



## **Independent Drug-Pricing Assessment Finds Vascepa® (icosapent ethyl) Cost-Effective as an Adjunct to Statins in Treating Patients at High Risk of Cardiovascular Events, such as Heart Attack, Stroke and Cardiac Death**

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DUBLIN, Ireland and BRIDGEWATER, N.J., Oct. 17, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN), a pharmaceutical company focused on improving cardiovascular health, today announced that an independent organization that evaluates pricing of prescription drugs has issued its final report assessing the cost-effectiveness of *Vascepa*® (icosapent ethyl) capsules. The final assessment confirms the cost-effectiveness of *Vascepa* across all the non-profit organization's analyses, including its most stringent criteria.<sup>1</sup>

The review was derived from results of the landmark phase 3 clinical trial REDUCE-IT®<sup>2</sup>, focusing on the clinical benefit-risk profile of *Vascepa* and its value as an additive therapy for cardiovascular disease. The conclusion from the report is that *Vascepa* easily meets "commonly cited thresholds for cost-effectiveness and therefore represent a high long-term value for money," based on the organization's value assessment framework.<sup>3</sup>

"We are proud to have priced *Vascepa* to be cost-effective, and we appreciate this positioning being recognized by third-parties," said Craig Granowitz, M.D., Ph.D., chief medical officer, Amarin. "However, despite the report's positive conclusion that *Vascepa* is cost-effective, we believe that it understates the true value of *Vascepa*. For example, the report's base-case analyses reflect only the costs of heart attack, stroke and cardiovascular death and exclude other high costs associated with other cardiovascular events demonstrated to be lowered by *Vascepa* in the REDUCE-IT cardiovascular outcomes study (e.g., revascularization procedures and hospitalization for unstable angina) as well as lower rates of recurring cardiovascular events in patients treated with *Vascepa* during the study."

### **Another Cost-Effectiveness Analysis of Vascepa to Be Presented at AHA**

A separate independent, academic cost-effectiveness analysis of *Vascepa* based on patient-specific data from the REDUCE-IT study will be presented at the American Heart Association Scientific Sessions 2019 on November 16 by William S. Weintraub, M.D., Director of Outcomes Research, MedStar Cardiovascular Research Network. Amarin provided an unrestricted grant for this academically driven analysis, titled "Cost-Effectiveness of Icosapent Ethyl in REDUCE-IT."

### **Cardiovascular Disease, an Urgent Public Health Issue**

"There is no doubt that cardiovascular disease is an urgent and growing public health issue, with more than half of U.S. adults impacted," Dr. Granowitz added. "The U.S. spends approximately \$555 billion on cardiovascular disease each year, and it is projected that these direct and indirect costs could increase to more than \$1.1 trillion by 2035.<sup>4</sup> Amarin has worked for over a decade to develop and test *Vascepa* to create a new preventative care solution that will potentially help many of our family, friends and neighbors within this population. Our goal is to make *Vascepa* accessible to as many patients as possible who can benefit."

*Vascepa* is currently approved in the United States as an adjunct to diet to reduce triglyceride levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia. Amarin has submitted a supplemental new drug application (sNDA) to the U.S. FDA for a label expansion based on the REDUCE-IT study results showing reduction of cardiovascular events in high-risk patients. The Prescription Drug User Fee Act (PDUFA) target action date set by the FDA to act on the sNDA is December 28, 2019. Assuming FDA approval, *Vascepa* is positioned to become the first drug indicated to reduce persistent residual cardiovascular risk in statin-managed patients with elevated triglycerides (135 mg/dL or greater) and other risk factors for cardiovascular disease. The approval of such label expansion and the wording of the indication statement is under regulatory review.

Today, many insurance plans, or payers, already broadly cover *Vascepa*. Upon assumed FDA label expansion, Amarin plans to use the results of the REDUCE-IT study, further objective health-economic analyses, and other medical information and data in negotiations with payers to seek expanded *Vascepa* insurance coverage.

### **About Amarin**

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 polyunsaturated fatty acids and lipid science. *Vascepa* (icosapent ethyl) is Amarin's first FDA-approved drug and is available by prescription in the United States, Lebanon and the United Arab Emirates. 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](http://www.amarincorp.com).

### **REDUCE-IT® Study**

REDUCE-IT, an 8,179-patient cardiovascular outcomes study, was completed in 2018. REDUCE-IT was the first multinational cardiovascular outcomes study that evaluated the effect of prescription pure EPA therapy as an add-on to statins in patients with high cardiovascular risk who, despite stable statin therapy, had elevated triglyceride levels (at least 135 mg/dL). A large portion of the male and female patients enrolled in this outcomes study were diagnosed with type 2 diabetes.

More information on the REDUCE-IT study results can be found at [www.amarincorp.com](http://www.amarincorp.com).

### **About Cardiovascular Disease**

Worldwide, cardiovascular disease (CVD) remains the #1 killer of men and women. In the United States CVD leads to one in every three deaths – one death approximately every 38 seconds – with annual treatment cost in excess of \$500 billion.<sup>5,6</sup>

Multiple primary and secondary prevention trials have shown a significant reduction of 25% to 35% in the risk of cardiovascular events with statin therapy, leaving significant persistent residual risk despite the achievement of target LDL-C levels.<sup>7</sup>

Beyond the cardiovascular risk associated with LDL-C, genetic, epidemiologic, clinical and real-world data suggest that patients with elevated triglycerides (TG) (fats in the blood), and TG-rich lipoproteins, are at increased risk for cardiovascular disease.<sup>8,9,10,11</sup>

### **About Vascepa® (icosapent ethyl) Capsules**

*Vascepa* (icosapent ethyl) capsules are a single-molecule prescription product consisting of the omega-3 acid commonly known as EPA in ethyl-ester form. *Vascepa* is not fish oil, but is derived from fish through a stringent and complex FDA-regulated manufacturing process designed to effectively eliminate impurities and isolate and protect the single molecule active ingredient from degradation. *Vascepa*, known in scientific literature as AMR101, has been designated a new chemical entity by the FDA. Amarin has been issued multiple patents internationally based on the unique clinical profile of *Vascepa*, including the drug's ability to lower triglyceride levels in relevant patient populations without raising LDL-cholesterol levels.

The FDA has not completed review and opined on a supplemental new drug application related to REDUCE IT. FDA has not reviewed the information herein or determined whether to approve *Vascepa* for use to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population.

#### Indication and Usage Based on Current FDA-Approved Label (not including REDUCE-IT results)

- *Vascepa* (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia.
- The effect of *Vascepa* on the risk for pancreatitis and cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

#### Important Safety Information for Vascepa Based on Current FDA-Approved Label (not including REDUCE-IT results) (Includes Data from Two 12-Week Studies (n=622) (MARINE and ANCHOR) of Patients with Triglycerides Values of 200 to 2000 mg/dL)

- *Vascepa* is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to *Vascepa* or any of its components.
- In patients with hepatic impairment, monitor ALT and AST levels periodically during therapy.
- Use with caution in patients with known hypersensitivity to fish and/or shellfish.
- The most common reported adverse reaction (incidence  $>2\%$  and greater than placebo) was arthralgia (2.3% for *Vascepa*, 1.0% for placebo). There was no reported adverse reaction  $>3\%$  and greater than placebo.
- Adverse events and product complaints may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088. Patients receiving treatment with *Vascepa* and other drugs affecting coagulation (e.g., anti-platelet agents) should be monitored periodically.
- Patients should be advised to swallow *Vascepa* capsules whole; not to break open, crush, dissolve, or chew *Vascepa*.

#### **FULL VASCEPA PRESCRIBING INFORMATION CAN BE FOUND AT [WWW.VASCEPA.COM](http://WWW.VASCEPA.COM).**

#### Important Safety Information for Vascepa based on REDUCE-IT, as previously reported in *The New England Journal of Medicine* publication of the primary results of the REDUCE-IT study:

- Excluding the major adverse cardiovascular events (MACE) results described above, overall adverse event rates in REDUCE-IT were similar across the statin plus *Vascepa* and the statin plus placebo treatment groups.
- There were no significant differences between treatments in the overall rate of treatment emergent adverse events or serious adverse events leading to withdrawal of study drug.
- There was no serious adverse event (SAE) occurring at a frequency of  $>2\%$  which occurred at a numerically higher rate in the statin plus *Vascepa* treatment group than in the statin plus placebo treatment group.
- Adverse events (AEs) occurring in 5% or greater of patients and more frequently with *Vascepa* than placebo were:
  - peripheral edema (6.5% *Vascepa* patients versus 5.0% placebo patients), although there was no increase in the rate of heart failure in *Vascepa* patients
  - constipation (5.4% *Vascepa* patients versus 3.6% placebo patients), although mineral oil, as used as placebo, is known to lower constipation, and

- atrial fibrillation (5.3% *Vascepa* patients versus 3.9% placebo patients), although there were reductions in rates of cardiac arrest, sudden death and myocardial infarctions observed in *Vascepa* patients
- There were numerically more SAEs related to bleeding in the statin plus *Vascepa* treatment group although overall rates were low with no fatal bleeding observed in either group and no significant difference in adjudicated hemorrhagic stroke or serious central nervous system or gastrointestinal bleeding events between treatments.
- In summary, *Vascepa* was well tolerated with a safety profile generally consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling of such products.

#### **Important Cautionary Information About These Data**

Further REDUCE-IT data assessment and data release could yield additional useful information to inform greater understanding of the trial outcome. For example, detailed data assessment by regulatory authorities, such as the FDA and Health Canada, will continue and take months to complete and announce. The FDA advisory committee process and the final evaluation by regulatory authorities of the totality of efficacy and safety data from REDUCE-IT may include some or all of the following, as well as other considerations: new information or analyses affecting the degree of treatment benefit on studied endpoints; study conduct and data robustness, quality, integrity and consistency; additional safety data considerations and risk/benefit considerations; and consideration of REDUCE-IT results in the context of other clinical studies. Because regulatory reviews are typically fluid and not definitive interactions between sponsor and agency on individual elements of an application and related information, Amarin does not plan to update investors on ongoing communications with regulatory authorities. Amarin plans to announce the final outcome of such regulatory reviews when appropriate.

#### **Forward-Looking Statements**

This press release contains forward-looking statements, including statements regarding the use of *Vascepa* to potentially help millions of patients. 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, clinical trials and related regulatory reviews and approvals; the risk that data interpretations or other information from third parties, the regulatory review process, regulatory authorities and in connection with an advisory committee could be made public that are negative or may delay approval or limit *Vascepa's* marketability; the risk that special protocol assessment (SPA) agreements with the FDA are not a guarantee that FDA will approve a product candidate; the risk associated with the FDA's rescinding the REDUCE-IT SPA agreement; the risk related to FDA advisory committee meetings; and the risk that the FDA may not complete its review of the REDUCE-IT sNDA within the timing expected. 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 Quarterly Report on Form 10-Q. 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.

#### **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](http://www.amarincorp.com)), the investor relations website ([investor.amarincorp.com](http://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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## References

- <sup>1</sup> [https://icer-review.org/wp-content/uploads/2019/02/ICER\\_CVD\\_Final\\_Evidence\\_Report\\_101719.pdf](https://icer-review.org/wp-content/uploads/2019/02/ICER_CVD_Final_Evidence_Report_101719.pdf)
- <sup>2</sup> Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. *N Engl J Med* 2019;380:11-22.
- <sup>3</sup> [https://icer-review.org/announcements/cvd\\_final\\_report/](https://icer-review.org/announcements/cvd_final_report/)
- <sup>4</sup> American Heart Association. 2017. Cardiovascular Disease: A Costly Burden for America. Projections Through 2035
- <sup>5</sup> American Heart Association. 2018. Disease and Stroke Statistics-2018 Update.
- <sup>6</sup> American Heart Association. 2017. Cardiovascular Disease: A Costly Burden for America Projections Through 2035.
- <sup>7</sup> Ganda OP, Bhatt DL, Mason RP, et al. Unmet need for adjunctive dyslipidemia therapy in hypertriglyceridemia management. *J Am Coll Cardiol*. 2018;72(3):330-343.
- <sup>8</sup> Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.
- <sup>9</sup> Toth PP, Granowitz C, Hull M, et al. High triglycerides are associated with increased cardiovascular events, medical costs, and resource use: A real-world administrative claims analysis of statin-treated patients with high residual cardiovascular risk. *J Am Heart Assoc*. 2018;7(15):e008740.
- <sup>10</sup> Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.
- <sup>11</sup> Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. *Lancet*. 2014;384:626–635.