However, a randomised trial found modified-release nicotinamide at 1.2 g/m^2 daily (to a maximum of 3 g daily) to be ineffective in preventing the onset of diabetes mellitus in first-degree relatives of patients with the disease.[3] Nicotinic acid can also raise high-density lipoprotein (HDL)-cholesterol concentrations (see below);[4,5] changes in glucose tolerance were mild enough for the drug to be considered as an alternative to statins and fibrates in diabetic patients.

1. Elliott RB, Chase HP. Prevention or delay of type 1 (insulin-dependent) diabetes mellitus in children using nicotinamide. *Diabetologia* 1991; **34:** 362–5.
2. Pozzilli P, *et al.* Meta-analysis of nicotinamide treatment in patients with recent-onset IDDM. *Diabetes Care* 1996; **19:** 1357–63.
3. European Nicotinamide Diabetes Intervention Trial Group. European Nicotinamide Diabetes Intervention Trial (ENDIT): a randomised controlled trial of intervention before the onset of type I diabetes. *Lancet* 2004; **363:** 925–31.
4. Elam MB, *et al.* Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: a randomized trial. *JAMA* 2000; **284:** 1263–70.
5. Grundy SM, *et al.* Efficacy, safety, and tolerability of once-daily niacin for the treatment of dyslipidemia associated with type 2 diabetes: results of the assessment of diabetes control and evaluation of the efficacy of Niaspan trial. *Arch Intern Med* 2002; **162:** 1568–76.

Hyperlipidaemias. The first-line treatment for hyperlipidaemias remains dietary and lifestyle modification; where this fails, drug therapy may be considered (p.1169). Nicotinic acid is reported to have a favourable effect on blood-lipid profiles, raising high-density lipoprotein (HDL)-cholesterol and lowering low-density lipoprotein (LDL)-cholesterol.[1-3] Nicotinic acid is used particularly in familial hypertriglyceridaemia, or in familial combined hyperlipidaemia when both triglyceride and cholesterol concentrations are similarly elevated. Nicotinic acid was less effective than lovastatin at reducing LDL-cholesterol in patients with primary hypercholesterolaemia, but more effective at increasing HDL-cholesterol; lovastatin was better tolerated.[4] A combination of nicotinic acid with lovastatin was found to be comparable to atorvastatin and more effective than simvastatin in reducing LDL-cholesterol, and more effective than either atorvastatin or simvastatin in increasing HDL-cholesterol, in a study of patients with dyslipidaemia.[5] Some have recommended that nicotinic acid be substituted for a statin to lower LDL-cholesterol when patients cannot tolerate a statin.[2] Combination therapy is recommended when the reduction in LDL-cholesterol is insufficient with statin monotherapy,[2,6] or when raising HDL-cholesterol would be beneficial,[7-9] as in patients with type 2 diabetes mellitus, or the metabolic syndrome.[8] The risk of muscle toxicity with this combination is not considered to be significantly different to that with statin monotherapy.[7]

1. McKenney JM, *et al.* A comparison of the efficacy and toxic effects of sustained- vs immediate-release niacin in hypercholesterolemic patients. *JAMA* 1994; **271:** 672–7.
2. McKenney J. Niacin for dyslipidemia: considerations in product selection. *Am J Health-Syst Pharm* 2003; **60:** 995–1005.
3. McCormack PL, Keating GM. Prolonged-release nicotinic acid: a review of its use in the treatment of dyslipidaemia. *Drugs* 2005; **65:** 2719–40.
4. Illingworth DR, *et al.* Comparative effects of lovastatin and niacin in primary hypercholesterolemia: a prospective trial. *Arch Intern Med* 1994; **154:** 1586–95.
5. Bays HE, *et al.* Comparison of once-daily, Niacin extended-release/lovastatin with standard doses of atorvastatin and simvastatin (The Advicor Versus Other Cholesterol-Modulating Agents Trial Evaluation [ADVOCATE]). *Am J Cardiol* 2003; **91:** 667–72.
6. Miller M. Niacin as a component of combination therapy for dyslipidemia. *Mayo Clin Proc* 2003; **78:** 735–42.
7. McKenney J. New perspectives on the use of niacin in the treatment of lipid disorders. *Arch Intern Med* 2004; **164:** 697–705.
8. Chapman MJ, *et al.* Raising high-density lipoprotein cholesterol with reduction of cardiovascular risk: the role of nicotinic acid—a position paper developed by the European Consensus Panel on HDL-C. *Curr Med Res Opin* 2004; **20:** 1253–68.
9. Yim BT, Chong PH. Niacin-ER and lovastatin treatment of hypercholesterolemia and mixed dyslipidemia. *Ann Pharmacother* 2003; **37:** 106–15.

Pemphigus. Oral treatment with nicotinamide and a tetracycline[1-6] has controlled lesions in pemphigus and pemphigoid (p.1582), including persistent pemphigoid gestationis,[5] and ocular cicatricial pemphigoid.[6]

1. Sawai T, *et al.* Pemphigus vegetans with oesophageal involvement: successful treatment with minocycline and nicotinamide. *Br J Dermatol* 1995; **132:** 668–70.
2. Kolbach DN, *et al.* Bullous pemphigoid successfully controlled by tetracycline and nicotinamide. *Br J Dermatol* 1995; **133:** 88–90.
3. Reiche L, *et al.* Combination therapy with nicotinamide and tetracyclines for cicatricial pemphigoid: further support for its efficacy. *Clin Exp Dermatol* 1998; **23:** 254–7.
4. Goon ATJ, *et al.* Tetracycline and nicotinamide for the treatment of bullous pemphigoid: our experience in Singapore. *Singapore Med J* 2000; **41:** 327–30.
5. Amato L, *et al.* Successful treatment with doxycycline and nicotinamide of two cases of persistent pemphigoid gestationis. *J Dermatol Treat* 2002; **13:** 143–6.
6. Dragan L, *et al.* Tetracycline and niacinamide: treatment alternatives in ocular cicatricial pemphigoid. *Cutis* 1999; **63:** 181–3.

Preparations

BP 2008: Nicotinamide Tablets; Nicotinic Acid Tablets; Vitamins B and C Injection;
BPC 1973: Compound Vitamin B Tablets; Strong Compound Vitamin B Tablets;
USP 31: Niacin Injection; Niacin Tablets; Niacinamide Injection; Niacinamide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: NB-3; Niaspan; Nicozinc; ***Austria:*** Direktan; Nicovitol; ***Belg.:*** Ucemine PP; ***Braz.:*** Papuless; ***Canad.:*** Niaspan; ***Chile:*** Cotina; Niacex; Niaspan; Vectidan†; ***Fin.:*** Niaspan; ***Fr.:*** Niaspan; Nicobion; ***Ger.:*** Niaspan; Nicobion; ***Hong Kong:*** Niaspan; ***India:*** Nialip; ***Indon.:*** Niacef; Niaspan; ***Irl.:*** Niaspan; Nicam; ***Mex.:*** Hipocol; Nacro; Pepevit; ***Neth.:*** Niaspan; ***Philipp.:*** Niaspan; ***Port.:*** Niaspan; ***Singapore:*** Niaspan; ***Swed.:*** Niaspan; Nicangin; ***Thai.:*** Nicotabs; ***UK:*** Freederm; Niaspan; Nicam; ***USA:*** Endur-acin; Niaspan; Nicotinex†; Slo-Niacin; ***Venez.:*** Niaspan.

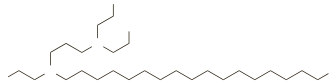
Multi-ingredient: ***Arg.:*** Antikatarata†; Centella Asiatica Compuesta; IP-6; Nicozinc; Parenciasˆ; ***Austral.:*** Bioglan Cirflo†; Chilblain Formula†; Gingo A†; Procholˆ; Silybum Complex†; ***Austria:*** Beneuran Vit B-Komplex†; Diligan; Pertrombon; Spasmocor; ***Belg.:*** Trihistalex; ***Braz.:*** Gaba†; Nicopaverina B6†; Nicopaverina†; ***Canad.:*** PML Crono†; ***Chile:*** Cicapost; Perfungol; Ureadin Forte; Ureadin Rx PS; Ureadin Rx RD; ***Fin.:*** Neurovitan; Vertipam; ***Fr.:*** TTD-B -B ; Vita-Dermacide; ***Ger.:*** Eukalisan N; Hepagrisevit Forte-N†; MerSolˆ; Petehaˆ; Telbibur Nˆ; ***Hung.:*** Paniverin; ***India:*** Diligan; Hepa-Merz; Nutrozyme; Sioneuron; Unienzyme; ***Indon.:*** Biocholes; Cereton; Kitoles; Sotens; ***Irl.:*** Effaclar Al; ***Israel:*** Babyzim; ***Ital.:*** Emazian B12†; Emoantitossina†; Emopon; Epargriseovit; Fisioreve; Folepar B12; Fosforilasi; Neuroftalˆ; Novostatin; Solvobil; Vit-Porphyrinˆ; ***Mon.:*** Monasens; ***Philipp.:*** Jetepar; ***Pol.:*** Dernilan; ***Port.:*** Diligan†; Ureadin Forte; ***Rus.:*** Lidevine (Лидевин); Oftan Catachrom (Офтан Катахром); ***S.Afr.:*** Cosaldonˆ; ***Singapore:*** Erase; ***Spain:*** Depurativo Richelet; Euzymina Lisina I; Euzymina Lisina II; Vitaphakol; ***Swed.:*** Theranylˆ; ***Thai.:*** B-100 Complex; ***Turk.:*** Epargriseovit; ***UK:*** Crampex; Quiet Life; S.P.H.P.; ***USA:*** Advicor; Simcor.

Olaflur *(BAN, USAN, rINN)*

Amine Fluoride 297; GA-297; Olaflurum; SKF-38095. 2,2′-(3-[*N*-(2-Hydroxyethyl)octadecylamino]propylimino)diethanol dihydrofluoride.

Олафлур

$C_{27}H_{60}F_2N_2O_3$ = 498.8.
CAS — 6818-37-7.
ATC — A01AA03.
ATC Vet — QA01AA03.



Profile
Olaflur is used as a source of fluoride (see Sodium Fluoride, p.1962) in the prevention of dental caries. For a report of stomatitis considered to be due to olaflur, see Hypersensitivity, under Sodium Fluoride, p.1963.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Elmexˆ; ***Israel:*** Elmexˆ; ***Pol.:*** Fluormex; ***Port.:*** Elmex.

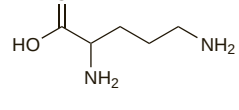
Multi-ingredient: ***Austria:*** Elmex; ***Belg.:*** Elmex; ***Cz.:*** Elmex; ***Fin.:*** Elmex; ***Fr.:*** Elmex Sensitive†; Elmexˆ; Meridolˆ; ***Ger.:*** Elmex; Lawefluor Nˆ; Multifluorid; ***Hung.:*** Elmex; ***Israel:*** Elmex; Meridol; ***Ital.:*** Elmex; ***Neth.:*** Elmex; ***Pol.:*** Fluormex; ***Switz.:*** Elmex; Paro aux fluorures d'amines Gelee.

Ornithine *(rINN)*

α,δ-Diaminovaleric Acid; Orn; L-Ornithine; Ornithinum; Ornitina. L-2,5-Diaminovaleric acid.

Орнитин

$C_5H_{12}N_2O_2$ = 132.2.
CAS — 70-26-8.



Pharmacopoeias. *Ger.* includes Ornithine Aspartate and Ornithine Hydrochloride.

Profile
Ornithine is an aliphatic non-essential amino acid. It is used as a dietary supplement.

The aspartate, hydrochloride, and oxoglurate (ornithine ketoglutarate, see also Parenteral and Enteral Nutrition under Glutamic Acid, p.1947) have been used in various indications including the treatment of hyperammonaemia (p.1929) and hepatic encephalopathy (p.1697).

◊ References.

1. Rapport L, Lockwood B. Ornithine ketoglutarate. *Pharm J* 2001; **266:** 688–90.
2. Coudray-Lucas C, *et al.* Ornithine alpha-ketoglutarate improves wound healing in severe burn patients: a prospective randomized double-blind trial versus isonitrogenous controls. *Crit Care Med* 2000; **28:** 1772–6.
3. Kircheis G, *et al.* Clinical efficacy of L-ornithine-L-aspartate in the management of hepatic encephalopathy. *Metab Brain Dis* 2002; **17:** 453–62.
4. Blonde-Cynober F, *et al.* Use of ornithine alpha-ketoglutarate in clinical nutrition of elderly patients. *Nutrition* 2003; **19:** 73–5.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Cere; Hepa; Ornicetil; ***Chile:*** Hepa-Merzˆ; ***Cz.:*** Hepa-Merzˆ; ***Fr.:*** Cetornan; Ornicetil; ***Ger.:*** Hepa-Merz; Hepa-Merz KT; Hepa-Vibolex; ***Hong Kong:*** Hepa-Merz; ***Hung.:*** Hepa-Merz; ***India:*** Hepa-Merz; ***Indon.:*** Hepa-Merz; Hevtin; ***Ital.:*** Ornicetilˆ; Ornil; Ornil KGF; ***Mex.:*** Hepa-Merz; ***Philipp.:*** Hepa-Merz; ***Pol.:*** Hepatil.

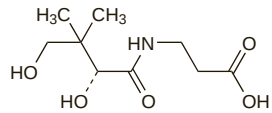
Multi-ingredient: ***Braz.:*** Ornihepatˆ; Ornitargin; ***Fr.:*** Epuramˆ; Ornitaine; ***Ger.:*** Polilevo Nˆ; ***India:*** Biohepˆ; Hepa-Merz; ***Ital.:*** Ipoazotal Complex; Ipoazotalˆ; Polilevoˆ; Somatron; ***Pol.:*** Hepa-Merz.

Pantothenic Acid *(BAN)*

Pantoténico, ácido; Vitamin B_5. (+)-(*R*)-3-(2,4-Dihydroxy-3,3-dimethylbutyramido)propionic acid.

Пантотеновая Кислота; Витамин B5

$C_9H_{17}NO_5$ = 219.2.
CAS — 79-83-4 (D-pantothenic acid); 599-54-2 (DL-pantothenic acid).
ATC — A11HA31; D03AX04.
ATC Vet — QA11HA31; QD03AX04.



(D-pantothenic acid)

Calcium Pantothenate *(BANM, rINN)*

Calcii pantothenas; Calcium, pantothénate de; Dextro Calcium Pantothenate; Kalcio pantotenatas; Kalciumpantotenat; Kalciumpantotenát; Kalsiumpantotenaatti; Pantotenato de calcio; Pantothenan vápenatý; Pantothénate de Calcium; Wapnia pantotenian.

Кальция Пантотенат

$(C_9H_{16}NO_5)_2Ca$ = 476.5.
CAS — 137-08-6 (calcium D-pantothenate); 6381-63-1 (calcium DL-pantothenate);.
ATC — A11HA31; D03AX04.
ATC Vet — QA11HA31; QD03AX04.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, *US*, and *Viet.* *US* also has a monograph for Racemic Calcium Pantothenate. *Ger.* also includes Sodium Pantothenate.

Ph. Eur. 6.2 (Calcium Pantothenate). A white or almost white, slightly hygroscopic powder. Freely soluble in water; slightly soluble in alcohol. A 5% solution has a pH of 6.8 to 8.0. Store in airtight containers.

USP 31 (Calcium Pantothenate). The calcium salt of the dextrorotatory isomer of pantothenic acid. A white, odourless, slightly hygroscopic powder. Soluble 1 in 3 of water; practically insoluble in alcohol, in chloroform, and in ether; soluble in glycerol. Store in airtight containers.

USP 31 (Racemic Calcium Pantothenate). A mixture of the calcium salts of the dextrorotatory and laevorotatory isomers of pantothenic acid. The physiological activity of Racemic Calcium Pantothenate is about one-half that of Calcium Pantothenate. A white, slightly hygroscopic powder, having a faint characteristic odour. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether; soluble in glycerol. Its solutions are neutral or alkaline to litmus. Store in airtight containers.

Adverse Effects
Pantothenic acid is reported to be generally non-toxic.

Eosinophilia. A report of life-threatening eosinophilic pleuropericarditis associated with the use of biotin and pantothenic acid.[1] Symptoms resolved on stopping the vitamins.

1. Debourdeau PM, *et al.* Life-threatening eosinophilic pleuropericardial effusion related to vitamins B and H. *Ann Pharmacother* 2001; **35:** 424–6.

Pharmacokinetics
Pantothenic acid is readily absorbed from the gastrointestinal tract after oral doses. It is widely distributed in the body tissues and appears in breast milk. About 70% of pantothenic acid is excreted unchanged in the urine and about 30% in the faeces.

Human Requirements
Pantothenic acid is widely distributed in foods. Meat, legumes, and whole grain cereals are particularly rich sources; other good sources include eggs, milk, vegetables, and fruits.

UK and US recommended dietary intake. In the UK neither a reference nutrient intake (RNI) nor an estimated average requirement (EAR) has been set (see p.1925) for pantothenic acid although an intake of 3 to 7 mg daily for adults was believed