

Amarin Corporation

Fifteen Medical Societies Now Recommend Icosapent Ethyl to Reduce Cardiovascular Risk, Further Supporting that VASCEPA® is Rapidly Becoming a New Standard of Care

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Recent recommendations or guidances, from Canada and Egypt, expand the global recognition of this important therapy and its demonstrated favorable outcomes study results

DUBLIN, Ireland and BRIDGEWATER, N.J., March 29, 2021 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN) today announced that the Canadian Cardiovascular Society (CCS) and the *Egyptian Heart Journal (EHJ)* (the official journal of the Egyptian Cardiovascular Society) have included icosapent ethyl in the 2021 Canadian Cardiovascular Society Guidelines¹ and in the *Egyptian Heart Journal's* Practical Guidance in Lipid Management² respectively, for the reduction of cardiovascular risk. These recommendations increase to 15 the number of global organizations or medical societies that recommend icosapent ethyl for cardiovascular risk reduction following its previously reported favorable outcomes study results. These independent recommendations support the company's view that this important drug, marketed in the United States as VASCEPA®, is rapidly becoming a new standard of care for the treatment of appropriate high-risk patients.

The CCS guideline recommends, "the use of icosapent ethyl to lower the risk of CV events in patients with atherosclerotic cardiovascular disease (ASCVD), or with diabetes and ≥ 1 CVD risk factors, who have an elevated fasting triglyceride level of 1.5-5.6 mmol/L despite treatment with maximally tolerated statin therapy". Further, CCS guideline authors, "do not recommend the use of over-the-counter omega-3 polyunsaturated fatty acids supplements (marketed as natural health products in Canada) to reduce CVD risk".¹ The reference to over-the-counter is understood in other parts of the world to refer to dietary supplements.

The *Egyptian Heart Journal* practical guidance in lipid management lists icosapent ethyl as a consideration in patients with high triglyceride (HTG) levels (above 200 mg/dL). The recommendation excludes secondary causes of HTG [TG levels > 200 mg/dL] as part of patient management and advises to treat them separately. Patients with HTG and at high risk must receive a statin as a first-line treatment to reduce cardiovascular disease (CVD) risk. In high-risk (or above) patients with TG levels between 135 and 499 mg/dL despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2g/day) should be considered in combination with a statin.²

"Inclusion in these new guidelines underscores the growing global acceptance of the clinical benefits of pure icosapent ethyl in reducing cardiovascular risk as supported by the landmark REDUCE-IT® study of VASCEPA and further validates the independent support of this unique agent by the scientific community," stated Craig B. Granowitz, M.D., Ph.D., senior vice president and chief medical officer of Amarin. "With these new recommendations, icosapent ethyl is now included in the treatment guidelines or otherwise recommended for use by 15 medical associations internationally, further validating icosapent ethyl as an important treatment option beyond cholesterol management for millions of patients worldwide at risk for a cardiovascular event."

The recommendation from the CCS was classified as 'Strong Recommendation; High-Quality Evidence' and supported by the results of the REDUCE-IT cardiovascular outcomes study. The results of REDUCE-IT cannot be extrapolated to other non-prescription omega-3 fatty acids.

The CCS and the *EHJ* do not provide endorsements of any brand name commercial product. Accordingly, the CCS "2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult" and the *EHJ* "Egyptian Practical Guidance in Lipid Management" reference icosapent ethyl. The guidelines do not reference VASCEPA, the brand name of icosapent ethyl in the United States, and such guidelines should not be construed as an endorsement or approval of VASCEPA by the CCS or *EHJ*.

Amarin acknowledges the rigor with which these documents are developed and approved by the CCS and the *EHJ*, which are comprised of leading medical professionals in Canada and Egypt who specialize in the care of patients with CVD.

The complete "2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult" addressing Primary and Secondary Prevention of Cardiovascular Diseases with icosapent ethyl published in the *Canadian Journal of Cardiology* can be accessed online [here](#). The "Egyptian Practical Guidance in Lipid Management" as published in *The Egyptian Heart Journal* can be accessed online [here](#).

Information on other medical societies that include icosapent ethyl in their guidelines can be accessed [here](#).

About Amarin

Amarin is a rapidly growing, innovative pharmaceutical company leading a new paradigm in cardiovascular disease management. From our scientific research foundation to our focus on clinical trials, and now our commercial expansion, we are evolving and growing. In 2009, Amarin had fewer than twenty employees. Today, with offices in Bridgewater, New Jersey in the United States, Dublin in Ireland, and Zug in Switzerland, Amarin has approximately 1,000 employees and commercial partners and suppliers around the world. We are committed to rethinking cardiovascular risk through the advancement of scientific understanding of the impact on society of significant residual risk that exists beyond traditional therapies, such as statins for cholesterol management.

About Cardiovascular Risk

The number of deaths in the United States attributed to cardiovascular disease continues to rise. There are 605,000 new and 200,000 recurrent heart attacks per year (approximately 1 every 40 seconds), in the United States. Stroke rates are 795,000 per year (approximately 1 every 40 seconds), accounting for 1 of every 19 U.S. deaths. Cardiovascular disease results in 859,000 deaths per year in the United States.³ In aggregate, there are more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, one every 13 seconds in the United States alone.

Controlling bad cholesterol, also known as LDL-C, is one way to reduce a patient's risk for cardiovascular events, such as heart attack, stroke or death. However, even with the achievement of target LDL-C levels, millions of patients still have significant and persistent risk of cardiovascular events, especially those patients with elevated triglycerides. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35%.⁴ Significant cardiovascular risk remains after statin therapy. People with elevated triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins.^{5,6,7}

About REDUCE-IT®

REDUCE-IT was a global cardiovascular outcomes study designed to evaluate the effect of VASCEPA in adult patients with LDL-C controlled to between 41-100 mg/dL (median baseline 75 mg/dL) by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides between 135-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or diabetes mellitus and at least one other cardiovascular risk factor (primary prevention cohort).

REDUCE-IT, conducted over seven years and completed in 2018, followed 8,179 patients at over 400 clinical sites in 11 countries with the largest number of sites located within the United States. REDUCE-IT was conducted based on a special protocol assessment agreement with FDA. The design of the REDUCE-IT study was published in March 2017 in *Clinical Cardiology*.⁸ The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.⁹ The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.¹⁰ These and other publications can be found in the R&D section on the company's website at www.amarinincorp.com.

About VASCEPA® (icosapent ethyl) Capsules

VASCEPA (icosapent ethyl) capsules are the first-and-only prescription treatment approved by the U.S. FDA comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. VASCEPA was launched in the United States in January 2020 as the first and only drug approved by the U.S. FDA for treatment of the studied high-risk patients with persistent cardiovascular risk after statin therapy. VASCEPA was initially launched in the United States in 2013 based on the drug's initial FDA approved indication for use as an adjunct therapy to diet to reduce triglyceride levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. Since launch, VASCEPA has been prescribed over ten million times. VASCEPA is covered by most major medical insurance plans. In addition to the United States, VASCEPA is approved and sold in Canada, Lebanon and the United Arab Emirates. In Europe, approval is anticipated in April 2021 following the January 28, 2021 favorable opinion of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommending that marketing authorisation be granted to icosapent ethyl in the European Union for the reduction of risk of cardiovascular events in patients at high cardiovascular risk, under the brand name VASKEPA.

Indications and Limitation of Use (in the United States)

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 triglyceride (TG) levels (≥ 150 mg/dL) and
 - established cardiovascular disease or
 - diabetes mellitus and two 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 (e.g., 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.
- It is 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 $\geq 3\%$ and $\geq 1\%$ 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 $\geq 1\%$ 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 should be monitored for bleeding.

Key clinical effects of VASCEPA on major adverse cardiovascular events are included in the Clinical Studies section of the prescribing information for VASCEPA as set forth below:

Effect of VASCEPA on Time to First Occurrence of Cardiovascular Events in Patients with Elevated Triglyceride levels and Other Risk Factors for Cardiovascular Disease in REDUCE-IT

	VASCEPA	Placebo	

					vs Placebo
	N = 4089 n (%)	Incidence Rate (per 100 patient years)	N = 4090 n (%)	Incidence Rate (per 100 patient years)	Hazard Ratio (95% CI)
Primary composite endpoint					
Cardiovascular death, myocardial infarction, stroke, coronary revascularization, hospitalization for unstable angina (5-point MACE)	705 (17.2)	4.3	901 (22.0)	5.7	0.75 (0.68, 0.83)
Key secondary composite endpoint					
Cardiovascular death, myocardial infarction, stroke (3-point MACE)	459 (11.2)	2.7	606 (14.8)	3.7	0.74 (0.65, 0.83)
Other secondary endpoints					
Fatal or non-fatal myocardial infarction	250 (6.1)	1.5	355 (8.7)	2.1	0.69 (0.58, 0.81)
Emergent or urgent coronary revascularization	216 (5.3)	1.3	321 (7.8)	1.9	0.65 (0.55, 0.78)
Cardiovascular death ^[1]	174 (4.3)	1.0	213 (5.2)	1.2	0.80 (0.66, 0.98)
Hospitalization for unstable angina ^[2]	108 (2.6)	0.6	157 (3.8)	0.9	0.68 (0.53, 0.87)
Fatal or non-fatal stroke	98 (2.4)	0.6	134 (3.3)	0.8	0.72 (0.55, 0.93)
[1] Includes adjudicated cardiovascular deaths and deaths of undetermined causality.					
[2] Determined to be caused by myocardial ischemia by invasive/non-invasive testing and requiring emergent hospitalization.					

FULL U.S. FDA-APPROVED VASCEPA [PRESCRIBING INFORMATION](#) CAN BE FOUND AT WWW.VASCEPA.COM.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential impact of VASCEPA in various clinical uses. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Among the factors that could cause actual results to differ materially from those described or projected herein include the following: uncertainties associated generally with research and development and clinical trials such as further clinical evaluations failing to confirm earlier findings. A further list and description of these risks, uncertainties and other risks associated with an investment in Amarin can be found in Amarin's filings with the U.S. Securities and Exchange Commission, including its most recent Annual Report on Form 10-K. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Amarin undertakes no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise. Amarin's forward-looking statements do not reflect the potential impact of significant transactions the company may enter into, such as mergers, acquisitions, dispositions, joint ventures or any material agreements that Amarin may enter into, amend or terminate.

Availability of Other Information About Amarin

Investors and others should note that Amarin communicates with its investors and the public using the company website (www.amarincorp.com), the investor relations website (investor.amarincorp.com), including but not limited to investor presentations and investor FAQs, Securities and Exchange Commission filings, press releases, public conference calls and webcasts. The information that Amarin posts on these channels and websites could be deemed to be material information. As a result, Amarin encourages investors, the media, and others interested in Amarin to review the information that is posted on these channels, including the investor relations website, on a regular basis. This list of channels may be updated from time to time on Amarin's investor relations website and may include social media channels. The contents of Amarin's website or these channels, or any other website that may be accessed from its website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

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VASCEPA and VAZKEPA are trademarks of Amarin Pharmaceuticals Ireland Limited. VAZKEPA is a registered trademark in Europe and other countries and regions and is pending registration in the United States.