

been investigated, with variable results; some consider that vitamin A and oily fish in the diet could be beneficial in terms of visual preservation.¹ Transplantation of the retina is being investigated as a treatment for retinitis pigmentosa.^{1,5} Devices to electrically stimulate the retina, optic nerve, or visual cortex are being developed.¹

1. Hartong DT, *et al.* Retinitis pigmentosa. *Lancet* 2006; **368**: 1795–1809.
2. Berson EL, *et al.* A randomized trial of vitamin A and vitamin E supplementation for retinitis pigmentosa. *Arch Ophthalmol* 1993; **111**: 761–2.
3. Yokota T, *et al.* Retinitis pigmentosa and ataxia caused by a mutation in the gene for the α -tocopherol-transfer protein. *N Engl J Med* 1996; **335**: 1770–1.
4. Sibulesky L, *et al.* Safety of <7500 RE (<25 000 IU) vitamin A daily in adults with retinitis pigmentosa. *Am J Clin Nutr* 1999; **69**: 656–63.
5. Anonymous. Transplantation as a therapy for retinitis pigmentosa? *Br J Ophthalmol* 1997; **81**: 430.

Retinopathy of prematurity. There is some suggestion that vitamin A supplementation may reduce the incidence of retinopathy of prematurity (p.1994).

Preparations

BP 2008: Paediatric Vitamins A, C and D Oral Drops;
BPC 1973: Vitamins A and D Capsules;
USP 31: Oleovitamin A and D; Oleovitamin A and D Capsules; Vitamin A Capsules.

Proprietary Preparations (details are given in Part 3)

Arg.: A-Vitel; Ademicina A Mama; Amenite A†; Andrioderma; Arovit; Atomoderma A; Bagovit A; Cazmar; Domsedan; Fiosen-A†; Flavostat†; Masivol; Metabolite-A†; Midermus†; Rogademis†; Skinderm A; **Austral.:** Ungvita; **Austria:** Arcavit A†; Avitol; Oleovit A; **Belg.:** Vitaminurine; **Braz.:** Arovit; Avitan†; Biocrin†; Lacrigel A; Retinar; **Canad.:** Arovit; **Chile:** Avitana; Bagovit A; Microret; **Cz.:** A-Mulsin†; Aserophthol; **Denm.:** A-vitamin; **Fin.:** A-Vitamin†; **Fr.:** A. 313; Arovit†; Avibon; **Ger.:** A-Mulsin†; A-Vicotrat†; Augenschutz NA; Oculetect; Oculetect sine; Solan-M†; Vitadral; Vitafluid; Vitagel; **Hung.:** Oculetect; **Israel:** Avipur; **Ital.:** Arovit; Euvitol; Repervit†; Vit-A-N†; **Malaysia:** Fairy ADE; **Mex.:** A Grin; A-Vicon†; Acon; Avinal-Ex†; Dermotin A; Microret; Microvita; Palmicaps†; Retigel-A; **Neth.:** Dagavit A Forte†; **NZ:** Dermalife; Ungvita; **Philipp.:** Afaxin; Alici-A; Hypotears; **Pol.:** Aksoderm; Dermosavit; Dermovit A; Masc. Ochronna z Witamina A; Masc. Vitaminowa Ochronna; **Port.:** A-Vite; Vitaminoflamin; **Rus.:** Vita-POS (Вита-ПОС); **S.Afr.:** Arovit; **Spain:** Auxina A Masiva; Biomino†; Dif Vitamin A Masivo†; Rinocusi Vitaminico; Rinovite†; **Swed.:** Arovit; **Switz.:** Arovit†; Oculetect; **Turk.:** Avicap; Avigen; Carovigen; **UK:** Biovit-A; **USA:** Aquasol A; Palmilate-A; Pedi-Vit-A; Retinol-A; **Venez.:** Alfa-Mon; Retiva.

Multi-ingredient: **Arg.:** A-D-C; A-Vitel E; AD Shock; Ademicina; Ademicina A; Atomoderma A-D; Atomoderma A-E; Aulo Gello Pie; Baby-Tex; Bagovit A Plus; Bagovit Avant Piel; Calusan Bebe; Celuvital†; Crema De Orden; Derivoco†; Dermanova; Dermosan; Epitheliale A-Derma; Factor Vit AE; Glossderm†; Herbaccion Nutriderm†; Hipoglos; Hipoglos con Hidrocortisona; Masivol Urea; Medicreme; Nemege†; O-Biol; Palant†; Panoxi; Platsul A; Puraloe Nutritivo; Redoxon A; Revital; Salvicutan†; Sulfadiazina de Plata; Sulfaplat; Ulcevarin†; Vagicular; Vansame; Vansame Plus; Vitapelen†; Zoedermia Cream; **Austral.:** Althaea Complex; Arthriforte; Bioglan Millelle A plus E; Bioglan Zn-A-C; Dermalife Plus; ER Cream†; Garlic, Horseradish, A & C Capsules†; Hydrastis Complex†; John Plunketts Protective Day Cream; Macro Natural Vitamin E Cream; Proyeast†; Sambucus Complex†; Trifolium Complex†; Verbascum Complex†; **Austria:** A-E-Mulsin; Arcavit A/E; Coldistop; Gelacet; Gerogelat; Lemual; Oleovit; Oleovit A; Oleovit A + D; Regenerin†; Rovigon; Ultrin; Vasovitol; **Belg.:** Neo-Cutigenol; Newderm†; Rovigon; Vita-Mefren†; **Braz.:** AD-Til; ADE 2 (Adedois); Adecal; Adederm; Adeforte; Aderogil D3; Babymed; Cariderm†; Dermalisan; Dermodyn; Epitezan; Gaduol†; Glossaliv; Hipoderme; Hipodermon; Hipodex; Hipoglos; Licovit; Multiderme; Pronenon; Regencel; Regenom; Sensibaby; Solemil†; Suavederm; Vitadesan; **Canad.:** A & D; A & D Ointment†; Antiseptic Skin Cream†; Lubiderm Advanced Moisture†; Nutrol A D; **Chile:** Brexon†; Dermaglos; Dermaglos Plus†; Droxel; Microret K; Nenegloss; Panthoderma-A; Peditaderm†; Platsul A; Pomada Vitaminica; Povin; Rovigon; Sanoderm; **Cz.:** A-E-Mulsin†; Coldastop; Hypotears; Infadolan; **Fin.:** A-Vita; Aesol; Oftan A-Pant; Wicarba; Wicnevit; **Fr.:** Alpha 5 DS†; Cirkan a la Prednisonone; Pommade Lelong†; Rovigon†; Seborheane; Solacy; **Ger.:** A + E Thilo†; A-E-Mulsin†; Coldastop; duraultra; Gelacet N†; Hewekzem novo N; Kwim†; Oculetect; Regepithel; Remeder†; Rovigon G†; Salus Augenschutz-Kapseln NA†; Tears Again; Unguentacid; Vita-POS; **Gr.:** Aquasol A+D; Aquasol A†; Avegon; Eviol-A; Novaquasol-A; **Hong Kong:** Aderma Epitheliale†; Hypotears†; Regepithel†; **Hung.:** Alksebör; Caldeat†; Coldastop; Neogranomron; Vita-Merfen†; **India:** Medithane; Ossivite; Sclerobion; Sharkomalt; Sharkovit; **Indon.:** Oculetect; Scott's E Vita; Visivit; Vita-Vision; **Israel:** Aquitol†; Aronal Forte; Baby A + D; Neocutan Silver; Oleovit A + D †; Vita-Merfen NF; Vitamidne A and D; **Ital.:** AD Pabym; Adisterolo; Babysteril; Derman-Oil; Dermana Crema; Dermana Pasta; Dicalcium†; Evitex; Granolein†; Midium; Neocuticals Spot Treatment; Provitamin A-E; Retinovit; Rinopanteina; Rovigon; Tocalfa; **Mex.:** Adekals; Adekon; Adekon C; Adeloren†; Adibal; Aquasol AD; Capent; Hipoglos; Hipoglos Cremosa; Kamiloderm; Microk; Microret K Nutrem; Quinoret; Sutin†; Vidamit; Vitalorange; **Neth.:** Dagavit A-E Forte†; Hallitrans; **Philipp.:** Remeder†; Rovigon; Vandol; **Pol.:** Alantavit; Capivit A + E; Oculetect; Tokovit A + E; Tranvit; **Port.:** Bacitracina Zima†; Dermabut; Esclerobion; Rovigon; Synchrovit; **S.Afr.:** Vandol†; **Spain:** Adiod; Antihermorrho†; Auxina A + E; Biomino A D; Calcio 20 Complex; Cicatral; Dermo Halbut; Epitelizante; Evitex A E Forte; Gramoce A; Grietalgen; Grietalgen Hidrocort†; Halbut; Halbut Hidrocortisona; Hubergrip†; Lacerdermol; Lacerdermol Complex; Mastiol; Mitos†; Vicomin A C; Vitaber A E; Wobenzimal†; **Swed.:** AD-vitamin; **Switz.:** Alphastrin; Antikeloides Creme; Carbamide Creme; Coldistop; Gelacet†; Leniderm†; Malvedrin; Oravil; Ricovitan†; Rovigon; Sanhelios Capsules a la vitamine A†; Unatol; Unguento-lan; Vita-Hexin; Vita-Merfen; **Turk.:** Balya; **UK:** S.H.I.P.; Se-Power; **USA:** A and D Medicated; Aloe Grande; Clocream; Diaper Guard; Lazercreme; Lobana Derm-Aide; Lobana Peri-Garde; Paladin; Phicon; **Venez.:** A-D-Vit; Adaderm; Ademina; Adenar; Dicalico†; Hipoglos†; Vandol; Vitenol†.

Vitamin B Substances

Vitamina B, grupo de la.

The B vitamin group includes the B₁ substances (thiamine and its derivatives), B₂ (riboflavin), B₆ (pyridoxine and derivatives), and B₁₂ (the cobalamins). In addition, nicotinic acid and its derivatives (p.1957) and folic acid (p.1940) are held to be part of the group, as is pantothenic acid (p.1959), but these latter substances are not generally referred to by their traditional B nomenclature.

Preparations

Proprietary Preparations (details are given in Part 3)

Philipp.: Vaneular.

Multi-ingredient: **Braz.:** Plex B; Xantina B12†; Xantion B12; **India:** Elfer†; Hycibex; JP Tone; Livogent†; Lupizyme; Terramycin SF; Toniazol†; Vitexid; **Indon.:** Gunabion; Lesifit; Tonikum; **Malaysia:** Hepavite; Time Release Nutrition Mega B + C Complex†; **Philipp.:** IBC; **Singapore:** Hepavite.

Used as an adjunct in: **Philipp.:** Trisofort.

Vitamin B₁ Substances

Vitamina B₁.

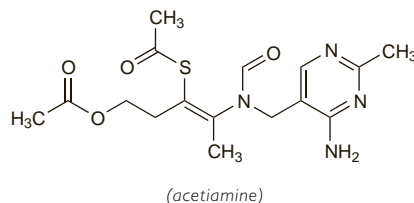
Acetiamine Hydrochloride (rINN)

Acetiamine Hydrochloride; Acétiamine, Chlorhydrate d'; Acetiamini Hydrochloridum; Diacetiamine Hydrochloride; Hidrocloruro de acetiamina. N-(5-Acetoxy-3-acetylthiopent-2-en-2-yl)-N-(4-amino-2-methylpyrimidin-5-ylmethyl)formamide hydrochloride monohydrate.

Ацетиамина Гидрохлорид

C₁₆H₂₂N₄O₄S.HCl.H₂O = 420.9.

CAS — 299-89-8 (acetiamine).



Benfotiamine (rINN)

Benfotiamina; Benfotiaminum; S-Benzoylthiamine O-Monophosphate. N-(4-Amino-2-methylpyrimidin-5-ylmethyl)-N-(2-benzoylthio-4-dihydroxyphosphinyloxy-1-methylbut-1-enyl)formamide.

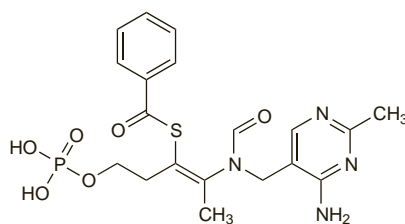
Бенфотиамин

C₁₉H₂₃N₄O₆PS = 466.4.

CAS — 22457-89-2.

ATC — A11DA03.

ATC Vet — QA11DA03.



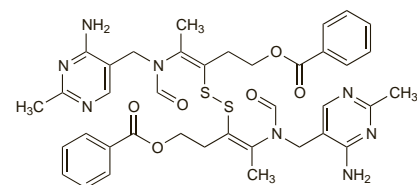
Bisbentiamine (rINN)

O-Benzoylthiamine Disulphide; Bisbentiamina; Bisbentiaminum. NN'-(Dithiobis[2-(2-benzoyloxyethyl)-1-methylvinylene])bis[N-(4-amino-2-methylpyrimidin-5-ylmethyl)formamide].

Бисбенйтиамин

C₃₈H₄₂N₈O₆S₂ = 770.9.

CAS — 2667-89-2.



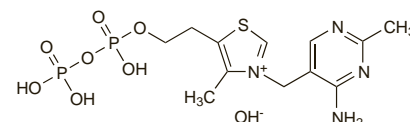
Cocarboxylase (BAN, rINN)

Cocarboxilasa; Co-carboxylase; Cocarboxylasum; Diphosphothiamine; Pyruvodehydraz; Thiamine Pyrophosphate. 3-(4-Amino-2-methylpyrimidin-5-ylmethyl)-5-{2-[dihydroxyphosphinyloxy-(hydroxy)phosphinyloxy]ethyl}-4-methylthiazolium hydroxide.

Кокарбоксилаза

C₁₂H₂₆N₄O₈P₂S (hydroxide form) = 442.3.

CAS — 154-87-0 (cocarboxylase chloride).



Pharmacopoeias. *Pol.* includes the chloride.

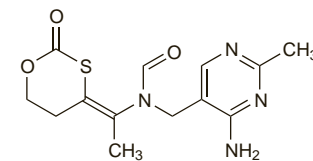
Cycotiamine (rINN)

CCT; Cicotiamina; Cyclocarbothiamine; Cycotiaminum. N-(4-Amino-2-methylpyrimidin-5-ylmethyl)-N-[1-(2-oxo-1,3-oxathian-4-ylidene)ethyl]formamide.

Цикотиамин

C₁₃H₁₆N₄O₃S = 308.4.

CAS — 6092-18-8.



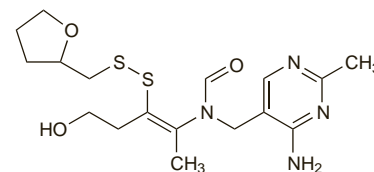
Fursultiamine (rINN)

Fursultiamina; Fursultiaminum; Thiamine Tetrahydrofurfuryl Disulphide; TTFD. N-(4-Amino-2-methylpyrimidin-5-ylmethyl)-N-[4-hydroxy-1-methyl-2-(tetrahydrofurfuryldithio)but-1-enyl]formamide.

Фурсультиамин

C₁₇H₂₆N₄O₃S₂ = 398.5.

CAS — 804-30-8.



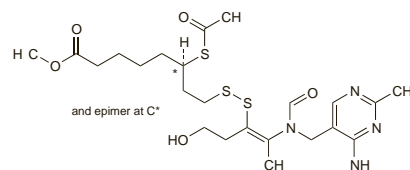
Octotiamine (rINN)

Octotiamina; Octotiaminum; Oktotiamiini; Oktotiamin; TATD; Thiocotthiamine. N-[2-(3-Acetylthio-7-methoxycarbonylheptyldithio)-4-hydroxy-1-methylbut-1-enyl]-N-(4-amino-2-methylpyrimidin-5-ylmethyl)formamide.

Октотиамин

C₂₃H₃₆N₄O₅S₃ = 544.8.

CAS — 137-86-0.



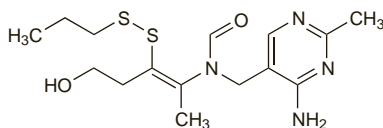
Prosultiamine (rINN)

DTPT; Prosultiamina; Prosultiaminum; Thiamine Propyl Disulphide. *N*-(4-Amino-2-methylpyrimidin-5-ylmethyl)-*N*-(4-hydroxy-1-methyl-2-propyldithio-but-1-enyl)formamide.

Просультіамин

$C_{15}H_{24}N_4O_2S_2 = 356.5$.

CAS — 59-58-5.

**Sulbutiamine** (rINN)

Bisubutiamine; *O*-isobutyrylthiamine Disulphide; Sulbutiamina; Sulbutiaminum. *NN'*-(Dithiobis[2-(2-isobutyryloxyethyl)-1-methyl-vinylene])bis[*N*-(4-amino-2-methylpyrimidin-5-ylmethyl)-formamide].

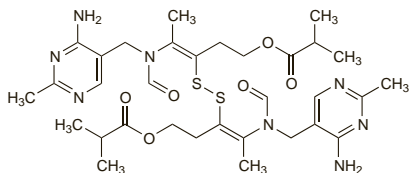
Сулбутиамин

$C_{32}H_{46}N_8O_6S_2 = 702.9$.

CAS — 3286-46-2.

ATC — A11DA02.

ATC Vet — QA11DA02.

**Thiamine Hydrochloride** (BANM, rINNM)

Aneurine Hydrochloride; Hidrocloruro de tiamina; Thiamin Hydrochloride; Thiamine, chlorhydrate de; Thiamine Chloride; Thiamin-hydrochlorid; Thiamini hydrochloridum; Thiaminii Chloridum; Thiaminihydrochlorid; Thiamin-hidroklorid; Thiaminihydroklorid; Tiamino hidrochloridas; Tiaminy chlorowodorek; Vitamin B₁. 3-(4-Amino-2-methylpyrimidin-5-ylmethyl)-5-(2-hydroxyethyl)-4-methylthiazolium chloride hydrochloride.

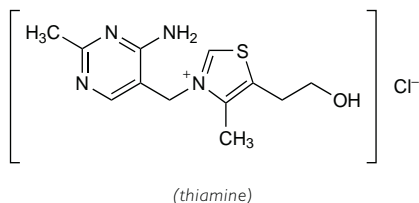
Тиаміна Гідрохлорид

$C_{12}H_{17}ClN_4OS.HCl = 337.3$.

CAS — 59-43-8 (thiamine); 67-03-8 (thiamine hydrochloride).

ATC — A11DA01.

ATC Vet — QA11DA01.



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

Thiamine hydrobromide is included in *Int*.

Ph. Eur. 6.2 (Thiamine Hydrochloride). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; slightly soluble in alcohol; soluble in glycerol. A 2.5% solution in water has a pH of 2.7 to 3.3. Store in nonmetallic containers. Protect from light.

USP 31 (Thiamine Hydrochloride). White crystals or crystalline powder, usually having a slight, characteristic odour. When exposed to air, the anhydrous product rapidly absorbs about 4% of water. Soluble 1 in 1 of water and 1 in 170 of alcohol; insoluble in ether and in benzene; soluble in glycerol. pH of a 1% solution in water is between 2.7 and 3.4. Store in airtight containers. Protect from light.

Stability. Sterile thiamine hydrochloride solutions of pH 4 or less lose activity only very slowly but neutral or alkaline solutions deteriorate rapidly, especially in contact with air.

Thiamine Nitrate (BANM, rINNM)

Aneurine Mononitrate; Nitrato de tiamina; Thiamine Mononitrate; Thiamine, nitrate de; Thiamini nitras; Thiamin-nitrat; Thiamini nitratt; Thiaminnitrat; Thiamin-nitrat; Tiamino nitratas; Tiaminy azotan; Vitamin B₁ Mononitrate. 3-(4-Amino-2-methylpyrimidin-5-ylmethyl)-5-(2-hydroxyethyl)-4-methylthiazolium nitrate.

Тиаміна Нитрат

$C_{12}H_{17}N_5O_4S = 327.4$.

CAS — 532-43-4.

ATC — A11DA01.

ATC Vet — QA11DA01.

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

Ph. Eur. 6.2 (Thiamine Nitrate). A white or almost white, crystalline powder or small, colourless crystals. Sparingly soluble in water; freely soluble in boiling water; slightly soluble in alcohol and in methyl alcohol. A 2% solution in water has a pH of 6.8 to 7.6. Store in nonmetallic containers. Protect from light.

USP 31 (Thiamine Mononitrate). White crystals or crystalline powder, usually having a slight characteristic odour. Soluble 1 in 44 of water; slightly soluble in alcohol; very slightly soluble in chloroform. pH of a 2% solution in water is between 6.0 and 7.5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

Adverse effects with thiamine are rare, but hypersensitivity reactions have occurred, mainly after parenteral doses. These reactions have ranged in severity from very mild to, very rarely, fatal anaphylactic shock (see below).

Breast feeding. Supplementation did not significantly affect thiamine concentration in breast milk of healthy, well-nourished women when compared with those not given thiamine; the authors supposed that absorptive capacity of the mammary gland may be saturable.¹ Based on this, the American Academy of Pediatrics considers its use to be usually compatible with breast feeding.²

1. Nail PA, *et al.* The effect of thiamin and riboflavin supplementation on the level of those vitamins in human breast milk and urine. *Am J Clin Nutr* 1980; **33**: 198–204.
2. 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)

Hypersensitivity. The UK CSM had received, between 1970 and July 1988, 90 reports of adverse reactions associated with the use of an injection containing high doses of vitamins B and C. The most frequent reactions were anaphylaxis (41 cases, including 2 fatalities), dyspnoea or bronchospasm (13 cases), and rash or flushing (22 cases); 78 of the reactions occurred during, or shortly after, intravenous injection and the other 12 after intramuscular injection.¹ They recommended that parenteral treatment be used only when essential, and that, when given, facilities for treating anaphylaxis should be available. They also recommended that, when the intravenous route was used, the injection be given slowly (over 10 minutes). Various authors^{2,3} have noted that parenteral treatment is essential for the prophylaxis and treatment of Wernicke's encephalopathy (see below). However, further reports of anaphylaxis to parenteral thiamine have since been described,^{4,6} including one with a fatal outcome.⁴

1. Committee on Safety of Medicines. Parentovite & allergic reactions. *Current Problems* 24 1989.
2. Wrenn KD, Slovis CM. Is intravenous thiamine safe? *Am J Emerg Med* 1992; **10**: 165.
3. Thomson AD, Cook CCH. Parenteral thiamine and Wernicke's encephalopathy: the balance of risks and concerns. *Alcohol Alcohol* 1997; **32**: 207–9.
4. Van Haecke P, *et al.* Thiamine-induced anaphylactic shock. *Am J Emerg Med* 1995; **13**: 371–2.
5. Morinville V, *et al.* Anaphylaxis to parenteral thiamine (vitamin B₁). *Schweiz Med Wochenschr* 1998; **128**: 1743–4.
6. Johri S, *et al.* Anaphylaxis from intravenous thiamine—long forgotten? *Am J Emerg Med* 2000; **18**: 642–3.

Pharmacokinetics

Small amounts of thiamine are well absorbed from the gastrointestinal tract after oral doses, but the absorption of doses larger than about 5 mg is limited. It is also rapidly absorbed on intramuscular injection. It is widely distributed to most body tissues, and appears in breast milk. Within the cell, thiamine is mostly present as the diphosphate. Thiamine is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine unchanged or as metabolites.

References.

1. Weber W, *et al.* Nonlinear kinetics of the thiamine cation in humans: saturation of nonrenal clearance and tubular reabsorption. *J Pharmacokinet Biopharm* 1990; **18**: 501–23.
2. Tallaksen CME, *et al.* Kinetics of thiamin and thiamin phosphate esters in human blood, plasma and urine after 50 mg intravenously or orally. *Eur J Clin Pharmacol* 1993; **44**: 73–8.

3. Loew D. Pharmacokinetics of thiamine derivatives especially of benfotiamine. *Int J Clin Pharmacol Ther* 1996; **34**: 47–50.

4. Greb A, Bitsch R. Comparative bioavailability of various thiamine derivatives after oral administration. *Int J Clin Pharmacol Ther* 1998; **36**: 216–21.

5. Frank T, *et al.* High thiamine diphosphate concentrations in erythrocytes can be achieved in dialysis patients by oral administration of benfotiamine. *Eur J Clin Pharmacol* 2000; **56**: 251–7.

6. Drewe J, *et al.* Effect of intravenous infusions of thiamine on the disposition kinetics of thiamine and its pyrophosphate. *J Clin Pharm Ther* 2003; **28**: 47–51.

Human Requirements

Thiamine requirements are directly related to the carbohydrate intake and the metabolic rate. A daily dietary intake of about 0.9 to 1.5 mg of thiamine is recommended for healthy men and about 0.8 to 1.1 mg for healthy women. Cereals, nuts, peas, beans, yeast, and pork are rich sources of thiamine. Some other meats especially liver or kidneys, and also fish, contain significant amounts. Flour and bakery products are often enriched with thiamine. Considerable losses of thiamine may result from cooking processes.

UK and US recommended dietary intake. In the UK dietary reference values (see p.1925) have been published for thiamine¹ and similarly in the USA recommended dietary allowances (RDAs) have been set.² In the UK for adult males and females the reference nutrient intake (RNI) is 0.4 mg per 1000 kcal daily and the estimated average requirement (EAR) is 0.3 mg per 1000 kcal daily. In the USA an RDA of 1.2 mg daily in adult males and 1.1 mg daily in females is recommended.

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 B₆, folate, vitamin B₁₂, 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

Thiamine is a water-soluble vitamin, although some of its derivatives have greater lipophilicity. It is an essential coenzyme for carbohydrate metabolism in the form of the diphosphate (thiamine pyrophosphate, cocarboxylase). Thiamine deficiency develops when the dietary intake is inadequate; severe deficiency leads to the development of a syndrome known as beri-beri. Chronic 'dry' beri-beri is characterised by peripheral neuropathy, muscle wasting and muscle weakness, and paralysis. Acute 'wet' beri-beri is characterised by cardiac failure and oedema. Wernicke-Korsakoff syndrome (demyelination of the CNS) may develop in severe cases of thiamine deficiency notably in association with chronic alcoholism. Severe thiamine deficiency, characterised by lactic acidosis and neurological deterioration, has been reported within a relatively short time of starting thiamine-free total parenteral nutrition; some deaths have occurred.

Thiamine is used in the treatment and prevention of thiamine deficiency. It is given orally, the preferred route, or if necessary by the intramuscular or intravenous routes (but see Hypersensitivity, above); intravenous injections should be given slowly over 30 minutes. In the treatment of mild chronic thiamine deficiency usual oral doses of 10 to 25 mg daily, in single or divided doses, have been recommended. In severe thiamine deficiency doses of up to 300 mg daily are given, and even higher daily doses may be used in Wernicke-Korsakoff syndrome by the intravenous route.

Thiamine is usually given as either the hydrochloride or nitrate salts although other salts such as the dicamylate, disulfide, monophosphate (monophosphothiamine) or pyrophosphate (cocarboxylase) may be used.

Other compounds that possess vitamin B₁ activity and may be given as alternatives to thiamine include benfotiamine, cycotiamine, octotiamine, prosultiamine, and sulbutiamine. Acetiamine, bisbentiamine, and fursultiamine have also been used.

Diabetes mellitus. Low plasma thiamine concentrations have been found¹ in patients with type 1 and type 2 diabetes mellitus (p.431). In a small placebo-controlled study, benfotiamine