
OMEGA-3 FATTY ACIDS (Fish Oil) Fact Sheet [G]

Bottom Line:

Omega-3 fatty acids form the lipid bilayers of cell membranes, and supplementing our natural dietary supply may have psychological and cardiological benefits. Based on the limited data available, the best use of omega-3 fatty acids (particularly 1–2 g with at least 60% EPA) is as an adjunct in the treatment of unipolar and bipolar depression. There is not enough evidence to recommend omega-3 fatty acids in other psychiatric disorders at this time.

FDA Indications:

High triglycerides (as Lovaza).

Off-Label Uses:

Unipolar and bipolar depression.

Dosage Forms:

- Supplied over the counter in various dosages and formulations; 500 mg, 1000 mg, and 1200 mg softgel capsules most common.
- By prescription only: Lovaza: 1000 mg softgel capsules (GSK). Dosage on label usually reflects fish oil dosage, which is not the same as omega-3 fatty acid dosage (eg, 1000 mg fish oil in some brands may provide 300 mg of omega-3 fatty acids, including EPA and DHA). Dosing recommendations are based on mg of fish oil.

Dosage Guidance:

Effective dose unclear, but studies have used 300 mg–6 g QD. For depression, start 500 mg/day, increase as tolerated (target dose 1–2 g/day); doses >3 g/day should be used cautiously. Dividing dose BID–TID helps with side effect tolerability.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$

Side Effects:

- Most common: Well tolerated up to 4 g/day. Nausea, loose stools, fishy aftertaste.
- Serious but rare: Caution in those who are allergic to seafood. Increased risk of bleeding, particularly at higher doses.
- Pregnancy/breastfeeding: Considered relatively safe.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Exact mechanism unknown, but may improve cell membrane fluidity and membrane function, change neurotransmitter binding, and promote anti-inflammatory effects.
- Metabolism is hepatic, primarily through CYP450; $t_{1/2}$: Unknown.
- For most patients, drug interactions not likely an issue; however, may prolong bleeding time. Fish oils may lower blood pressure and have additive effects when used with antihypertensives.

Clinical Pearls:

- Fish oils contain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA); both are omega-3 fatty acids. Although the body can synthesize these fats from alpha-linolenic acid (ALA), this is believed to be inefficient in many people.
- EPA and DHA are derived from fish; ALA is derived from flax seed and other vegetable matter. Mercury accumulates in fish meat more than in fish oil, which might explain the lack of detectable mercury in most fish oil supplements. Also, the manufacturing process that is used to deodorize fish oil supplements seems to lower the levels of PCBs and other contaminants.
- Omega-3 fatty acids have been tested in the treatment of schizophrenia, bipolar disorder, depression, anxiety, OCD, ADHD, autism, aggression, borderline personality disorder, substance use disorder, anorexia nervosa, and dementia. With the exception of depressive disorders, overall consensus is still lacking for the majority of these uses due to limited sample sizes, selection of patients, doses and formulations used, and study durations.
- Omega-3 fatty acids appear helpful as augmentation in unipolar depression in some individual studies, but several meta-analyses have not been able to show robust benefit. In positive studies, the most benefit was seen at 1 g/day, with EPA more effective than DHA and more severely ill patients showing greater improvement.

Fun Fact:

Inuit people have been reported to ingest up to 16 g/day (via fish) with no dangerous side effects.