevramin; Princi-B Fort; Vibion; Vida Neurotab; Vidaclofen-Plus; ***Hung.:*** Atherovit; Beres Magnezium + B ; Magne-B ; Magurlit†; Milgamma N; Neurobion; Pregmag; Vitacalc†; ***India:*** Blosyn; Conviron-TR; Cx-3; Cx-4; Cx-5; Doxinate; Eternex; Gocox Compound; Gocox-4†; Ipcacin Kid; Ipcazide; Isokin-300; Rifa; Rifa E; Sclerobion; Sioneuron; Vitneurin; Vominate; Wokex-2; Wokex-3; Wokex-4; ***Indon.:*** Abajos; Anvomer B6; Arsinal; Avogin; Betrion; Bicitron; Biocombin; Biomega; Biomex; Corobion; Corsaneuron; Daneuron; Deprex; Dolo Scanneuron; Dolo-Licobion; Dolo-Neurobion; Dolofenac; Dramasine; Farbion; Foraneural; Fundamin-E; Goralgin; Ikaneuron; Ikaneuron Plus; Lapibion; Licobion; Mediamer B6; Mersibion; Myoviton; Nervitone; Nervitone E; Neuralgin RX; Neuro Panstop; Neuro-Beston; Neurobat; Neurobat A; Neurobion; Neurobiovit; Neurodex; Neurohax; Neurophil; Neuropyramin; Neurosanbe; Neurosanbe Plus; Neurotrat; Neurotropic Plus; Neurovit E; Nevradin; Nevramin; Penagon; Ponconeuron; Pregnasea; Pregvomit; Primabion; Pritagesic; Scanneuron; Sohobion; Solaneuron; Stileran; Tocobion; Trimate-E; Tropineuron; Vitap; Vomilat; ***Israel:*** Calmanervin; Tribemin; Tricardia; ***Ital.:*** Acutil Fosforo; Adenoplex; Adenovit†; Alcalosio; Benexol B12; Coxanturenasi; Dobetin Totale; Emoantitossina†; Esaglut†; Fosforilasi; Miazide B6†; Midium; Mionevrasi; Neuraben; Sedofit; Trinevrina B6; ***Jpn:*** Neurovitan†; ***Malaysia:*** 3B; Becoloxin†; Flavettes Neuroforte; Fundamin-E; Navidoxine†; Neuro B†; Neurobion; Neurorubine; Neurovit†; Nevramin; Princi-B Fort; Re-B; Vitabion; ***Mex.:*** Aniflam Forte; Benexol B12; Betrox; Bomine; Bonadoxina; Bonalen; Bonazin; Cobotiaxina; Dexabion; Diclovith-B; Dodemina Tri; Dolo-Neurobion; Dolo-Pangavit; Dolo-Tiaminal; Doxemina; Duciclon; Emediba; Forvin; Innobion; Lecifar-K†; Liatriz; Macrox-5; Meclifar; Meclison; Neuralin; Neurobion; Nuro-B; Odexan; Pangavit B; Pangavit Hypak; Pangavit Pediatrico; Pidoxina; Revitaliv-C; Selectadoce; Suma-B; Tiaminal B Trivalente; Tribedoce; Tribedoce Compuesto; Tribedoxyl†; Trineurovita; Trineurovita Compuesto; Uni-Dox; Vo-Remi; ***Neth.:*** Emesafene; Neurobion; Princi B1 + B6; ***Philipp.:*** Catarstat; Dolo-Neurobion; Godex; Hinuron-E; Meganerv F-A; Neuroforte-E; Nevramin; Nuron-E; Vitanerv; ***Pol.:*** Filomag B ; Maglek B ; Magne-B ; Magnefar B ; Magsolvit B ; Magvit B ; MBE; Milgamma N; Slow-Mag B ; ***Port.:*** Detoxergon; Esclerobion; Linamin Plus†; Nausefe; Neurobion; Phakan†; ***Rus.:*** Lysobact (Лизобакт); Magne B6 (Магне B6); Milgamma (Мильгамма); Neuromultivit (Нейромультивит); Vectrum Calcium (Вектрум Кальций); ***S.Afr.:*** Asic; Neurobion; Vomifene; ***Singapore:*** Daneuron; Navidoxine†; Neurobion; Neurodex; Neuroforte; Neurorubine; Neurovit; Neuroxel; Nevramin; Princi-B Fort; ***Spain:*** Acetuber; Aftasone B C; Agudil; Antineurina; Benexol B1 B6 B12; Bester Complex; Biodramina Cafeina; Cariban; Cefabol; Dalamon†; Dorken; Duplicalcio 150†; Gamalate B6; Hidroxil B12 B6 B1; Mederebro; Menalgil B6; Nervobion; Neuromade; Neurostop Complex; Nuclesecrina; Pazbronquial; Pleocortex B6†; Quimpedor; Redutona; Sirodina†; Taurobetina†; Tepazepan; ***Swed.:*** Neurobion; ***Switz.:*** Acne Gel; Antemin compositum; Benexol B12; Catarstat; Itinerol B ; Linervidol†; Lyso-6†; Neurorubin; Phakolen†; Suracton†; Trawell compositum; Trilagavit; ***Thai.:*** 3B; B-100 Complex; Beromin; Cydoxmine-B†; Cyriamine; Douzabox; Ferli-6; Ferosix; Genavit; Hemolax; Neubee; Neurobex; Neurobion; Nevramin; Nuro-B; Nuvit; Princi-B; Re-B Forte; Roxine; Tribesian; Tricortin†; Trivit-B; Vita-B; Vitabion; Vitamedin†; Vitron; ***Turk.:*** Benexol; Benol; Benoral; Bevitab; Bevitol; Nerox-B; Neurogriseovit; Neurovit; Tribeksol; ***UAE:*** 3V; ***UK:*** HealthAid Boldo-Plus; Kelp Plus 3; ***USA:*** Beelith; Cerefolin; FOLTX; KLB6; Lurline PMS; Marlyn Formula 50; Metanx; PremesisRx; Releaf for PMS; ***Venez.:*** Bedoyecta; Bonadoxina; Briomet; Deca-Lentermina Complex; Dermagran; Dobetin Compuesto; Etizil†; Lecivar Plus; Lentermina Complex; Mebax†; Mega-Neubion; Miovit; Neubion; Neuribe; Rubrinal; Rubrinex; Tres-Be.

Used as an adjunct in: ***Ger.:*** Isozid comp N; tebesium; ***India:*** Rifacomb†; ***Indon.:*** bacbutINH; Erabutol Plus; INH-Ciba; INHA; Inoxin; Medinh-OD; Meditam-6; Mycothambin-INH; Niacifort-6; Niazitol; Pulmolin; Pulna; Pyravit; Pyrifort; Santibi Plus; Suprazid; TB Vit 6; ***Ital.:*** Etanicozid B6; ***Philipp.:*** CombiKids; Comprilex; Curazid (Reformulated); Ethamizid; Ethi 400; Eurocoxin; Isodexid; Isoxin; Kidz Kit 2; Kidz Kit 3; Nicetal; Odinah; Refam Duo; Refam Pedia Kit; Sthamizide; SVM-Polypac-A; Techxafort; Terozid; Vamsoxid; ***Pol.:*** Laktomag B ; ***Rus.:*** Isocomb (Изокомб); Lomecomb (Ломекомб); Protiocomb (Протиокомб); Repin B (Репин B); Rifacomb (Рифакомб); ***Spain:*** Cemidon B6; Tisobrif; ***Turk.:*** Isovit.

Vitamin B_{12} Substances

Vitamina B_{12}.

Vitamin B_{12} is the name generally used for a group of related cobalt-containing compounds, also known as cobalamins, of which cyanocobalamin and hydroxocobalamin are the principal forms in clinical use.

Cobamamide *(pINN)*

Adenosylcobalamin; Cobamamida; Cobamamidum; Coenzyme B_{12}; Dibencozide; Dibenzocozamide; Dimebenzcozamide; Kobamamid. Inner salt of the *Co*-(5′-deoxyadenosine-5′) derivative of the 3′-ester of cobinamide phosphate with 5,6-dimethyl-1-α-D-ribofuranosylbenzimidazole.

Кобамамид

$C_{72}H_{100}CoN_{18}O_{17}P$ = 1579.6.
CAS — 13870-90-1.
ATC — B03BA04.
ATC Vet — QB03BA04.

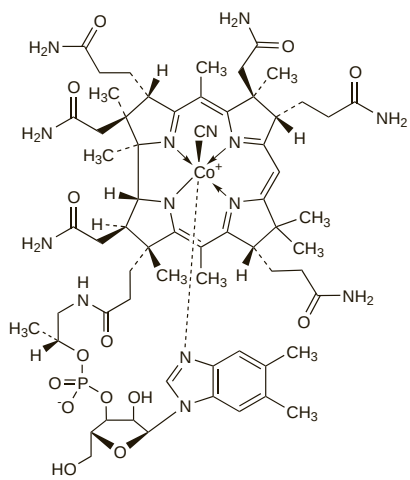
Pharmacopoeias. In *Chin.*

Cyanocobalamin *(BAN, rINN)*

Cianocobalamina; Cianokobalamin; Cianokobalaminas; Cobamin; Cyanocobalamine; Cyanocobalaminum; Cyanokobalamin; Cycobemin; Cyjanokobalamina; Kyanokobalamin; Siyanokobalamin; Syanokobalamiini. *Co*α-[α-(5,6-Dimethylbenzimidazolyl)]-*Co*β-cyanocobamide.

Цианокобаламин

$C_{63}H_{88}CoN_{14}O_{14}P$ = 1355.4.
CAS — 68-19-9.
ATC — B03BA01.
ATC Vet — QB03BA01.



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

Ph. Eur. 6.2 (Cyanocobalamin). A dark red, crystalline powder or dark red crystals. The anhydrous substance is very hygroscopic. Sparingly soluble in water and in alcohol; practically insoluble in acetone. Store in airtight containers. Protect from light.

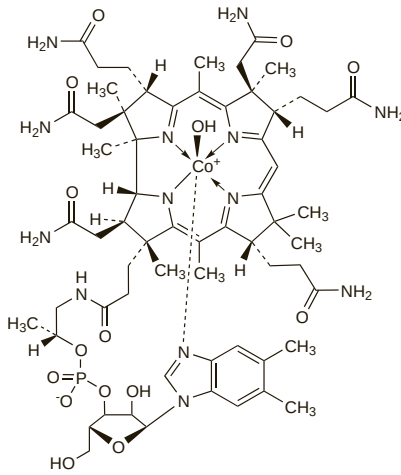
USP 31 (Cyanocobalamin). Dark red crystals or amorphous or crystalline red powder. In the anhydrous form it is very hygroscopic and when exposed to air it may absorb about 12% of water. Soluble 1 in 80 of water; soluble in alcohol; insoluble in acetone, in chloroform, and in ether. Store in airtight containers. Protect from light.

Hydroxocobalamin *(BAN, USAN, rINN)*

Hidroksokobalamin; Hidroxocobalamina; Hydroksikobalamiini; Hydroxikobalamin; Hydroxocobalamine; Hydroxocobalaminum; Hydroxycobalaminum; Idrossocobalamina. *Co*α-[α-(5,6-Dimethylbenzimidazolyl)]-*Co*β-hydroxocobamide.

Гидроксокобаламин

$C_{62}H_{89}CoN_{13}O_{15}P$ = 1346.4.
CAS — 13422-51-0.
ATC — B03BA03; V03AB33.
ATC Vet — QB03BA03; QV03AB33.



NOTE. The hydrated form of hydroxocobalamin has been referred to as aquocobalamin.

Pharmacopoeias. In *Int.* and *US.*

USP 31 (Hydroxocobalamin). Dark red crystals or red crystalline powder. Is odourless or has not more than a slight acetone odour. The anhydrous form is very hygroscopic. Soluble 1 in 50 of water and 1 in 100 of alcohol; practically insoluble in acetone, in chloroform, in ether, and in benzene; sparingly soluble in methyl alcohol. pH of a 2% solution in water is between 8.0 and 10.0. Store in airtight containers at a temperature of 8° to 15°. Protect from light.

Hydroxocobalamin Acetate *(BANM, rINNM)*

Acetato de hidroxocobalamina; Acetatocobalamin; Hidroksokobalamino acetatas; Hidroxokobalamin-acetát; Hydroksokobalamiiniasetaatti; Hydroxocobalamine, acétate d'; Hydroxocobalamini acetas; Hydroxokobalamin acetát; Hydroxokobalaminacetat.

Гидроксокобаламина Ацетат

$C_{64}H_{93}CoN_{13}O_{17}P$ = 1406.4.
CAS — 22465-48-1.

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

Ph. Eur. 6.2 (Hydroxocobalamin Acetate). A dark red, very hygroscopic, crystalline powder or dark red crystals. Soluble in water. Some decomposition may occur on drying. Store at a temperature between 2° and 8° in airtight containers. Protect from light.

Hydroxocobalamin Chloride *(BANM, rINNM)*

Cloruro de hidroxocobalamina; Hidroksokobalamino chloridas; Hidroxokobalamin-klorid; Hydroksokobalamiinikloridi; Hydroxocobalamine, chlorure d'; Hydroxocobalamini chloridum; Hydroxocobalamini Hydrochloridum; Hydroxokobalamin hydrochlorid; Hydroxokobalaminklorid.

Гидроксокобаламина Хлорид

$C_{62}H_{90}ClCoN_{13}O_{15}P$ = 1382.8.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *Viet.*

Ph. Eur. 6.2 (Hydroxocobalamin Chloride). A dark red, very hygroscopic, crystalline powder or dark red crystals. Soluble in water. Some decomposition may occur on drying. Store at a temperature between 2° and 8° in airtight containers. Protect from light.

Hydroxocobalamin Sulfate *(BANM, rINNM)*

Hidroksokobalamino sulfatas; Hidroxokobalamin-szulfát; Hydroksokobalamiinisulfaatti; Hydroxocobalamin Sulphate; Hydroxocobalamine, sulfate d'; Hydroxocobalamini sulfas; Hydroxokobalamin sulfát; Hydroxokobalaminsulfat; Sulfato de hidroxocobalamina.

Гидроксокобаламина Сульфат

$C_{124}H_{180}Co_2N_{26}O_{34}P_2S$ = 2790.8.