Adverse effects. For reference to life-threatening eosinophilic pleuropericarditis in a patient receiving biotin and pantothenic acid see p.1959.

Deficiency states. Biotin has been used to treat deficiency of biotinidase or holocarboxylase synthetase, enzymes responsible for the recycling and incorporation of biotin. In the UK, the *BNFC* suggests the following doses:

- for isolated carboxylase defects, biotin may be given to neonates in a dose of 5 mg once daily by mouth or slow intravenous injection, adjusted according to response; older patients may be given 10 mg daily. The usual maintenance dose ranges from 10 to 50 mg daily, though up to 100 mg daily may be needed
- for defects of biotin metabolism, 10 mg once daily may be given by mouth or slow intravenous injection, adjusted according to response. Usual maintenance doses are 5 to 20 mg daily but higher doses may be needed

References.

1. Baumgartner ER, Suormala T. Multiple carboxylase deficiency: inherited and acquired disorders of biotin metabolism. *Int J Vitam Nutr Res* 1997; **67:** 377–84.
2. Tsao CY, Kien CL. Complete biotinidase deficiency presenting as reversible progressive ataxia and sensorineural deafness. *J Child Neurol* 2002; **17:** 146.
3. Wolf B. Biotinidase deficiency: new directions and practical concerns. *Curr Treat Options Neurol* 2003; **5:** 321–8.
4. Seymons K, *et al.* Dermatologic signs of biotin deficiency leading to the diagnosis of multiple carboxylase deficiency. *Pediatr Dermatol* 2004; **21:** 231–5.
5. Grünewald S, *et al.* Biotinidase deficiency: a treatable leukoencephalopathy. *Neuropediatrics* 2004; **35:** 211–16.
6. Puertas Bordallo D, *et al.* Neuropatía óptica por déficit de biotinidasa. *Arch Soc Esp Oftalmol* 2004; **79:** 393–6.
7. Hoffman TL, *et al.* Biotinidase deficiency: the importance of adequate follow-up for an inconclusive newborn screening result. *Eur J Pediatr* 2005; **164:** 298–301.
8. Wilson CJ, *et al.* Severe holocarboxylase synthetase deficiency with incomplete biotin responsiveness resulting in antenatal insult in Samoan neonates. *J Pediatr* 2005; **147:** 115–18.

Human requirements. In the UK neither a reference nutrient intake (RNI) nor an estimated average requirement (EAR—see p.1925) has been set for biotin although it was considered that an intake of between 10 and 200 micrograms daily was both safe and adequate.[1] Similarly in the USA an adequate intake of 30 micrograms daily has been set for adults.[2]

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)

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Aminosam; Panabiotin; ***Austria:*** Bio-H-Tin; Curatin; Medobiotin; Merzbiotin; ***Canad.:*** D Biotin†; ***Chile:*** Hvit; ***Fin.:*** Biotisan; ***Ger.:*** Bio-H-Tin; Biokur†; Biotin-Asmedic; Deacura; Gabunat; Medobiotin†; Natubiotin; Natuderm†; Rombellin†; ***Hung.:*** Bio-H-Tin; ***Ital.:*** Biodermatin; Diathynil; Nebiotin; ***Spain:*** Medebiotin; ***Switz.:*** Bio-H-Tin; Rombellin; ***USA:*** Appearex; Hard Nails.

Multi-ingredient: ***Arg.:*** Folimax B; Megaplus; Tersoderm Anticaspa†; ***Fr.:*** Zeniac LP†; Zeniac†; ***Ger.:*** Carotin; ***Indon.:*** Alicron; ***Spain:*** Doctodermis; Lacerdermol.

Calcium Ferrous Citrate

Ferrous Calcium Citrate. Dicalcium iron(2+) bis(2-hydroxypropane-1,2,3-tricarboxylate).

$C_{12}H_{10}Ca_2FeO_{14}$ = 514.2.
CAS — 53684-61-0.

Profile

Calcium ferrous citrate is used as a source of iron (p.1949) for iron-deficiency anaemia (p.1951).

Preparations

Proprietary Preparations (details are given in Part 3)
Israel: Ferrocal.

Multi-ingredient: ***India:*** Raricap; Raricap L.

Calcium Fluoride

Fluoruro cálcico.

CaF_2 = 78.07.
CAS — 7789-75-5.

Pharmacopoeias. In *Ger.*

Profile

Calcium fluoride is used as a fluoride supplement (see Sodium Fluoride, p.1962) for the prevention of dental caries. Calcium fluoride is also used as a source of calcium.

Homoeopathy. Calcium fluoride has been used in homoeopathic medicines under the following names: Calcarea Fluorica; Calc. Fluor; Calcium Fluoratum; Cal. fl.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Calcifluor†.

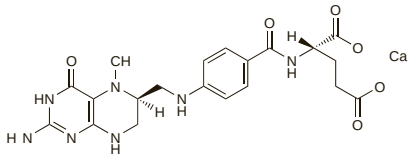
Multi-ingredient: ***Cz.:*** Bifluorid†; ***Denm.:*** Bifluorid; ***India:*** Calcinol; ***Ital.:*** Bifluorid†; ***Pol.:*** Bifluorid; ***Swed.:*** Bifluorid.

Calcium Mefolinate

Calcii Mefolinas; Calcio Mefolinato; Calcium L-Methylfolate; Calcium (6S)-5-Methyltetrahydrofolate.

Кальция L-Метилфолат

$C_{20}H_{23}CaN_7O_6$ = 497.5.
CAS — 26560-38-3.



NOTE. Metafolin is a trade name that has been used for calcium mefolinate.

Profile

Calcium mefolinate is the calcium salt of 5-methyltetrahydrofolate, the biologically active metabolite of folic acid (p.1940). It is used as a food supplement and also has similar uses to folic acid.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Biofolic; Furoic; Prefolic; ***USA:*** Deplin.

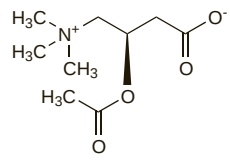
Multi-ingredient: ***USA:*** Cerefolin; Metanx.

Carnitine Derivatives

Acetylcarnitine Hydrochloride

Acetilcarnitina, hidrocloruro de; Acetyl-L-carnitine Chloride; Levacecarnine Hydrochloride; Levocarnitinum acetilum hydrochloricum; ST-200. (3-Carboxy-2-hydroxypropyl)trimethylammonium acetate (ester) chloride.

$C_9H_{17}NO_4$,HCl = 239.7.
CAS — 5080-50-2.
ATC — N06BX12.
ATC Vet — QN06BX12.



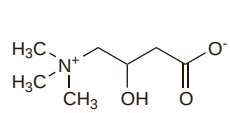
(acetyl-L-carnitine)

Carnitine *(rINN)*

Carnitina; Carnitinum; Karnitin; ST-198; Vitamin B_T. (3-Carboxy-2-hydroxypropyl)trimethylammonium hydroxide, inner salt; 3-Hydroxy-4-trimethylammoniobutyrate.

Карнитин

$C_7H_{15}NO_3$ = 161.2.
CAS — 461-06-3.

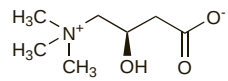


Levocarnitine *(BAN, USAN, rINN)*

L-Carnitine; L-Karnitin; Levocarnitina; Lévocarnitine; Levocarnitinum; Levokarnitiini; Levokarnitin; Levokarnitinas. (*R*)-(3-Carboxy-2-hydroxypropyl)trimethylammonium hydroxide, inner salt; (*R*)-3-Hydroxy-4-trimethylammoniobutyrate.

Левокарнитин

$C_7H_{15}NO_3$ = 161.2.
CAS — 541-15-1.
ATC — A16AA01.
ATC Vet — QA16AA01.



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

Ph. Eur. 6.2 (Levocarnitine). A white or almost white, hygroscopic, crystalline powder or colourless crystals. Freely soluble in water; soluble in warm alcohol; practically insoluble in acetone. A 5% solution in water has a pH of 6.5 to 8.5. Store in airtight containers.

USP 31 (Levocarnitine). White, hygroscopic, crystals or crystalline powder. Freely soluble in water and in hot alcohol; practically insoluble in acetone, in ether, and in benzene. pH of a 5% solution in water is between 5.5 and 9.5. Store in airtight containers.

Levocarnitine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de levocarnitina; Lévocarnitine, Chlorhydrate de; Levocarnitini Hydrochloridum. (*R*)-3-Hydroxy-4-trimethylammoniobutyrate hydrochloride.

Левокарнитина Гидрохлорид

$C_7H_{15}NO_3$,HCl = 197.7.
CAS — 6645-46-1.

Levocarnitine Propionate *(rINNM)*

L-Carnitine propionate; Lévocarnitine, Propionate de; Levocarnitini Propionas; Propionato de levocarnitina; Propionylcarnitine; L-Propionylcarnitine; Propionyl-L-carnitine; ST-261.

Левокарнитина Пропионат

$C_{10}H_{19}NO_4$ = 217.3.
CAS — 20064-19-1.

Levocarnitine Propionate Hydrochloride *(USAN)*

Propionyl-L-carnitine Hydrochloride; STI-261. (2*R*)-3-Carboxy-*N*,*N*,*N*-trimethyl-2-(propanoyloxy)propan-1-aminium chloride.

$C_{10}H_{20}ClNO_4$ = 253.7.
CAS — 119793-66-7.

Adverse Effects and Precautions

Gastrointestinal disturbances such as nausea, vomiting, diarrhoea, and abdominal cramps have been reported after the use of levocarnitine. Body odour has also been noticed in some patients, possibly due to the formation of the metabolite trimethylamine (see Fish Odour Syndrome, p.1923). Decreasing the dosage may reduce or eliminate these effects; oral levocarnitine should be consumed slowly to decrease gastrointestinal disturbances. Seizures have been reported.

Patients with severe renal impairment should not be given high oral doses of levocarnitine for long periods, because of the accumulation of the metabolites trimethylamine and trimethylamine-*N*-oxide. This is said not to occur to the same extent after intravenous dosage. Diabetic patients given carnitine while receiving insulin or hypoglycaemic drugs should be monitored for hypoglycaemia.

Renal impairment. Of 30 patients given DL-carnitine intravenously after dialysis sessions 3 developed myasthenia-like symptoms but when these 3 were given only levocarnitine the symptoms did not occur.[1] It was considered that in anuric uraemic patients the D-isomer was not excreted adequately and that accumulation had blocked neuromuscular transmission. It was therefore suggested that levocarnitine, rather than the DL-form, should be used. (High and prolonged oral doses of levocarnitine should, however, be avoided—see above.)

1. Bazzato G, *et al.* Myasthenia-like syndrome after but not - carnitine. *Lancet* 1981; **i:** 1209.

Pharmacokinetics

Oral doses of levocarnitine are absorbed slowly and incompletely from the small intestine. Bioavailability has been reported to be only about 10 to 15%, with peak plasma concentrations attained about 3 to 4 hours after an oral dose. Plasma concentrations after oral doses represent the sum of endogenous and exogenous material. Levocarnitine does not appear to bind to plasma proteins. It is mainly eliminated by the kidneys, undergoing extensive tubular reabsorption. After intravenous doses, levocarnitine appears to undergo minimal metabolism. Levocarnitine given orally may undergo degradation in the gastrointestinal tract, leading to the