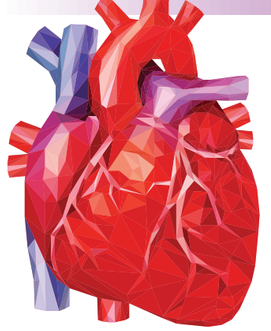


CARDIOVASCULAR RISK REDUCTION

BEYOND THE CURRENT STANDARD OF CARE

Between 2013 and 2016, 121.5 million people had some form of cardiovascular disease (CVD) in the US, and 92.8 million had a total cholesterol of 200 mg/dL or higher.[1] Statin therapy is considered the first-line treatment for CVD prevention in patients at risk of CVD and those between 40 and 75 years of age with diabetes mellitus.[2] However, despite the benefits of statin therapy, patients remain at high persistent risk for cardiovascular (CV) events, including persistent cholesterol risk, persistent inflammatory risk, persistent thrombotic risk, and persistent triglyceride (TG) risk.[3,4]

Generic omega-3 (OM3) fatty acid drugs or supplements have been recommended as a means of secondary prevention to address persistent CV risk.[5] In a recent survey of more than 700 cardiology patients, nearly half (48%) were taking dietary supplement fish oil for heart health (28%) or to treat a CV condition (20%).[5] However, OM3 supplements are not approved or indicated for any disease. In clinical trials, OM3 drugs have not been proven to be better than placebo in reducing the risk of CV events.[5-10]

Generic OM3 ethyl esters have failed to demonstrate statistically significant reduction risk of major adverse CV events in CV outcomes trials: ORIGIN, OMEGA, ASCEND, and VITAL.[7-10]

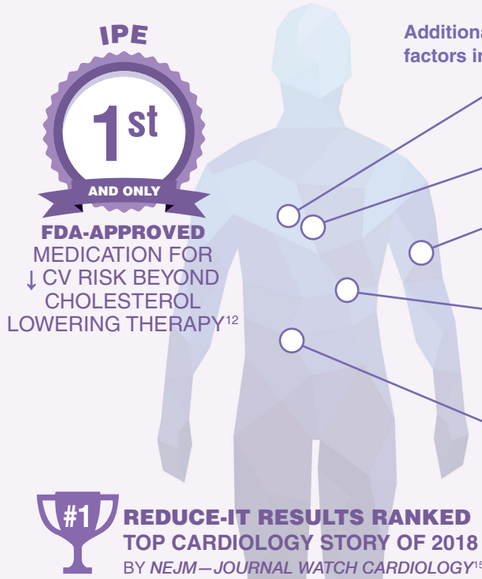
Despite current treatment options in the US, there is

1 STROKE AND 1 HEART ATTACK

occurring on average EVERY

There are two main types of OM3 fatty acids— eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[5] EPA is considered beneficial in the CV system, while DHA-containing products are important in the nervous system. DHA may raise median low-density lipoprotein cholesterol (LDL-C) compared to placebo, contributing to plaque buildup.[6] Most dietary OM3 supplements can contain up to 36% saturated fat and DHA.[11]

Icosapent ethyl (IPE) is the first and only drug approved by the FDA as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with TG levels ≥150 mg/dL and established CVD or diabetes mellitus and two or more additional risk factors for CVD.[12,13] IPE is an ethyl ester of EPA that has undergone a proprietary purification process to extract toxins, saturated fats, and LDL-raising DHA.[6,13] It is estimated that millions of high-risk patients in the US could benefit from this one-of-a-kind prescription therapy.[14]



#1 REDUCE-IT RESULTS RANKED TOP CARDIOLOGY STORY OF 2018
BY *NEJM—JOURNAL WATCH CARDIOLOGY*[15]

IPE is the only CV risk reducing agent that has met all primary and secondary endpoints in a multinational, double-blind, randomized, placebo-controlled, event-driven trial (REDUCE-IT).[13,16] 8,179 statin-treated adult patients with LDL-C between 40 mg/dL and 100 mg/dL, elevated TG levels, and either established CVD or diabetes and other risk factors for CVD were enrolled in the REDUCE-IT trial across 11 countries and were followed for a median of 4.9 years.[13,16] IPE significantly reduced the risk of CV events by 25% compared with placebo.[16]

Regardless of secondary or primary prevention, statin tolerance, gender, smoking status, renal dysfunction, diabetes, or TG levels above or below 150 mg/dL (see patient baseline characteristics at left and below), IPE in combination with statins provided better CV outcomes compared with statins taken with a placebo.[12,13,16] Moreover, within a year, patients using IPE experienced a median 18% decrease in TG levels from baseline compared to those using placebo; rather, the latter showed a median 2% increase in TG levels from baseline.[13] The overall rates of adverse events and serious adverse events in REDUCE-IT were similar between IPE-treated and placebo-treated patients.[12,16]

Most patients were taking moderate-intensity (63%) or high-intensity (31%) statin therapy at baseline.[13] Most patients were taking at least 1 other standard CV medication, including:[13]

ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker

The results of the REDUCE-IT trial for IPE cannot be extrapolated to generic OM3 supplements.[7-10] The amount of beneficial OM3 (ie, EPA) in fish oil supplements is inadequate to reduce the risk of CVD, and patients may need to take **more than 20 capsules to achieve the same dose** as what was used with IPE in the REDUCE-IT trial.[6,16]

Pharmacists have a role in communicating differences between IPE and generic OM3 drugs or supplements.[17-21]

As the most accessible health care professionals, pharmacists can educate patients about these developments and guide patient decision-making—especially patients that are on long-term management for reducing CVD risk and frequently visit pharmacies.[17-20] Patient education about the impurity of most fish oil supplements would bring to the forefront their potential risk of increasing cholesterol.[21] Fortunately, patients have an FDA-approved alternative with demonstrated CV risk reduction—IPE.[13,16] The American Diabetes Association has updated its guidelines to include IPE as recommended therapy for CV risk reduction.[22] Confidence in the outcomes of IPE in the REDUCE-IT trial is further supported by recommendations from the European Society of Cardiology/European Atherosclerosis Society and National Lipid Association.[23,24] This growing acknowledgment of IPE potentially positions it as a possible next foundational treatment in evidence-based CV risk reduction.

To learn more about how IPE can help lower CVD risk, visit www.vascepahcp.com.

INDICATIONS AND LIMITATIONS OF USE FROM THE VASCEPA® (ICOSAPENT ETHYL) FDA-APPROVED LABEL

VASCEPA is indicated:

- As an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated TG levels (≥150 mg/dL) and
  - established cardiovascular disease or
  - diabetes mellitus and 2 or more additional risk factors for cardiovascular disease.
- As an adjunct to diet to reduce TG levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

IMPORTANT SAFETY INFORMATION

- VASCEPA is contraindicated in patients with known hypersensitivity (eg, anaphylactic reaction) to VASCEPA or any of its components.
- VASCEPA was associated with an increased risk (3% vs 2%) of atrial fibrillation or atrial flutter requiring hospitalization in a double-blind, placebo-controlled trial. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter.
- Is it not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Patients with such allergies should discontinue VASCEPA if any reactions occur.
- VASCEPA was associated with an increased risk (12% vs 10%) of bleeding in a double-blind, placebo-controlled trial. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel or warfarin.
- Common adverse reactions in the cardiovascular outcomes trial (incidence ≥3% and ≥1% more frequent than placebo): musculoskeletal pain (4% vs 3%), peripheral edema (7% vs 5%), constipation (5% vs 4%), gout (4% vs 3%) and atrial fibrillation (5% vs 4%).
- Common adverse reactions in the hypertriglyceridemia trials (incidence ≥1% more frequent than placebo): arthralgia (2% vs 1%) and oropharyngeal pain (1% vs 0.3%).
- Adverse events may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.
- Patients receiving VASCEPA and concomitant anticoagulants and/or anti-platelet agents for bleeding should be monitored.

Please see full Prescribing Information for more information on VASCEPA or visit www.vascepahcp.com.

AMARIN®

VAS-02231 12/19

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