

Are drugmakers fishing for a market with prescription omega-3s?

The market for fish oil supplements dates back more than two centuries to when British fishermen started selling the oil oozing from cod livers as a miracle cure for many ailments. Today, fish oil is enjoying a renaissance for a slew of purported health benefits, from reducing cholesterol and lessening asthma to treating dry skin and slowing aging. But, rather than pouring crude oil products from a decanter, most people nowadays tend to get their health-promoting omega-3s in the form of squishy gel-capsules containing refined fatty acids, which have grown to become the third most popular dietary supplement in the US.

Aiming to capture part of the growing market, big pharma has recently cast its hook into the fish oil frenzy. London-based GlaxoSmithKline (GSK) now offers a prescription omega-3 fatty acid pill called Lovaza, which posted sales of more than \$820 million in 2010. And, on 25 November, the US Food and Drug Administration (FDA) accepted a new drug application for an omega-3 medication known as AMR101, developed by Dublin-based Amarin.

But, even as drugmakers perfect their prescription versions, some onlookers remain skeptical. “Frankly, nobody knows for sure how the prescription compares to the supplement in terms of effectiveness,” says Charles Serhan, a biochemist who studies omega-3s at the Brigham and Women’s Hospital in Boston.

Lovaza—which, at around \$400 per month, costs at least sixfold more than over-the-counter pills—is a defined formulation of two different kinds of omega-3s. Importantly, its manufacturers stress, the drug is free of impurities such as heavy metals and other toxins that are sometimes found in the nonprescription supplements. In clinical trials, Lovaza has been shown to reduce circulating blood fats in people with high triglyceride levels by up to 47% (*Am. J. Cardiol.* **98**, 71i–76i, 2006). But Lovaza, which is marketed as Omacor outside the US by a number of companies under license from the Norwegian drugmaker Pronova BioPharma, has also been shown to raise people’s levels of ‘bad’ cholesterol by a few percentage points—an adverse effect that has been linked to one of the drug’s two ingredients, docosahexaenoic acid (*J. Nutr.* **142**, 99–104, 2012).

Regulatory concerns about this side effect have kept Lovaza from reaching a larger market. At present, the drug is approved only



Fishing for a deal: Drugmakers cast their net into prescription fish oil market.

for those with triglyceride levels exceeding 500 milligrams per milliliter. GSK has applied twice—in 2004 and again in 2009—for the drug to be approved for people with triglyceride levels as low as 200 milligrams per milliliter of blood. In both cases, the FDA rejected the company’s application, citing the cholesterol bump.

A fine kettle of fish oil

AMR101, by comparison, doesn’t contain the docosahexaenoic acid. Instead, the Amarin drug is a pure formulation of the other omega-3 in Lovaza, called eicosapentaenoic acid, and so it is thought to be safer than its competitor for people with cardiovascular disease. In September 2011, Amarin reported the results of a 229-person, phase 3 trial showing that AMR101 does not significantly raise levels of bad cholesterol (*Am. J. Cardiol.* **108**, 682–690, 2011). As a result, the company is now seeking approval for people currently taking cholesterol-lowering statins who also have triglycerides above just 200 milligrams per milliliter. On 7 December, Amarin announced that the phase 3 trial on which that extended approval rests had begun enrolling participants.

“If the current trial is successful, the addition of those patients increases Amarin’s potential market by tenfold over Lovaza’s market,” says Joseph Schwartz, an analyst at the New York investment bank Leerink Swann. He predicts annual sales of AMR101

will top \$3.2 billion by 2024.

Yet, without any head-to-head clinical trials of over-the-counter fish oil and its prescription cousins, many experts caution that consumers might be getting a raw deal with these prescription medications. Worse, many physicians worry whether the touted medicines are providing much of a clinical benefit at all. Some studies have shown that taking prescription omega-3s can moderately reduce the likelihood that an average person will die from heart disease. But several recent reviews, including a meta-analysis published in November 2011 by researchers at the Harvard School of Public Health in Boston (*J. Am. Coll. Cardiol.* **58**, 2047–2067, 2011), have failed to find a reduction in cardiovascular mortality in people taking prescription fish oil.

Those findings don’t faze Kevin Maki, president and chief scientific officer of Biofortis-Provident Clinical Research, a contract research organization based in Chicago that has run more than a dozen trials for the makers of Lovaza, AMR101 and other fish oils. “There are clearly benefits,” he maintains. But with so many different triggers for chronic heart failure, he says that more research is needed to tease apart which people are most likely to respond favorably to the drugs. “It’s a matter of isolating exactly what [the benefits] are,” he notes, “and we haven’t managed to do that yet.”

Rebecca Hersher

istockphoto