

## Omega-3 Fatty Acids

Ácidos grasos omega 3.

Омега-3 Жирные Кислоты

ATC — C10AX06.

ATC Vet — QC10AX06.

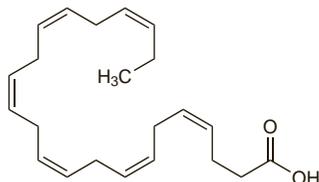
### Docosahexaenoic Acid

Doconexent (*nINN*); Cervonic Acid; DHA; Doconexento; Doconexentum. (*all-Z*)-Docosahexa-4,7,10,13,16,19-enoic acid.

Доконоксент

$C_{22}H_{32}O_2 = 328.5$ .

CAS — 6217-54-5; 25167-62-8.



NOTE. DHA is also used as a synonym for dihydroxyacetone (p.1594).

### Docosahexaenoic Acid Ethyl Ester

Doconexent Ethyl (*nINN*); Cervonic Acid Ethyl Ester; Doconexent d'Éthyle; Doconexento de etilo; Ethyl Docosahexaenoate; Ethylum Doconexentum.

Этил Доконоксент

$C_{24}H_{36}O_2 = 356.5$ .

CAS — 81926-94-5 (*all-Z*); 84494-72-4.

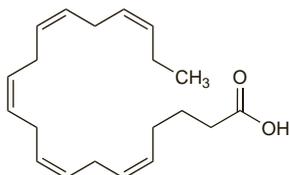
### Eicosapentaenoic Acid

Icosapent (*nINN*); Acidum Eicosapentaenoicum; Eikosapentaeni-happo; Eikosapentaensyra; EPA; Icosapento; Icosapentum; Timnodonic Acid. (*all-Z*)-Eicosapenta-5,8,11,14,17-enoic acid.

Икозапент

$C_{20}H_{30}O_2 = 302.5$ .

CAS — 10417-94-4 (*all-z*); 1553-41-9.



NOTE. EPA is also used as a synonym for pheneturide.

### Eicosapentaenoic Acid Ethyl Ester

Icosapent Ethyl (*nINN*); Ethyl Eicosapentaenoate; Ethyl Icosapentate; Ethylum Icosapentum; Icosapent d'Éthyle; Icosapento de etilo; Timnodonic Acid Ethyl Ester.

Этил Икозапент

$C_{22}H_{34}O_2 = 330.5$ .

CAS — 73310-10-8 (*all-Z*); 86227-47-6 (*all-Z*); 84494-70-2.

Pharmacopoeias. In *Jpn*.

### Linolenic Acid

ALA; Alpha-linolenic Acid; Kwas linolenowy;  $\alpha$ -Linolenic Acid. (*all-Z*)-9,12,15-Octadecatrienoic acid.

Линоленовая Кислота

$C_{18}H_{30}O_2 = 278.4$ .

CAS — 463-40-1.



NOTE. Do not confuse with  $\gamma$ -linolenic acid (Gamolenic Acid, p.2308)

### Omega-3-acid Ethyl Esters (USAN)

Ethylestery omega-3-kyselin; K-85; Omega-3 Acidorum Esteri Ethylici; Omega-3 Acidorum Esteri Etylicy; Omega-3 rűgűcűi etilo esteria; Omega-3-sav-etilűszterek.

Омега-3-кислоты Этиловых Эфиров

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

**Ph. Eur. 6.2** (Omega-3-Acid Ethyl Esters 60). A mixture of ethyl esters of omega-3 acids. They are obtained by transesterification of the body oil of fat fish species coming from families such as Engraulidae, Carangidae, Clupeidae, Osmeridae, Salmonidae, and Scombridae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The total amount of omega-3 acid ethyl esters, eicosapentaenoic acid ethyl esters, and docosahexaenoic acid ethyl esters should be stated on the label. For a total omega-3 acid ethyl ester content of 55%, the amount of eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is not less than 50% and the content of eicosapentaenoic acid ethyl esters is not less than 40%; for a total omega-3 acid ethyl ester content of 60%, the amount of eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is not less than 50% and the content of docosahexaenoic acid ethyl esters is not less than 40%; and for a total omega-3 acid ethyl ester content of 65%, the amount of eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is not less than 50%, the content of eicosapentaenoic acid ethyl esters is not less than 25%, and the content of docosahexaenoic acid ethyl esters is not less than 20%. Tocopherol may be added as an antioxidant.

A light yellow liquid with a slight fish-like odour. Practically insoluble in water; very soluble in acetone, in dehydrated alcohol, in heptane, and in methyl alcohol. Store in airtight containers under inert gas. Protect from light.

**Ph. Eur. 6.2** (Omega-3-Acid Ethyl Esters 90). A mixture of ethyl esters of omega-3 acids. They are obtained by transesterification of the body oil of fat fish species coming from families such as Engraulidae, Carangidae, Clupeidae, Osmeridae, Salmonidae, and Scombridae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The total amount of omega-3 acid ethyl esters is not less than 90%, and that of both eicosapentaenoic acid ethyl esters and docosahexaenoic acid ethyl esters together is 80%; the content of eicosapentaenoic acid ethyl esters is not less than 40% and of docosahexaenoic acid ethyl esters is not less than 34%. Tocopherol may be added as an antioxidant.

A light yellow liquid with a slight fish-like odour. Practically insoluble in water; very soluble in acetone, in dehydrated alcohol, in heptane, and in methyl alcohol. Store in airtight containers under inert gas. Protect from light.

### Omega-3 Marine Triglycerides

Deniz Kaynaklı Omega-3 Trigliseridler; Poisson (huile de) riche en acides oméga-3 (fish oil, rich in omega-3-acids); Saumon d'élevage, huile de (salmon oil, farmed); Triglicéridos marinos omega 3.

Омега-3 Триглицериды Морского Происхождения

NOTE. Omega-3 Marine Triglycerides (BAN) is a mixture of triglycerides of fatty acids from marine fish containing the equivalent of about 18% of eicosapentaenoic acid and 12% of docosahexaenoic acid. The content of triglycerides is not the same as that in Omega-3-Marine Triglycerides BP.

Pharmacopoeias. *Eur*. (see p.vii) includes Omega-3-Acid Triglycerides, Fish Oil, Rich in Omega-3-Acids, and Salmon Oil, Farmed. *US* includes Fish Oil containing Omega-3 Acids.

**Ph. Eur. 6.2** (Omega-3-Acid Triglycerides; Omega-3 Acidorum Triglycerida; Omega-3-Marine Triglycerides). A mixture of mono-, di-, and triesters of omega-3 acids with glycerol, containing mainly triesters. They are obtained by esterification of concentrated and purified omega-3 acids with glycerol or by transesterification of the omega-3 acid ethyl esters with glycerol. The omega-3 acids are from the body oil of fatty fish species coming from families such as Engraulidae, Carangidae, Clupeidae, Osmeridae, Salmonidae, and Scombridae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexaenoic acid (cervonic acid). The total amount of omega-3 acids expressed as triglycerides is not less than 60% and that of both eicosapentaenoic acid and docosahexaenoic acid together, expressed as triglycerides, is not less than 45%. Tocopherol may be added as an antioxidant.

A pale yellow liquid. Practically insoluble in water; slightly soluble in dehydrated alcohol; very soluble in acetone and in heptane. Store in well-filled, airtight containers under inert gas. Protect from light.

**Ph. Eur. 6.2** (Fish Oil, Rich in Omega-3-Acids; Piscis Oleum Omega-3 Acidis Abundans). The purified, winterised, and deodorised fatty oil obtained from fish of the families Engraulidae, Carangidae, Clupeidae, Osmeridae, Scombridae, and Ammodytidae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (timnodonic acid), heneicosapentaenoic acid, clupanodonic acid, and docosahexa-

noic acid (cervonic acid). The minimum content, expressed as triglycerides, is eicosapentaenoic acid 13%, docosahexaenoic acid 9%, and total omega-3 acids 28%. Antioxidants may be added.

A pale yellow liquid. Practically insoluble in water; slightly soluble in dehydrated alcohol; very soluble in acetone and in heptane. Store in well-filled, airtight containers under inert gas. Protect from light.

**Ph. Eur. 6.2** (Salmon Oil, Farmed; Salmonis Domestici Oleum). The purified fatty oil obtained from fresh farmed *Salmo salar*. The positional distribution ( $\beta(2)$ -acyl) is 60 to 70% for docosahexaenoic acid (cervonic acid), 25 to 35% for eicosapentaenoic acid (timnodonic acid), and 40 to 55% for moroctic acid. The sum of the contents of eicosapentaenoic acid and docosahexaenoic acid, expressed as triglycerides, is 10.0 to 28.0%. Authorised antioxidants may be added. A pale pink liquid. Practically insoluble in water; slightly soluble in dehydrated alcohol; very soluble in acetone and in heptane. Store in well-filled airtight containers under an inert gas. Protect from light.

**USP 31** (Fish Oil containing Omega-3 Acids). The purified, winterised, and deodorised fatty oil obtained from fish of the families Engraulidae, Carangidae, Clupeidae, Osmeridae, Scombroidea, and Ammodytidae. The acids consist of alpha-linolenic acid, moroctic acid, eicosatetraenoic acid, eicosapentaenoic acid (EPA), heneicosapentaenoic acid, docosapentaenoic acid, and docosahexaenoic acid (DHA). It contains not less than 28% (w/w) of total omega-3 acids (expressed as free acids) consisting of not less than 13% of EPA and not less than 9% of DHA. Antioxidants may be added. A pale yellow liquid. Practically insoluble in water; slightly soluble in anhydrous alcohol; very soluble in acetone and in heptane. Store in airtight containers at a temperature of 20° to 25°, excursions permitted between 15° and 30°. It may be stored under vacuum or under an inert gas. Protect from light.

### Adverse Effects and Precautions

The most common adverse effects of omega-3 fatty acid preparations are gastrointestinal disturbances, particularly at high doses, including nausea, eructation, vomiting, abdominal distension, diarrhoea, and constipation. There have been rare reports of acne and eczema. Moderate increases in hepatic transaminases have been reported in patients with hypertriglyceridaemia.

Preparations vary widely in concentration and purity. Some preparations contain significant amounts of vitamins A and D and long-term use could cause toxicity. There is a theoretical possibility of vitamin E deficiency with long-term use, although many preparations contain vitamin E as an antioxidant. Concern has been expressed over the high calorific value and cholesterol content of some preparations.

Omega-3 fatty acids have antithrombotic activity and should be given with caution to patients with haemorrhagic disorders or to those receiving anticoagulants or other drugs affecting coagulation. Hepatic function should be monitored in patients with hepatic impairment, particularly if receiving high doses. Caution may also be required in asthmatic patients sensitive to aspirin since omega-3 fatty acids may affect prostaglandin synthesis (but see Inflammatory and Auto-immune Disorders, below, for studies of fish oils in the management of asthma).

◇ Reviews.

1. Bays HE. Safety considerations with omega-3 fatty acid therapy. *Am J Cardiol* 2007; **99** (suppl): 35C-43C.

**Effects on the blood.** Omega-3 fatty acids have antithrombotic effects and may increase bleeding. In a study<sup>1</sup> in adolescents with familial hypercholesterolaemia, epistaxis occurred in 8 of 11 patients treated with a fish oil supplement; prolonged bleeding time was noted in 3 patients. There have also been case reports of INR elevation and haematoma in patients taking fish oil preparations with antithrombotics (see Lipid Regulating Drugs under Interactions of Warfarin, p.1431), although controlled studies have failed to show an effect.

1. Clarke JTR, *et al*. Increased incidence of epistaxis in adolescents with familial hypercholesterolemia treated with fish oil. *J Pediatr* 1990; **116**: 139-41.

**Effects on glucose metabolism.** Although a deterioration in glycaemic control has been reported in diabetic patients taking omega-3 fatty acids and fish oil preparations, a meta-analysis<sup>1</sup> of studies in type 1 and type 2 diabetics, and a systematic review<sup>2</sup>

of controlled studies in type 2 diabetics, both concluded that fish oils effectively lowered triglycerides without a deleterious effect on glycaemic control.

1. Friedberg CE, et al. Fish oil and glycaemic control in diabetes: a meta-analysis. *Diabetes Care* 1998; **21**: 494–500.
2. Hartweg J, et al. Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 30/05/08).

## Uses and Administration

Omega-3 fatty acids are long-chain polyunsaturated fatty acids containing 18 to 22 carbon atoms and a varying number of double bonds, the first of which is in the n-3 position. They are essential fatty acids and must be obtained from the diet. They have an important role as eicosanoid precursors and as components of cell membranes; in humans, they compete with arachidonic acid, an omega-6 fatty acid precursor. Their actions in humans include a hypolipidaemic action (especially a reduction in plasma triglycerides), an anti-inflammatory action, and an antiplatelet effect. The main dietary omega-3 fatty acids are eicosapentaenoic acid and docosahexaenoic acid and are derived from marine fish; other omega-3 fatty acids found in fish oils (defined in terms of number of carbon atoms and number of double bonds) include alpha-linolenic acid, moroticic acid (C18:4), eicosatetraenoic acid (C20:4), heneicosapentaenoic acid (C21:5), and clupanodonic acid (C22:5). Alpha-linolenic acid is also found in some plant sources and is converted to a limited extent in the body to eicosapentaenoic acid and docosahexaenoic acid.

Fish oils and purified omega-3 fatty acid preparations are used in patients with severe hypertriglyceridaemia (see Hyperlipidaemias, p.1169) and for secondary prevention after myocardial infarction (see Cardiovascular Disorders below). They are also marketed as dietary supplements, and are used in preparations for parenteral nutrition.

The preparations available vary widely in purity and omega-3 fatty acid content, usually expressed in terms of eicosapentaenoic acid and docosahexaenoic acid; the fatty acids may be present as triglycerides or as ethyl esters. Typical oral doses of fish oil for the treatment of hypertriglyceridaemia are 5 g twice daily of a preparation containing 17% eicosapentaenoic acid and 11.5% docosahexaenoic acid, or 2 to 4 g daily of a preparation containing 46% eicosapentaenoic acid and 38% docosahexaenoic acid. For the secondary prevention of myocardial infarction, 1 g daily of a preparation containing 46% eicosapentaenoic acid and 38% docosahexaenoic acid may be given. Eicosapentaenoic acid ethyl ester may also be used alone in the treatment of hyperlipidaemia, and to improve the symptoms associated with arteriosclerosis obliterans.

**Action.** Interest in omega-3 fatty acids arose from observations that populations with a diet rich in marine fish oils generally have a low incidence of cardiovascular disease, while the incidence of asthma, psoriasis, and auto-immune diseases appears to be lower among Eskimos (Inuit) than in populations consuming a typical western diet (although the incidence of haemorrhagic stroke and epilepsy may be higher). Increased omega-3 fatty acid intake has been suggested to underlie these differences, and fish oil and other omega-3 preparations have therefore been promoted as dietary supplements, with benefit suggested for many conditions.

The beneficial health effects of omega-3 fatty acids have been attributed to their effects on eicosanoid balance, lipid metabolism, and cell membranes. Essential fatty acids of both the omega-3 and omega-6 series have an important role as components of cell membranes and as precursors of eicosanoids (prostaglandins, leukotrienes, and thromboxanes). Eicosanoids derived from omega-3 fatty acids generally have anti-inflammatory, antithrombotic, antiarrhythmic, and vasodilator effects, while those derived from omega-6 fatty acids tend to be pro-inflammatory and prothrombotic. Since omega-3 and omega-6 fatty acids compete for the same enzymatic pathways, increasing the intake of omega-3 fatty acids promotes the formation of anti-inflammatory and antithrombotic eicosanoids, and may have beneficial effects. Production of inflammatory cytokines such as interleukins and tumour necrosis factor alpha may also be affected.

For further information on the actions of omega-3 fatty acids in cardiovascular disorders, inflammatory and auto-immune disorders, malignant neoplasms, and neurological and psychiatric disorders, see below.

References.

1. Connor WE. Importance of n-3 fatty acids in health and disease. *Am J Clin Nutr* 2000; **71** (suppl): 171S–175S.
2. Covington MB. Omega-3 fatty acids. *Am Fam Physician* 2004; **70**: 133–40.

**Cardiovascular disorders.** Omega-3 fatty acids have a number of actions that are potentially beneficial for patients at risk of cardiovascular disease.<sup>1,6</sup> They have a hypolipidaemic effect due to inhibition of very-low-density lipoprotein (VLDL) synthesis in the liver, and this particularly reduces triglyceride concentrations.<sup>7</sup> Heart rate may be reduced,<sup>8</sup> and they also have an antiarrhythmic effect,<sup>2</sup> possibly due to a direct action on myocardial cells. Omega-3 fatty acids may also reduce blood pressure in hypertensive patients,<sup>9</sup> as well as increasing erythrocyte deformability and decreasing blood viscosity. They appear to stabilise atherosclerotic plaques,<sup>10</sup> and may reduce progression of atherosclerosis<sup>11</sup> and of restenosis after percutaneous coronary intervention.<sup>12</sup>

Despite these benefits, the role of dietary or supplementary omega-3 fatty acids for cardiovascular risk reduction (p.1164) remains controversial. Epidemiological studies have suggested that increased dietary fish intake is associated with a reduced risk of fatal coronary events,<sup>13</sup> and possibly also ischaemic stroke.<sup>14,15</sup> and there is also evidence for benefit with omega-3 fatty acid supplements, particularly for secondary prevention.<sup>14,16</sup> In the GISSI-Prevenzione study,<sup>17</sup> long-term use of omega-3 fatty acid supplements reduced the risk of fatal cardiovascular events in a large group of Italian post-infarction patients studied for 3.5 years,<sup>17</sup> while the JELIS investigators<sup>18</sup> reported a reduction in primary and secondary cardiovascular events in Japanese patients with hypercholesterolaemia. However, a systematic review<sup>19</sup> found no clear benefit from omega-3 fatty acids, whether dietary or supplemental, in people with or without cardiac risk factors.

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3. Din JN, et al. Omega 3 fatty acids and cardiovascular disease—fishing for a natural treatment. *BMJ* 2004; **328**: 30–5.
4. Holub BJ. Clinical nutrition 4: omega-3 fatty acids in cardiovascular care. *CMAJ* 2002; **166**: 608–15.
5. Breslow JL. n-3 Fatty acids and cardiovascular disease. *Am J Clin Nutr* 2006; **83** (suppl 6): 1477S–1482S.
6. Lee JH, et al. Omega-3 fatty acids for cardioprotection. *Mayo Clin Proc* 2008; **83**: 324–32.
7. McKenney JM, Sica D. Prescription omega-3 fatty acids for the treatment of hypertriglyceridemia. *Am J Health-Syst Pharm* 2007; **64**: 595–605.
8. Mozaffarian D, et al. Effect of fish oil on heart rate in humans: a meta-analysis of randomized controlled trials. *Circulation* 2005; **112**: 1945–52.
9. Geleijnse JM, et al. Blood pressure response to fish oil supplementation: metaregression analysis of randomized trials. *J Hypertens* 2002; **20**: 1493–9.
10. Thies F, et al. Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomised controlled trial. *Lancet* 2003; **361**: 477–85.
11. von Schacky C, et al. The effect of dietary omega-3 fatty acids on coronary atherosclerosis: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1999; **130**: 554–62.
12. Balk EM, et al. Effects of omega-3 fatty acids on coronary restenosis, intima-media thickness, and exercise tolerance: a systematic review. *Atherosclerosis* 2006; **184**: 237–46.
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16. Wang C, et al. n-3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review. *Am J Clin Nutr* 2006; **84**: 5–17.
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19. Hooper L, et al. Omega 3 fatty acids for the prevention and treatment of cardiovascular disease. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 30/05/08).

**Inflammatory and auto-immune disorders.** Omega-3 fatty acids have effects on several immunological and inflammatory mediators<sup>1,2</sup> and have been tried in a number of inflammatory and auto-immune disorders. Beneficial effects have been reported in rheumatoid arthritis<sup>3</sup> (p.11) and in glomerular kidney disease<sup>4,6</sup> (p.1504), but results in kidney transplantation (p.1813) have been mixed, and systematic reviews<sup>7,8</sup> suggest no significant effect on rejection episodes or graft survival. Some studies have shown benefit in psoriasis (p.1583), but with oral<sup>9,10</sup> and with intravenous dosage,<sup>11,12</sup> but other studies found neither the

oral<sup>13</sup> nor the topical<sup>14</sup> route to be effective. Variable benefit has been seen in inflammatory bowel disease<sup>15</sup> (p.1697) although this may relate to the different formulations used. In Crohn's disease, a systematic review found that enteric-coated formulations helped to maintain remission,<sup>16</sup> but a subsequent randomised study using a gelatin capsule formulation found no benefit.<sup>17</sup> Similarly, a systematic review found that conventional formulations were not of benefit in patients with ulcerative colitis.<sup>18</sup> Fish oils have also been tried in lung disorders, although systematic reviews have found little evidence of benefit in asthma;<sup>19,20</sup> in cystic fibrosis, limited benefit has been reported,<sup>21</sup> with one study<sup>22</sup> reporting that fish oil supplementation reduced the need for antibacterial treatment. Preliminary evidence<sup>23</sup> also suggests that omega-3 supplementation may reduce inflammatory markers and improve dyspnoea in chronic obstructive pulmonary disease.

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5. Donadio JV, et al. The long-term outcome of patients with IgA nephropathy treated with fish oil in a controlled trial. *J Am Soc Nephrol* 1999; **10**: 1772–7.
6. Donadio JV, et al. A randomized trial of high-dose compared with low-dose omega-3 fatty acids in severe IgA nephropathy. *J Am Soc Nephrol* 2001; **12**: 791–9.
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**Malignant neoplasms.** There is some evidence that the incidence of cancer may be lower in populations with a high fish intake, and animal studies have suggested that omega-3 fatty acids may slow the progression of some cancers.<sup>1</sup> However, studies of omega-3 fatty acid intake and cancer incidence in humans have given conflicting results, and systematic reviews<sup>2,3</sup> have found no evidence of a beneficial effect. It has also been suggested that omega-3 fatty acids might be beneficial in patients with cancer cachexia, but a randomised study<sup>4</sup> found that eicosapentaenoic acid supplementation was less effective than megestrol acetate, and a systematic review<sup>5</sup> found insufficient evidence to establish whether eicosapentaenoic acid was more effective than placebo.

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**Neurological and psychiatric disorders.** Omega-3 fatty acids concentrate in neuronal membranes and appear to have an important role in brain development and function. Supplementation during pregnancy and in infants has been investigated, but there is little evidence that maternal supplements improve neonatal outcomes,<sup>1</sup> and only limited evidence of a benefit on growth and neurodevelopment in preterm infants given milk formulas supplemented with both omega-3 and omega-6 fatty acids.<sup>2,3</sup> However, in older children with phenylketonuria treated with dietary restriction, omega-3 fatty acid supplements may improve motor skills.<sup>4</sup>

Omega-3 fatty acids have also been tried in the treatment of neurological and psychiatric disorders.<sup>5,6</sup> There appears to be a link between deficient fatty acid intake and mood disorders,<sup>7</sup> and there is reasonable evidence to support the use of omega-3 fatty acids as adjuncts in the treatment of depression, including possible benefit in the depressive symptoms of bipolar disorder, but further studies are needed to confirm this.<sup>8–10</sup> Benefit has been shown in schizophrenia, but results have been mixed and the role of omega-3 fatty acids is not established.<sup>11</sup> Some positive results have been reported in hyperactivity and in autism, but further studies are needed.<sup>12</sup> Omega-3 fatty acids have also been tried in dementia, but there is not yet sufficient evidence<sup>13</sup> to recommend them for prevention.

Eicosapentaenoic acid ethyl ester has been tried in Huntington's disease, and may improve motor function,<sup>14</sup> but this remains to be confirmed.

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## Preparations

**USP 31:** Fish Oil containing Omega-3 Acids Capsules.

**Proprietary Preparations** (details are given in Part 3)

**Arg:** Regulip; **Austral:** Bioglan Maxepe; Fishaphos; Maxepe†; **Austria:** Eicosapen; Omacor; Omegaven; **Belg:** Omacor; **Braz:** Votag; **Canada:** Focus 425; **Chile:** Epasan Omega 3; Eykosacol; Neuromin†; Omegaven; Sanepa Forte†; **Cz:** Omacor; Omegaven; **Denm:** Omegaven; **Fr:** Epabiol; Maxepe; OM3; Omacor; Omega 3; Omega 3†; Omegaven; Psoriacalm; Triglistab; **Ger:** Ameu; Eicosan; Eicosapen; Lipicor; Omacor; Omegaven; Zodin; **Gr:** Farlipid; Maxepe; Omacor; Zodin; **Hong Kong:** Lipomega; Smartfish; **Hung:** Omacor; Omegaven; **India:** Maxepe; **Indon:** Champs DHA; Proclacta with DHA; Proclacta with DHA for Mother; **It:** Maxepe; Omacor; **Israel:** Omegaven; **Ital:** Almic; Esapent; Eskim; Fish Factor; Maxepe; Omegaven; Seacor; Triolip; Triomar; **Jpn:** Epadel; **Malaysia:** Champs DHA; Hovid Omega-3†; Mlepa; Quest Gamma EPA Plus; VitaEPA†; **Mex:** Colega-3; Fresomega; **Neth:** Omacor; Omegaven; Zodin; **Norw:** Omacor; **Philipp:** Fisol; Omacor; Zymechol; **Pol:** BioCardine; Galomega†; Omega-3; Omegaven; Trienyl; **Port:** Omacor; Omegaven; Zodin; **Rus:** Omacor (Омакор); **Singapore:** Champs DHA; **Spain:** Omacor; **Swed:** Omegaven; **Switz:** Ameu†; Eicosapen; Epacaps; Omega-3; Omegaven; **Thai:** Omacor; **Turk:** Marincap; Omega III; Omegaven; **UK:** Maxepe; Omacor; Pure Omega; **USA:** Cardi-Omega 3; Cholestin; Lovasa; Lovaza; Maxepe; Promega; SuperEPA; **Venez:** Epax; Fizoll; Marina; Maxepe; Ometrix.

**Multi-ingredient:** **Arg:** Cholesterol Reducing Plan†; **Austral:** APR Cream†; Arthriforte; Bioglan Arthri Plus; Bioglan Zellulean with Escin; Curaderm†; Efalex†; Efamarine†; ER Cream†; Himegast; LifeChange Circulation

Aid†; Macro Maxepe†; Maxepe & EPO†; Naudicelle Marine†; Pre Natal†; Vita-Preg†; **Austria:** SMOFlipid; **Braz:** Borag; Glavit; Lipcor†; Lisacol†; **Canada:** Bionagre plus E; Efalex†; **Chile:** Acnoxyf Jabon†; Celtech Gold; **Cz:** Lipoplus; SMOFlipid; **Denm:** SMOFlipid; **Fin:** Lipoplus; **Fr:** A-Flam; Arthrolib; Bio-Marine Plus†; Bionagrol Plus; Cardiom3; Dioptec; Efadiane relipidantes; Elteans; Molva; OM3 Junior; Omegacoer; Phytophanere; Reti-Nat; Synerbiol; **Ger:** SMOFlipid; **Gr:** Atrol; Dynapen-3; Emfrastop; Epadoc; Lipemia; Pazeril; Prolipid; Salmon Oil; SMOFlipid; **Hong Kong:** Biomega-3†; Doctor's Choice Omega 3; Eye Q; Himegast; Mumomega; **Hung:** SMOFlipid; **India:** Cadvion; Dicloran MS; Megasoft-E; **Indon:** Co-Q-10; Flexasur; Maxtrin; Nulacta Li; Objiluz; Prenatin-DF; Vitazym; **It:** MorD-HA; MorEPA; **Israel:** Triomar; **Ital:** Agedin Plus; Derman-Oil; Dermana Crema; Dermana Pasta; DHA; Ditrevit; Fitogenase; Fotrec DHA; Gamma-plus; Ictom 3†; Memoactive†; Secri; Trofinerv; Trofinerv Antiox; Venactive†; Venoton; **Malaysia:** Adult Citrex Multivitamin + Ginseng + Omega 3; VitaEPA Plus†; **Neth:** Lipoplus; SMOFlipid; **Norw:** SMOFlipid; **NZ:** Efaclat; Efalex; Efamarine; Efamax; **Philipp:** Memori Plus; OB Smart SG; **Pol:** SMOFlipid; **Port:** Lipoplus; **Singapore:** CardioCare; Celatrac; Gissicor; Seven Seas JointCare; Seven Seas JointCare High Strength; Seven Seas Joint-Care Max; VitaEPA; VitaEPA Plus; **Swed:** Lipoplus; SMOFlipid; **Switz:** Vitafissan N; **UK:** Chol-Aid; Efalex; Efamarine; GlucOsamax; Lipidem; Omegaven; Pregnacare Plus; ProBrain; SMOFlipid; **USA:** Animi-3; Citracal Prenatal + DHA; Duet DHA; Marine Lipid Concentrate; Optinate Omega-3; Sea-Omega; **Venez:** Eidoca; Piscis 3.

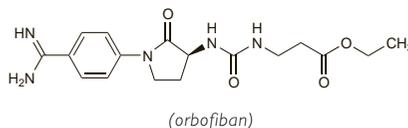
## Orbofiban Acetate (USAN, rINNM)

Acetato de orbofibrán; CS-511; Orbofiban, Acétate d'; Orbofiban Acetate; SC-57099-B. N-[[[(3S)-1-(p-Amidinophenyl)-2-oxo-3-pyrrolidiny]carbonyl]-β-alanine ethyl ester monoacetate quadrant hydrate.

Орбофібана Ацетат

C<sub>17</sub>H<sub>23</sub>N<sub>5</sub>O<sub>4</sub>·C<sub>2</sub>H<sub>4</sub>O<sub>2</sub>·H<sub>2</sub>O = 426.0.

CAS — 163250-90-6 (orbofiban); 165800-05-5 (orbofiban acetate).



## Profile

Orbofiban is a glycoprotein IIb/IIIa-receptor antagonist. It has been investigated as an oral antiplatelet drug in unstable angina and myocardial infarction but has been associated with an increase in mortality.

## References

- Cannon CP, et al. Oral glycoprotein IIb/IIIa inhibition with orbofiban in patients with unstable coronary syndromes (OPUS-TIMI 16) trial. *Circulation* 2000; **102**: 149–56.

## Ouabain

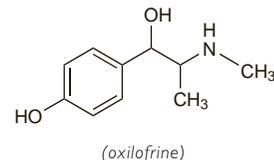
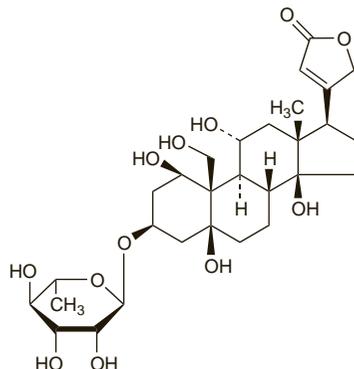
Acocantherin; G-Strophanthin; Ouabaini; Ouabain oktahydrát; Ouabaina; Ouabainas; Ouabaine; Ouabainum; Ouabainum Octahydricum; Strophanthin-G; Strophanthinum; Strophanthoside-G; Uabaina; Uabaina. 3β-(α-L-Rhamnopyranosyloxy)-1β,5,11α-,14,19-pentahydroxy-5β,14β-card-20(22)-enolide octahydrate.

C<sub>29</sub>H<sub>44</sub>O<sub>12</sub>·8H<sub>2</sub>O = 728.8.

CAS — 630-60-4 (anhydrous ouabain); 11018-89-6 (ouabain octahydrate).

ATC — C01AC01.

ATC Vet — QC01AC01.



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

**Ph. Eur. 6.2** (Ouabain). Colourless crystals or white or almost white, crystalline powder. Sparingly soluble in water and in dehydrated alcohol; practically insoluble in ethyl acetate. Protect from light.

## Profile

Ouabain is a cardiac glycoside with positive inotropic activity that is obtained from the seeds of *Strophanthus gratus* or from the wood of *Aconanthera schimperii* or *A. ouabain* (Apocynaceae). It has general properties similar to those of digoxin (p.1259) and may be used in the treatment of heart failure (p.1165). Ouabain is given orally in a dose of up to 24 mg daily; it has also been given intravenously.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Ger:** Strodival.

## Oxedrine (BAN) ⓧ

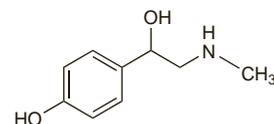
Oksedriini; Oxedrin; Oxedrinum; Sinefrina; Sympaethaminum; Synephrine; p-Synephrine. (R5)-1-(4-Hydroxyphenyl)-2-(methylamino)ethanol.

C<sub>9</sub>H<sub>13</sub>NO<sub>2</sub> = 167.2.

CAS — 94-07-5.

ATC — C01CA08; S01GA06.

ATC Vet — QC01CA08; Q501FB90; Q501GA06.



NOTE: Synephrine and p-synephrine have been used as synonyms for oxedrine. Care should be taken to avoid confusion with m-synephrine, which is phenylephrine (p.1568).

## Oxedrine Hydrochloride (BANM) ⓧ

Sinefrina, hidrocloruro de.

C<sub>9</sub>H<sub>13</sub>NO<sub>2</sub>·HCl = 203.7.

ATC — C01CA08; S01GA06.

ATC Vet — QC01CA08; Q501GA06.

## Oxedrine Tartrate (BANM) ⓧ

Aetaphen. Tartrat; Aethaphenum Tartaricum; Oksedriintartraatti; Oxedriini Tartras; Oxedrintartrat; Oxyphenylmethylaminoethanol Tartrate; Sinefrina Tartrato; Sinefrina, tartrato de; Synephrine Tartrate.

(C<sub>9</sub>H<sub>13</sub>NO<sub>2</sub>)<sub>2</sub>·C<sub>4</sub>H<sub>6</sub>O<sub>6</sub> = 484.5.

CAS — 16589-24-5 (oxedrine tartrate); 67-04-9 (±oxedrine tartrate).

ATC — C01CA08; S01GA06.

ATC Vet — QC01CA08; Q501GA06.

## Profile

Oxedrine is a sympathomimetic (p.1407) given as the tartrate in the treatment of hypotensive states in oral doses of about 100 to 150 mg three times daily; it has also been given by subcutaneous, intramuscular, or intravenous injection.

Oxedrine is also used in eye drops as an ocular decongestant, usually as the tartrate in a concentration of 0.5% in combination preparations. The hydrochloride has also been used.

## Preparations

**Proprietary Preparations** (details are given in Part 3)

**Austria:** Sympatol; **Hong Kong:** Ocuton; **Hung:** Sympathomim; **Ital:** Sympatol; **Switz:** Sympalept.

**Multi-ingredient:** **Austria:** Dacrin; Pasuma-Dragees; **Fr:** Dacryne; Dacryboraline; Polyfira; Posinet†; Sedacollyre; Uvicol.

## Oxilofrine Hydrochloride (rINNM) ⓧ

Hidrocloruro de oxilofrina; p-Hydroxyephedrine Hydrochloride; Methylsynephrine Hydrochloride; Oxilofrine, Chlorhydrate d'; Oxilofrini Hydrochloridum; Oxyphephrine Hydrochloride. erythro-p-Hydroxy-α-[1-(methylamino)ethyl]benzyl alcohol hydrochloride.

Оксиліофрина Гідрохлорид

C<sub>10</sub>H<sub>15</sub>NO<sub>2</sub>·HCl = 217.7.

CAS — 942-51-8.