

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<sub>6</sub>, folate, vitamin B<sub>12</sub>, 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 tetrabutrylate 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.<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup>

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<sup>1,2</sup> and a placebo-controlled trial<sup>3</sup> 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. Boenke 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:** Belfavine; **Ger:** B2-ASmedic; **Hong Kong:** FAD Ophthalmic Soln; Hilon; **Indon:** Alinamin; **Thai:** Boflavin.

**Multi-ingredient:** **Austral:** Antioxidant Forte Tablets; Antioxidant Tablets; Extralife Eye-Care; Liv-Detox†; **Austria:** Beneruan Vit B-Komplex†; **Braz:** Sulfatofer†; **Ger:** Kwim†; **Hong Kong:** Alinamin-F; **India:** Hepamerz; **Indon:** Matase; **Ital:** Emazian B12†; Emoantitossina†; Facovit; Fos-

forilis; Neurofal†; **Jpn:** Neurovitant†; **Mex:** Pangavit Pediatrica; **Philipp:** Godex; **Pol:** Biovision; **Singapore:** Alinamin-F; **Spain:** Aftasone B C; **Thai:** Alinamin-F; B-100 Complex; **Turk:** Neurovit; **UK:** Quiet Life; Se-Power; **USA:** Cerefolin.

## Vitamin B<sub>6</sub> Substances

Vitamina B<sub>6</sub>.

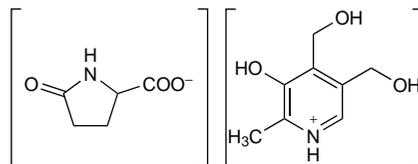
Vitamin B<sub>6</sub> is usually available as pyridoxine but the term is also used to refer to the related compounds, pyridoxal and pyridoxamine.

### Metadoxine

Metadoxina; Pyridoxine Pidolate. Pyridoxine 1-5-oxopyrrolidine-2-carboxylate.

$C_8H_{11}NO_3$ ,  $C_5H_7NO_3 = 298.3$ .

CAS — 74536-44-0.



### Pyridoxal Phosphate

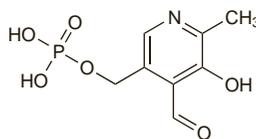
Codecarboxylase; MC-I; Piridoxal, fosfato de; Pyridoxal 5-Phosphate. 3-Hydroxy-5-hydroxymethyl-2-methylpyridine-4-carboxaldehyde 5'-phosphate.

$C_8H_{10}NO_6P = 247.1$ .

CAS — 54-47-7.

ATC — A11HA06.

ATC Vet — QA11HA06.

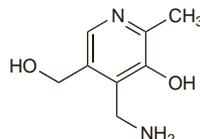


### Pyridoxamine Hydrochloride

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

$C_8H_{12}N_2O_2 \cdot 2HCl = 241.1$ .

CAS — 524-36-7.



(pyridoxamine)

### Pyridoxine Hydrochloride (BANM, rINNM)

Adermine Hydrochloride; Hidrokloruro de piridoxina; Piridoksin Hidroklorid; Piridoksin hidrokloridas; Piridossina Cloridrat; Piridoxin-hidroklorid; Pirydoksyn chlorowodorek; Pyridoksiini-hidroklorid; Pyridoxine, chlorhydrate de; Pyridoxin-hydrochlorid; Pyridoxinhydrochlorid; Pyridoxini hydrochloridum; Pyridoxinii Chloridum; Pyridoxinium Chloride; Pyridoxol Hydrochloride; Vitamin B<sub>6</sub>, 3-Hydroxy-4,5-bis(hydroxymethyl)-2-picoline hydrochloride.

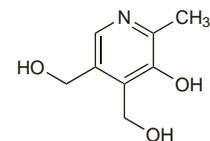
Пиридоксина Гидрохлорид

$C_8H_{11}NO_3 \cdot HCl = 205.6$ .

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<sub>6</sub> is excreted into breast milk.<sup>1,2</sup> While some have expressed concern over the inhibition of breast milk secretion by pyridoxine,<sup>3</sup> others have cautioned that pyridoxine deficiency may cause seizures in the neonate.<sup>4</sup> The American Academy of Pediatrics considers the use of pyridoxine to be usually compatible with breast feeding.<sup>5</sup>

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 nutrition during pregnancy and lactation: I. 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.<sup>1</sup> 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.<sup>2,3</sup> However, there have been some case reports<sup>4,5</sup> 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.<sup>6</sup> 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.<sup>7</sup> These proposals were heavily contested.<sup>7,8</sup> An upper limit of 100 mg daily has been suggested in the USA.<sup>8</sup>

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 al-tretamine. 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