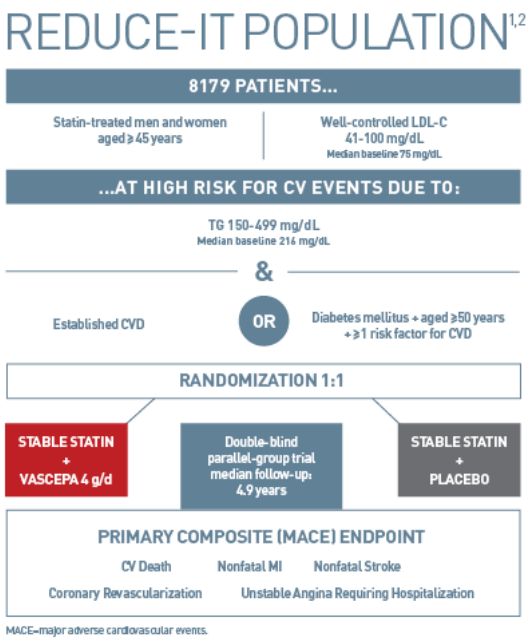
VASCEPA® (ICOSAPENT ETHYL) CARDIOVASCULAR OUTCOMES TRIAL: REDUCE-IT™

WHAT IS REDUCE-IT?

REDUCE-IT is a landmark global outcomes study that investigated the cardioprotective effects of 4 grams daily VASCEPA. In REDUCE-IT, VASCEPA was studied as an add-on to statin therapy to reduce the risk of major adverse cardiovascular (CV) events in patients with bad (LDL) cholesterol controlled to between 41-100 mg/dL who have other CV risk factors, including persistent elevated triglyceride levels (150-499 mg/dL), diabetes or established CV disease.

WHAT IS THE REDUCE-IT TRIAL DESIGN?[1]



The primary endpoint of REDUCE-IT was a composite of ~1,612 events:

- cardiovascular death
- non-fatal myocardial infarction (heart attack)
- non-fatal stroke
- coronary revascularization (procedures, such as stents) or,
- unstable angina

The key secondary endpoint of REDUCE-IT was a composite of:

- cardiovascular death
- non-fatal myocardial infarction (heart attack)
- non-fatal stroke

There are >30 additional, pre-specified secondary and tertiary endpoints.
The REDUCE-IT trial was an event-driven CV outcomes study and was not designed to validate the effect of lowering triglycerides (a type of fat in the blood) on a stand-alone basis.

WHY IS REDUCE-IT AN IMPORTANT STUDY?

Risk of heart attack, stroke and other MACE remains despite statins. To date, large, randomized clinical trials have failed to show that lowering triglycerides on top of statin therapy improves cardiovascular outcomes. REDUCE-IT is the first to evaluate whether treatment with VASCEPA will have benefit in statin-treated patients with additional risk factors beyond LDL-C.[1]

HOW BIG A PROBLEM IS CARDIOVASCULAR DISEASE (CVD)?

In the United States, CVD is the #1 killer – 1 in 3 deaths (1 death every 38 seconds) – with annual treatment cost in excess of $500 billion.[2,3] After decades of decline, the number of deaths from heart disease began to rise starting in 2011.[4,5] Even after all the progress that has been made with managing bad (LDL) cholesterol, the majority of CV risk remains. Cholesterol management reduces CV risk by 25-35%, leaving 65-75% risk remaining.

WHAT IS VASCEPA?

Vascepa consists of a single molecule, FDA-approved, prescription drug, icosapent ethyl, in an oral capsule form.[6] In addition to the landmark REDUCE-IT trial, VASCEPA had been studied in two successful Phase 3 clinical trials in which it was shown to provide a broad spectrum of effect on lipid, lipoprotein and inflammatory biomarkers and to have a safety profile comparable to placebo.[7,8] VASCEPA has been approved by the U.S. Food & Drug Administration (FDA) to reduce triglyceride levels in adults with very high triglycerides as an adjunct to diet, and was evaluated in the REDUCE-IT trial for its potential cardioprotective effects as an add-on to statin. VASCEPA capsules have been prescribed in the U.S. more than 4 million times since 2013, and are affordably priced and covered by insurance for most patients.

For more information about VASCEPA, visit www.vascepa.com. Additional information on the VASCEPA cardiovascular outcomes trial, REDUCE-IT, and other VASCEPA clinical studies can be found at www.clinicaltrials.gov. The publication of the design of the REDUCE-IT trial is available at: http://onlinelibrary.wiley.com/doi/10.1002/clc.22692/full.

Please see second page for VASCEPA's full indication, limitations of use and important safety information.

ABOUT AMARIN CORPORATION – GUIDED BY SCIENCE; DRIVEN TO HELP IMPROVE PATIENT CARE

Amarin Corporation plc. is a rapidly growing, innovative pharmaceutical company focused on developing therapeutics to improve cardiovascular health. Amarin's product development program leverages its extensive experience in lipid science and the potential therapeutic benefits of polyunsaturated fatty acids. This focus includes a commitment to ground-breaking research and education in cardiovascular health – including approximately $300M invested to complete the VASCEPA cardiovascular outcomes study, REDUCE-IT. VASCEPA (icosapent ethyl) is Amarin's first FDA-approved drug and available by prescription in the United States, UAE & Lebanon. Amarin's commercial partners are pursuing additional regulatory approvals for VASCEPA in Canada, China and the Middle East. For more information about Amarin, visit www.amarincorp.com.

ABOUT VASCEPA (ICOSAPENT ETHYL) CAPSULES FDA APPROVED INDICATION & IMPORTANT SAFETY INFORMATION

WHAT IS VASCEPA?

VASCEPA (vas-EE-puh) is a prescription medicine used along with a low-fat and low-cholesterol diet to lower high levels of triglycerides (fats) in adults.

- It is not known if VASCEPA changes your risk of having inflammation of your pancreas (pancreatitis).
- It is not known if VASCEPA prevents you from having a heart attack or stroke.
- It is not known if VASCEPA is safe and effective in children.

IMPORTANT SAFETY INFORMATION

WHO SHOULD NOT TAKE VASCEPA?

- Do not take VASCEPA if you are allergic to icosapent ethyl or any of the ingredients in VASCEPA.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF VASCEPA?

- It is not known if people who are allergic to fish or shellfish are also allergic to VASCEPA.
- If you have liver problems and are taking VASCEPA, your doctor should do blood tests during treatment.
- The most common side effect of VASCEPA is joint pain. Talk to your doctor for medical advice about side effects.

As with all drugs, you may experience a serious side effect when taking VASCEPA.
You may report side effects by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.

Tell your doctor if you take medicines that affect your blood clotting (anticoagulants or blood thinners).

Take VASCEPA capsules whole. Do not break, crush, dissolve, or chew VASCEPA capsules before swallowing.

For more information on VASCEPA, click here to see the full Patient Information or call 1-855-VASCEPA (1-855-827-2372).

Sources:

1. Bhatt DL, Steg PG, Brinton EA, et al. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. Clin Cardiol. 2017;40:138-148.
2. Benjamin EJ, Virani SS, Callaway CW, et al; on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics 2018 at-a-glance. https://healthmetrics.heart.org/wp-content/uploads/2018/02/At-A-Glance-Heart-Disease-and-Stroke-Statistics-2018.pdf. Accessed February 26, 2018.
3. American Heart Association. Cardiovascular disease: a costly burden for America. Projections through 2035. http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_491543.pdf. Accessed February 7, 2018.
4. Adapted from Heron M, Anderson RN. NCHS Data Brief. 2016;(254):1-8. Figure 1: Number of deaths due to heart disease and cancer: United States, 1950-2014.
5. Kochanek KD et al. NCHS Data Brief. 2017;(293):1-8.
6. Bays HE, Ballantyne CM, Kastelein JJ, Isaacsohn JL, Braeckman RA, Soni PN. Eicosapentaenoic acid ethyl ester (AMR101) therapy in patients with very high triglyceride levels (from the Multi-center, plAcebo-controlled, Randomized, double-blINd, 12-week study with an open-label Extension [MARINE] trial). Am J Cardiol. 2011;108(5):682-690.
7. Ballantyne CM, Bays HE, Kastelein JJ, et al. Efficacy and safety of eicosapentaenoic acid ethyl ester (AMR101) therapy in statin-treated patients with persistent high triglycerides (from the ANCHOR study). Am J Cardiol. 2012;110(7):984-992.
8. Bays HE, Ballantyne CM, Braeckman RA, Stirtan WG, Soni PN. Icosapent ethyl, a pure ethyl ester of eicosapentaenoic acid: effects on circulating markers of inflammation from the MARINE and ANCHOR studies. Am J Cardiovasc Drugs. 2013;13(1):37-46.

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