

Tardive dyskinesia. In a double-blind, controlled, crossover study, daily oral doses of vitamin B₆ 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:** Dicllo-B; **Belg.:** Bedoxine; **Braz.:** Dimedriñ; Fonto-Vit B6; **Neuri B6;** **Seis-B;** **Canad.:** Carthame; **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.:** Comploment Continus; **Israel:** Anacrodine; B-Six; **Ital.:** Benadon; Memosprint; Metadoxil; Xanturensia; **Mex.:** Abrixone; Fortical; Metasin; Valparina; **Philipp.:** Drexabin; Hybutin; Jaga; Lixtrex; 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; Comploment Continus; **Thai.:** B-6; Metadoxil; **Turk.:** B. Vigen; Libavit B; Postadoxine; **USA:** Vitelle Nestrex; **Venez.:** Benadon; Beplus; Biprin; Clodoxin; Suprabion; Vibrant.

Multi-ingredient: **Arg.:** 6 Copin; Algio Nervomax; Algio Nervomax Fuerte; Blastop; Butineuron; Cadenal Plus; Calcinam; Magnesio; Centella Incaico; Cobenexol Forte; Cobenexol Fuerte; CVP B1 B6 B12; Dexabion; Dolo Nervobion; Dolo Nervobion 10000; Dorixina B1 B6 B12; Flexicamin B12; Florigatin B12; Holomagnesio B6; KLB6 Fruit Diet; Klossidol B1 B6 B12; Lohp; Magnebe; Megacistin; Megapuls; Nervobion Fuerte; Nervomax TB12; Neuronal Vascular; Plenovit Melatonin; Presterin; QX 10; Sindrone; Total Magnesiano B6; **Austral.:** Bio Magnesium; Extralife Flow-Care; Extralife Fluid-Care; Extralife PMS-Care; Extralife Uri-Care; Liv-Detox; Mag-Oro; Medinat PMT-Ezet; Zinc Zenith; **Austria:** Arca-B; Aslavit; Astronauta; Beneran compositum; Beneran Vit B-Komplex; Contravert B; Diclavit; Dolo-Neurobion; Echnatol B; Neurobion; Neuromerck; Neuromultivit; Pronerv; Signalin B; Signalin B forte; Signalin B ohne Coffein; Vertirosan Vitamin B; **Belg.:** Betapyr; Neurobion; Vioneurin; **Braz.:** Alergo Final; Aminocid; Aminotox; Anekron; Benistina; Betaliver; Bicavine; Biohepax; Bronquitos; Cianotrat-Dexa; Citoneurin; Dexa-Citoneurin; Dexa-Cronob; Dexa-Neuribion; Dexacoba; Dexador; Dexadoze; Dexagil; Dexaneurin; Dexaneval; Diagrin; Doxal; Dramavit B6; Dramin B-6; Dramin B-6 DL; Emetrol; Enjoil; Epativan; Epocler; Estact; Gabax; Hepacitron; Hepatobex; Hepatox; Hormo Hepatico; Levordiol; Megestran; Montrean B6; Nausical; Nausilon B6; Negro B-6; Nicopaverina B6; Pantevit; Plagon; Trirubin; Vitatonus; Vominil; Xantion Complex; **Canad.:** Dialectin; Penta-3B; Penta-3B + C; ProstGard; **Chile:** Activator; Betonvit; Dolutol 12; Ferro Vitaminico; Gamlate B6; Glutacyl Vitaminado; Hexalecto; Nefersil B; Neurobion; Neurocam; Tol 12; Tol 12 Plus; **Cz.:** Magne-B; Milgamma NA; Neuromultivit; **Fin.:** Neurobion; Neurovit; Wicnecarb; Wicnevit; **Fr.:** Arthrolib; Catarstat; Cysti-C; Cystine B; Lyso-6; Magne-B; Phakan; Uvimag B; **Ger.:** B-Komplex forte; Bevit Forte; Bramin-hepa; Dolo-Neurobion forte; Dolo-Neurobion N; Hepagisevit Forte-N; Hewedolor neuro; Medivitan N; Medivitan N Neuro; Medyn; Milgamma; Milgamma N; Milgamma-NA; Milneuron NA; Neuralsan S; Neuro; Neuro uno; Neuro-AS N; neuro-B forte; Neuro-Effektin B; Neuro-Lichtenstein M; Neuro-Lichtenstein N; Neuro-ratiopharm N; Neuro-ratiopharm; Neuro-Vibex; Neurobion; Neurobion N; Neurotrat S; Nifurantin B 6; Novirel B Duo; Pleomix-B; Reigold; Telbibur N; Vitaject; Vitamin B duo; **Gr.:** Lyso-6; Neurobion; **Hong Kong:** B6; C-Six; Milgamma; Navidoxine; Neuro B1-6-12; Neurobion; Neuromin; Neurorubine; Nevramin; Princi-B Fort; Vibion; Vida Neurotab; Vidalofen-Plus; **Hung.:** Atherovit; Beres Magnezium + B; Magne-B; Maguril; Milgamma N; Neurobion; Pregmag; Vitacalc; **India:** Blosyn; Convion-TR; Cx-3; Cx-4; Cx-5; Dioxinate; Eternex; Gocox Compound; Gocox-4; Ipcacin Kid; Ipcazine; Isokin-300; Rifa; Rifa E; Sclerobion; Soneuron; Viturum; Vominate; Wokex-2; Wokex-3; Wokex-4; **Indon.:** Abajos; Anvomer B6; Arsinol; Avogin; Betrión; Bicitron; Biocombin; Biomega; Biomec; Corobion; Corsaneuron; Daneuron; Deprex; Dolo Scanneuron; Dolo-Licobion; Dolo-Neurobion; Doloferac; Dramasine; Farbion; Foraneural; Fundamin-E; Goralgin; Ikeuron; Kaneuron-Lus; Laphibion; Licobion; Mediamer B6; Mersibion; Myoviton; Nervitone; Nervitone E; Neuralgin RX; Neuro Panstop; Neuro-Beston; Neurobat; Neurobat A; Neurobion; Neurobiotiv; Neurodex; Neurohax; Neurophil; Neuropyramin; Neuronasbe; Neuronasbe Plus; Neurotrat; Neurotropic Plus; Neurovit E; Nevradin; Nevramin; Penagon; Ponconeuron; Pregnasae; Pregvomit; Primabion; Prtagase; Scanneuron; Sohobion; Solaneuron; Stileran; Tobicion; Trimate-E; Tropineuron; Vitap; Vomilat; **Israel:** Calmanervin; Trimbion; Tricardia; **Ital.:** Acutif Fosforo; Adenoplex; Adenovit; Alcalosio; Benexol B12; Coxanturensia; Dobetin Totale; Emoantossina; Esaglut; Fosforilasi; Miazide B6; Midium; Mionevras; Neurben; Sedoff; Trinevria B6; **Jpn.:** Neurovitant; **Malaysia:** 3B; Becoloxin; Flavettes Neuroforte; Fundamin-E; Navidoxine; Neuro B; Neurobion; Neurobion; Neurovit; Nevramin; Princi-B Fort; Re-B; Vitabion; **Mex.:** Ariflam Forte; Benexol B12; Betrox; Bomin; Bonadoxina; Bonalin; Bonazin; Cobotixina; Dexabion; Diclavit-B; Dodelima Tri; Dolo-Neurobion; Dolo-Pangavit; Dolo-Tiaminal; Dolemina; Ducidin; Emedba; Forvin; Innobion; Lecifar-K; Liatrix; Macrox-5; Medifar; Medison; 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.:** Emsesafe; Neurobion; Princi B1 + B6; **Philipp.:** Catarstat; Dolo-Neurobion; Godeix; Hinuron-E; Meganerv F-A; Neuroforte-E; Nevramin; Nuron-E; Vitaneur; **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.:** Lyso-bact (Лизобакт); Magne B6 (Мане Б6); Milgamma (Милгамма); Neuro-multivit (Нейромултивит); Vectrum Calcium (Вектрум Кальций); **S.Afr.:** Asic; Neurobion; Vomifene; **Singapore:** Daneuron; Navidoxine; Neurobion; Neurodex; Neuroforte; Neurorubine; Neurovit; Neuroxol; Nevramin; Princi-B Fort; **Spain:** Acetuber; Aftasone B C; Agudil; Antineurina; Benexol B1 B6 B12; Bester Complex; Biodramina Cafeina; Cariban; Cefabol; Dalamin; Dorken; Duplicalcio 150; Gamalate B6; Hidroxil B12 B6 B1; Mederebro; Menaligil B6; Nervobion; Neuromade; Neurostop Complex; Nucleseina; Pazbrinqual; Pleocortex B6; Qimpedro; Redone; Sirodin; Tauracetina; Tepazepan; **Swed.:** Neurobion; **Switz.:** Actus Gel; Antinam compositum; Benexol B12; Catarstat; Itinerol B; Linervidol; Lyso-6; Neuro-rubion; Phakolent; Suracton; Travell compositum; Trilavagat; **Thai.:** 3B; B-100 Complex; Beromin; Cydoxime-B6; Cyamine; Douzabox; Ferli-6; Ferios; Genavit; Hemolax; Neumex; Neurohex; 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; Bevitit; Nerex-B; Neurogrisevit; Neurovit; Tribeksol; **UAE:** 3V; **UK:** HealthAid Boldo-Plus; Kelp Plus 3; **USA:** Beelith; Cerefolin; FOLTX; KLB6; Lurline PMS; Marilyn Formula 50; Metanx; PremisRx; Release for PMS; **Ven.:** Bedyecta; Bonadoxina; Biomet; Dexa-Lentemina Complex; Derna; Dobetin Compuesto; Etizil; Lecifar Plus; Lentemina Complex; Mebax; Mega-Neubion; Miovit; Neubion; Neunber; Rubinal; Rubrinex; Tres-B.

Used as an adjunct in: **Ger.:** Isozid comp N; tesbesium; **India:** Rifacomb; **Indon.:** bacutlNH; Erabulol Plus; INH-Ciba; INHA; Innox; 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; Eth 400; Eurocoxin; Isodexid; Isoxin; Kidz Kit 2; Kidz Kit 3; Nicetal; Odinah; Refam Duo; Refam Pedia Kit; Sthamizid; SVM-Polypac-A; Techsafort; Terozid; Vamsoxid; **Pol.:** Laktomag B; **Rus.:** Isocomb (Изокомб); Lomecomb (Ломекомб); Protiocomb (Протиокомб); Repin B (Репин В); Rifacomb (Рифакомб); **Spain:** Cemidon B6; Tisobrin; **Turk.:** Isovit.

Vitamin B₁₂ Substances

Vitamina B₁₂.

Vitamin B₁₂ 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 B₁₂; Dibenzocido; Dibenzozamide; Dimebenzozamide; Kobamamin. 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

C₇₇H₁₀₀CoN₁₈O₁₇P = 1579.6.

CAS — 13870-90-1.

ATC — B03BA04.

ATC Vet — QB03BA04.

Pharmacopoeias. In *Chin.*

Cyanocobalamin (BAN, rINN)

Cianocobalamina; Cianokobalamina; Cianokobalaminas; Cobamin; Cyanocobalamine; Cyanocobalaminum; Cyanocobalamin; Cycobemine; Cyanokobalamina; Kyanokobalamina; Siyanokobalamina; Syanokobalamini. Coa-[α -(5,6-Dimethylbenzimidazolyl)]-CoB-cyanocobamide.

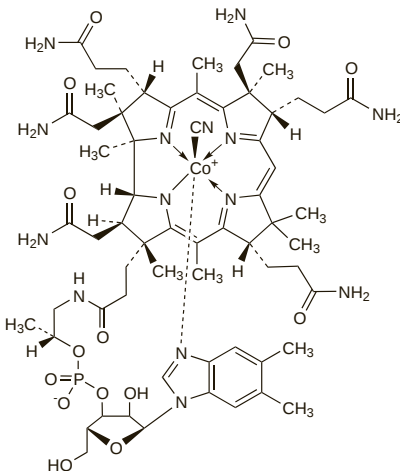
Цианокобаламин

C₆₃H₈₈CoN₁₄O₁₄P = 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)

Hidroksokobalamina; Hidroxocobalamina; Hidroksikobalamini; Hidroksikobalamina; Hidroxocobalamine; Hidroxocobalaminum; Hidroxocobalaminum; Idrossocobalamina. Coa-[α -(5,6-Dimethylbenzimidazolyl)]-CoB-hydroxocobamide.

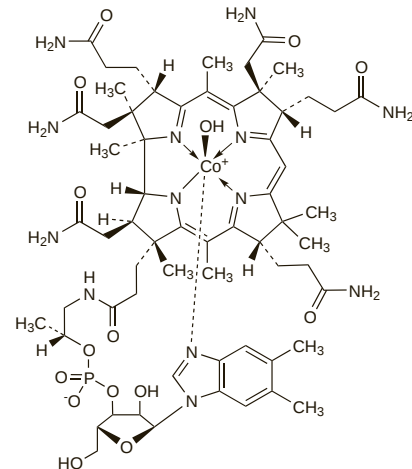
Гидрококобаламин

C₆₂H₈₉CoN₁₃O₁₅P = 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, rINN)

Acetato de hidroxcobalamina; Acetatocobalamina; Hidroksokobalamino acetatas; Hidroxokobalamina-acetát; Hidroksokobalaminiacetat; Hydroxocobalamine, acétate d'; Hydroxocobalamini acetat; Hydroxokobalamina acetát; Hydroxokobalamina-cetát.

Гидрококобаламина Ацетат

C₆₄H₉₃CoN₁₃O₁₇P = 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, rINN)

Cloruro de hidroxcobalamina; Hidroksokobalamino chloridas; Hidroxokobalamina-klorid; Hidroksokobalaminiiklorid; Hydroxocobalamine, chloride d'; Hydroxocobalamini chloridum; Hydroxocobalamini Hydrochloridum; Hydroxokobalamini hydrochlorid; Hydroxokobalaminklorid.

Гидрококобаламина Хлорид

C₆₂H₉₀ClCoN₁₃O₁₅P = 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, rINN)

Hidroksokobalamino sulfatas; Hidroxokobalamina-szulfát; Hidroksokobalaminiisulfat; Hidroxocobalamini Sulphate; Hydroxocobalamine, sulfate d'; Hydroxocobalamini sulfas; Hydroxokobalamini sulfát; Hydroxokobalaminsulfat; Sulfato de hidroxcobalamina.

Гидрококобаламина Сульфат

C₁₂₄H₁₈₀Co₂N₂₆O₃₄P₂S = 2790.8.

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

Ph. Eur. 6.2 (Hydroxocobalamin Sulphate). 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.

Mecobalamin (BAN, USAN, pINN)

Mecobalamin; Mécobalamine; Mecobalaminum; Methylcobalamin. Coa-[α-(5,6-Dimethylbenzimidazolyl)]-Coβ-methylcobamide.

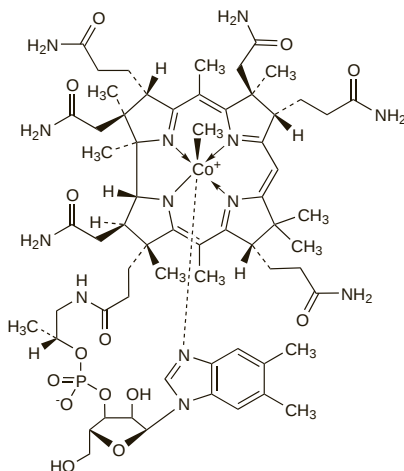
Мекобаламин

C₆₃H₉₁CoN₁₃O₁₄P = 1344.4.

CAS — 13422-55-4.

ATC — B03BA05.

ATC Vet — QB03BA05.



Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions

Allergic hypersensitivity reactions have occurred rarely after parenteral doses of the vitamin B₁₂ compounds cyanocobalamin and hydroxocobalamin. Antibodies to hydroxocobalamin-transcobalamin II complex have developed during hydroxocobalamin therapy.

Arrhythmias secondary to hypokalaemia have occurred at the beginning of parenteral treatment with hydroxocobalamin.

Intranasal cyanocobalamin may cause rhinitis, nausea, and headache.

Cyanocobalamin or hydroxocobalamin should, if possible, not be given to patients with suspected vitamin B₁₂ deficiency without first confirming the diagnosis. Regular monitoring of the blood is advisable. Use of doses greater than 10 micrograms daily may produce a haematological response in patients with folate deficiency; indiscriminate use may mask the precise diagnosis. Conversely, folate may mask vitamin B₁₂ deficiency (see p.1940).

Cyanocobalamin should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.

Breast feeding. Vitamin B₁₂ is distributed into breast milk.¹ The American Academy of Pediatrics considers its use to be usually compatible with breast feeding.²

1. Samson RR, McClelland DBL. Vitamin B in human colostrum and milk. *Acta Paediatr Scand* 1980; **69**: 93-9.

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. Analysis, by the Boston Collaborative Drug Surveillance Program, of data on 15 438 patients hospitalised between 1975 and 1982 detected 3 allergic skin reactions attributed to cyanocobalamin among 168 recipients of the drug.¹ For the purposes of the study, reactions were defined as being generalised morbilliform exanthems, urticaria, or generalised pruritus only.

In a patient with a generalised pruritic reaction to hydroxocobalamin (with subsequent urticaria, bronchospasm, and oropharyngeal angioedema), cyanocobalamin was relatively well-tolerated, with only one episode of delayed urticaria.²

1. Bigby M, et al. Drug-induced cutaneous reactions: a report from the Boston Collaborative Drug Surveillance Program on 15 438 consecutive inpatients, 1975 to 1982. *JAMA* 1986; **256**: 3358-63.

2. Heyworth-Smith D, Hogan PG. Allergy to hydroxocobalamin, with tolerance of cyanocobalamin. *Med J Aust* 2002; **177**: 162-3.

Local reactions. After 3 years of monthly intramuscular vitamin B₁₂ injections, a patient presented with a sclerotic plaque at the injection site, which was successfully treated by excision and local fat transfer. It was unclear as to whether the patient had reacted to the vehicle, the preservative, or to the cyanocobalamin.¹ Fascial haematoma after vitamin B₁₂ injection leading to local compression (posterior arm compartment syndrome) has also been reported.²

1. Ho J, et al. Vitamin B12-associated localized scleroderma and its treatment. *Dermatol Surg* 2004; **30**: 1252-5.

2. Knapke D, Truumees E. Posterior arm and deltoid compartment syndrome after vitamin B12 injection. *Orthopedics* 2004; **27**: 520-1.

Interactions

Absorption of vitamin B₁₂ from the gastrointestinal tract may be reduced by neomycin, aminosalicylic acid, histamine H₂-antagonists, omeprazole, and colchicine. Serum concentrations may be decreased by use of oral contraceptives. Many of these interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations. Parenteral chloramphenicol may attenuate the effect of vitamin B₁₂ in anaemia.

Pharmacokinetics

Vitamin B₁₂ substances bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa, and are then actively absorbed from the gastrointestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy. Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used therapeutically. After intranasal dosage, peak plasma concentrations of cyanocobalamin have been reached in 1 to 2 hours. The bioavailability of the intranasal preparation is about 7 to 11% of that by intramuscular injection.

Vitamin B₁₂ is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. Vitamin B₁₂ is stored in the liver, excreted in the bile, and undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Vitamin B₁₂ diffuses across the placenta and also appears in breast milk.

Retention in the body. After injection of cyanocobalamin a large proportion is excreted in the urine within 24 hours; the body retains only 55% of a 100-microgram dose and 15% of a 1000-microgram dose. Body stores of vitamin B₁₂ amount to 2000 to 3000 micrograms which is believed to be enough for 3 to 4 years. If 1000 micrograms is injected monthly, the 150 micrograms retained lasts for about 1 month. Hydroxocobalamin is better retained than cyanocobalamin; 90% of a 100-microgram dose and 30% of a 1000-microgram dose are retained and that range is believed to be enough for 2 to 10 months.¹

1. Anonymous. Time to drop cyanocobalamin? *Drug Ther Bull* 1984; **22**: 43.

Human Requirements

For adults, the daily requirement of vitamin B₁₂ is probably about 1 to 2 micrograms and this amount is present in most normal diets. Vitamin B₁₂ occurs only in animal products; it does not occur in vegetables, therefore strict vegetarian (vegan) diets that exclude dairy products may provide an inadequate amount although it has been said that many years of vegetarianism are necessary before a deficiency is produced, if at

all. Meats, especially liver and kidney, milk, eggs, and other dairy products, and fish are good sources of vitamin B₁₂.

UK and US recommended dietary intake. In the UK¹ dietary reference values (see p.1925) have been published for vitamin B₁₂ and similarly in the USA recommended dietary allowances (RDAs) have been set.² Differing amounts are recommended for infants and children of varying ages, adults and pregnant and lactating women. In the UK the reference nutrient intake (RNI) is 1.5 micrograms daily for adult males and females and the estimated average requirement (EAR) is 1.25 micrograms daily. In the USA the RDA for adults is 2.4 micrograms 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 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

Vitamin B₁₂, a water-soluble vitamin, occurs in the body mainly as methylcobalamin (mecobalamin) and as adenosylcobalamin (cobamide) and hydroxocobalamin. Mecobalamin and cobamide act as coenzymes in nucleic acid synthesis. Mecobalamin is also closely involved with folic acid in several important metabolic pathways.

Vitamin B₁₂ deficiency can occur in strict vegetarians with an inadequate dietary intake, although it may take many years before a deficiency is produced. Deficiency is more likely in patients with malabsorption syndromes or metabolic disorders, nitrous oxide-induced megaloblastosis, or after gastrectomy or extensive ileal resection. Deficiency leads to the development of megaloblastic anaemias and demyelination and other neurological damage. A specific anaemia known as pernicious anaemia develops in patients with an absence of the intrinsic factor necessary for good absorption of the vitamin from dietary sources.

Vitamin B₁₂ preparations are used in the treatment and prevention of vitamin B₁₂ deficiency. It is essential to identify the exact cause of deficiency, preferably before starting therapy. Hydroxocobalamin is generally preferred to cyanocobalamin; it binds more firmly to plasma proteins and is retained in the body longer (see under Pharmacokinetics, above). Cyanocobalamin and hydroxocobalamin are generally given by the intramuscular route, although cyanocobalamin may be given orally or subcutaneously, or intranasally (see also under Administration, below). Oral cyanocobalamin may be used in treating or preventing vitamin B₁₂ deficiency of dietary origin.

In the UK, recommended doses for **pernicious anaemia** and other macrocytic anaemias *without neurological involvement* are hydroxocobalamin (or cyanocobalamin) 250 to 1000 micrograms intramuscularly on alternate days for 1 to 2 weeks, then 250 micrograms weekly until the blood count returns to normal. Maintenance doses of 1000 micrograms of hydroxocobalamin are given every 2 to 3 months (or monthly for cyanocobalamin). If there is *neurological involvement*, hydroxocobalamin or cyanocobalamin may be given in doses of 1000 micrograms on alternate days and continued for as long as improvement occurs. For the *prophylaxis* of anaemia associated with vitamin B₁₂ deficiency resulting from gastrectomy or malabsorption syndromes hydroxocobalamin may be given in doses of 1000 micrograms intramuscularly every 2 or 3 months or cyanocobalamin in doses of 250 to 1000 micrograms intramuscularly each month. For vitamin B₁₂ deficiency of *dietary* origin, oral cyanocobalamin 50 to 150 micrograms may be taken daily between meals.

Lower doses of both cyanocobalamin and hydroxocobalamin are recommended in the USA. For the *treatment* of deficiency, the usual intramuscular or subcutaneous dose of cyanocobalamin is 100 micrograms