TOPLINE RESULTS FROM THE VASCEPA® (icosapent ethyl) CV OUTCOMES TRIAL (REDUCE-IT™) ANNOUNCED SEPTEMBER 2018

REDUCE-IT investigated the effects of VASCEPA on CV risk in statin-treated adults with well-controlled LDL-C 41-100 mg/dL (median baseline LDL-C: 75 mg/dL) and other CV risk factors, including persistent elevated TG 150-499 mg/dL (median baseline TG: 216 mg/dL).1,2

Pure EPA VASCEPA 1-g capsules contain 1 g of icosapent ethyl, a form of the omega-3 fatty acid known as EPA and inactive ingredients. VASCEPA is also available in 0.5-g capsules.

FDA has not reviewed and opined on a new drug application related to the REDUCE-IT data. FDA has thus not determined whether to approve VASCEPA for use to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population.*

FDA-APPROVED INDICATION AND LIMITATIONS OF USE FOR VASCEPA3

- VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (>500 mg/dL) hypertriglyceridemia
- In patients with severe hypertriglyceridemia, the effect of VASCEPA on cardiovascular mortality or morbidity or on the risk of pancreatitis has not been determined

*This information is intended to ensure Amarin meets its continuing obligation to update healthcare professionals regarding off-label use of VASCEPA to assure that its communications remain truthful and non-misleading, consistent with the federal court approved settlement under Amarin Pharma, Inc. et al. v. United States Food and Drug Administration et al., 119 F.Supp. 3d 196, 236 (S.D.N.Y. 2015).

Please see Important Safety Information for VASCEPA on page 2. Please see accompanying full Prescribing Information for VASCEPA or go to www.vascepahcp.com.
FDA-APPROVED INDICATION AND LIMITATIONS OF USE FOR VASCEPA³

- VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia

- In patients with severe hypertriglyceridemia, the effect of VASCEPA on cardiovascular mortality or morbidity or on the risk of pancreatitis has not been determined

IMPORTANT SAFETY INFORMATION FOR VASCEPA FROM FDA-APPROVED LABEL

Includes Data from Two 12-Week Studies (MARINE and ANCHOR) of Patients with Triglycerides Values of 200 to 2000 mg/dL (n=622 on VASCEPA, n=309 on placebo)³

- 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% VASCEPA, 1.0% placebo)

- Adverse events 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

Pay as little as $9 for 90 days.*

Expiration Date: 12/31/2019

*Limitations apply. See reverse side for details.

Powered by:
Change Healthcare
BIN# 004682
PCN# CN
GRP# ECVASCEPA
ID# 59021139303

Commercially insured patients† can pay as little as $9 for a 90-day supply with the VASCEPA Savings Card. Subject to eligibility. Restrictions apply.‡

Your patients can download the VASCEPA Savings Card§ at www.VASCEPASavings.com

†Offer Restrictions: May not be used to obtain prescription drugs paid in part by Federal or State Programs including Medicare, Medicaid, Medicare Advantage, Medicare Part D, Tricare, VA. Most eligible, insured patients will pay as little as $9 of their copay for either each month or a 90 day fill, with a maximum savings of up to $80 per month or $240 on a 90 day fill. Not for use by residents of VT, nor medical professionals licensed in VT. This offer is not valid for those patients under 18 years of age or patients whose plans do not permit use of a copay card. Void where prohibited by law, taxed, or restricted. Eligible patients include those who participate in commercial insurance, through a healthcare exchange, or pay cash. Offer good through December 31, 2019.

‡As of August 31, 2018.

§Universal Pharmacy Card (UPC) may be applied for any eligible patient by entering all 4 codes into the notes section of an e-prescription.

Please see accompanying full Prescribing Information for VASCEPA or go to www.vascepahcp.com.
THE MARINE TRIAL

VASCEPA lowers VHTG and atherogenic lipids without raising LDL-C:

- The effects of VASCEPA 4 g/d were assessed in a randomized, placebo-controlled, double-blind, parallel-group study evaluating adult patients with fasting TG levels >500 mg/dL and ≤2000 mg/dL (with or without statin therapy)

- The primary study endpoint was the placebo-adjusted median percent change in TG levels from baseline to study end (Week 12)

**MARINE overall population**

Median percent change from baseline vs placebo

<table>
<thead>
<tr>
<th></th>
<th>TG (n=76)</th>
<th>LDL-C (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median baseline</td>
<td>680 mg/dL</td>
<td>91 mg/dL</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>not significant</td>
</tr>
</tbody>
</table>

**Results:**

- TG: VASCEPA (n=76), 27% median decrease from baseline; placebo (n=75), 10% increase from baseline. LDL-C: VASCEPA (n=76), 5% median decrease from baseline; placebo (n=75), 3% decrease from baseline.

VASCEPA 4 g/d significantly reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with VASCEPA was not associated with elevations in LDL-C levels relative to placebo.

In a pre-specified subgroup analysis, there was a 45% TG decrease in patients with TG >750 mg/dL (median baseline TG level 902 mg/dL; median change vs baseline: VASCEPA (n=28): -27%, placebo (n=32): +19%; \( P<0.001 \)).

\( \downarrow \) As compared to placebo.

Please see Important Safety Information for VASCEPA on page 2.
IMPORTANT INFORMATION FOR HCPs ABOUT VASCEPA®

IMPORTANT NEW INFORMATION FROM THE RECENTLY COMPLETED REDUCE-IT™ CARDIOVASCULAR OUTCOMES STUDY²*

Top Line Results Announced—September 2018:

- REDUCE-IT cardiovascular (CV) outcomes study of VASCEPA (icosapent ethyl) capsules met its pre-specified primary composite endpoint in the intent-to-treat population:
  - Showed reduction in a composite of major adverse cardiovascular events (MACE) of approximately 25%
  - P value <0.001 (highly statistically significant)
  - Composite endpoint consisted of CV death, nonfatal myocardial infarction (MI, including silent MI), nonfatal stroke, coronary revascularization, and unstable angina requiring hospitalization
  - Primary endpoint result supported by robust demonstrations of efficacy across multiple secondary endpoints

- REDUCE-IT safety: VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups

- FDA has not reviewed and opined on a new drug application related to the REDUCE-IT data. FDA has thus not determined whether to approve VASCEPA for use to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population*

- REDUCE-IT design overview:
  - REDUCE-IT enrolled adult patients with LDL-C controlled to between 41-100 mg/dL (median baseline 75 mg/dL) by statin therapy and with various cardiovascular risk factors including persistent elevated TGs between 150-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention) or diabetes mellitus and at least one other CV risk factor (primary prevention)
  - REDUCE-IT randomized 8,179 patients on a 1:1 basis to statin plus VASCEPA 4g/day or statin plus placebo and compared the incidence of MACE between treatment arms over a median period of 4.9 years
  - REDUCE-IT was a global trial conducted based on a special protocol assessment agreement with the FDA with statistical power based on 1,612 primary endpoint events

- Additional updates on REDUCE-IT study results are planned in a peer-reviewed publication and presentation of REDUCE-IT results will occur at the late-breaker session at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018 in Chicago, Illinois

*This information is intended to ensure Amarin meets its continuing obligation to update healthcare professionals regarding off-label use of VASCEPA to assure that its communications remain truthful and non-misleading, consistent with the federal court approved settlement under Amarin Pharma, Inc. et al. v. United States Food and Drug Administration et al., 119 F.Supp.3d 196, 236 (S.D.N.Y. 2015).

Please see Important Safety Information related to REDUCE-IT for VASCEPA above.
Please see accompanying full Prescribing Information for VASCEPA or go to www.vascepahcp.com.
• As with any topline CV outcomes trial result, further REDUCE-IT data assessment and data release will yield additional useful information to inform greater understanding of study outcome:
  - Detailed trial data assessment may take several months to complete and record
  - Aspects that could change and impact the final evaluation of the totality of the efficacy/safety data from REDUCE-IT may include some or all of the following:
    o The magnitude of the treatment benefit on the primary composite endpoint, its components, secondary endpoints and the primary and secondary risk prevention cohorts
    o Consideration of which components of the composite or secondary endpoints have the most clinical significance
    o The consistency of the primary and secondary outcomes
    o The consistency of findings across cohorts and important subgroups
    o Safety considerations and risk/benefit considerations
    o Consideration of REDUCE-IT results in the context of other clinical studies
    o Study conduct and data quality, integrity and consistency

• VASCEPA may not be eligible for reimbursement under government healthcare programs (such as Medicare and Medicaid) and certain commercial plans to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population. We encourage you to check that for yourself

• REDUCE-IT was sponsored by Amarin Pharma, Inc. and its affiliates

IMPORTANT INFORMATION FOR HCPs ABOUT VASCEPA AS AN ADD-ON TO STATINS IN PATIENTS WITH HIGH (200-499 mg/dL) TG LEVELS

• VASCEPA is not FDA-approved to lower TG levels in statin-treated patients with mixed dyslipidemia and persistent high (>200 mg/dL and <500 mg/dL) TG levels due to current uncertainty regarding the benefit, if any, of drug-induced changes in lipid/lipoprotein parameters beyond statin-lowered LDL-C on cardiovascular risk among statin-treated patients with residually high TG
  - Other cardiovascular outcomes trials (ACCORD Lipid, AIM-HIGH, and HPS2-THRIVE), while not designed to test the effect of lowering TG levels in patients with high TG levels after statin therapy, each failed to demonstrate incremental cardiovascular benefit of adding a second lipid-altering drug (fenofibrate or formulations of niacin), despite raising HDL-C and reducing TG levels, among statin-treated patients with well-controlled LDL-C
• Other cardiovascular outcomes trials in the omega-3 class that studied fish oil or mixtures of omega-3 acids that include the omega-3 acid, DHA, have reported negligible impact on cardiovascular events
• No head-to-head, randomized, well-controlled studies have been conducted to compare the effects of VASCEPA with other FDA-approved TG-lowering therapies
THE VASCEPA CV OUTCOMES TRIAL (REDUCE-IT™) IS THE FIRST OF ITS KIND

- The REDUCE-IT trial was a global, rigorously designed, placebo-controlled, double-blind, event-driven trial—not a biomarker trial (e.g., not a TG-lowering trial)¹
- REDUCE-IT was a CV outcomes study with statistical power based on 1612 primary endpoint events¹

REDUCE-IT was specifically designed to study prescription Pure EPA VASCEPA at 4 g/d in statin-treated adults with well-controlled LDL-C and other CV risk factors, including persistent elevated TG.¹*

Additional updates on REDUCE-IT study results are planned in a peer-reviewed publication and presentation of REDUCE-IT results will occur at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018 in Chicago, Illinois.

*LDL-C 41-100 mg/dL, TG 150-499 mg/dL.

REDUCE-IT safety: VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups.²
REDUCE-IT safety: VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups.

The VASCEPA CV Outcomes Trial (REDUCE-IT™) is the first of its kind. The REDUCE-IT trial was a global, rigorously designed, placebo-controlled, double-blind, event-driven trial—not a biomarker trial. REDUCE-IT was a CV outcomes study with statistical power based on 1612 primary endpoint events.

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*LDL-C 41-100 mg/dL, TG 150-499 mg/dL.

8179 PATIENTS...

Statin-treated men and women aged ≥45 years

Well-controlled LDL-C 41-100 mg/dL

Median baseline 75 mg/dL

...AT HIGH RISK FOR CV EVENTS DUE TO:

TG 150-499 mg/dL

Median baseline 216 mg/dL

&

Established CVD

OR

Diabetes mellitus + aged ≥50 years + ≥1 risk factor for CVD

RANDOMIZATION 1:1

STABLE STATIN + VASCEPA 4 g/d

Double-blind parallel-group trial median follow-up: 4.9 years

STABLE STATIN + PLACEBO

PRIMARY COMPOSITE (MACE) ENDPOINT

CV Death Nonfatal MI Nonfatal Stroke

Coronary Revascularization Unstable Angina Requiring Hospitalization

MACE=major adverse cardiovascular events.
In statin-treated adults with well-controlled LDL-C and other CV risk factors, including persistent elevated TG*

**ADDING VASCEPA 4 g/d SHOWED AN APPROXIMATELY 25% RRR IN CV EVENTS BASED ON TOPLINE RESULTS**\(^2\)

Median follow-up was 4.9 years with a composite primary MACE endpoint of:

- CV Death
- Nonfatal MI
- Nonfatal Stroke
- Coronary Revascularization
- Unstable Angina Requiring Hospitalization

RRR=relative risk reduction.

*LDL-C 41-100 mg/dL, TG 150-499 mg/dL. The median baseline LDL-C was 75 mg/dL and median baseline TG was 216 mg/dL.

\(^1\)As compared to placebo in the intent-to-treat population.

FDA has not reviewed and opined on a new drug application related to the REDUCE-IT data. FDA has thus not determined whether to approve VASCEPA for use to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population.

As with any topline CV outcomes trial result, further REDUCE-IT data assessment and data release will yield additional useful information to inform greater understanding of study outcome.

**IMPORTANT SAFETY INFORMATION RELATED TO REDUCE-IT FOR VASCEPA**

REDUCE-IT safety: VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups.\(^2\)
TOPLINE RESULTS ARE IN:\nAPPROXIMATELY 25% RELATIVE RISK REDUCTION P<0.001

This result was supported by robust demonstrations of efficacy across multiple secondary endpoints\n
REDUCE-IT safety: VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups\n
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Includes Data from Two 12-Week Studies (MARINE and ANCHOR) of Patients with Triglycerides Values of 200 to 2000 mg/dL (n=622 on VASCEPA, n=309 on placebo)\n
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- 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% VASCEPA, 1.0% placebo)
- Adverse events 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
HOW IS PURE EPA VASCEPA DIFFERENT?*

Pure EPA VASCEPA²:

- Topline results from REDUCE-IT showed reduction in MACE of approximately 25% in statin-treated adults with well-controlled LDL-C and other CV risk factors, including persistent elevated TG†
- This result was supported by robust demonstrations of efficacy across multiple secondary endpoints
- VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups

- CV outcomes studies of earlier generation drug therapies including fenofibrates and omega-3 mixture products containing DHA have failed to demonstrate CV benefits on top of statins⁵-⁸*
- REDUCE-IT results stand alone as positive and confirm the hypothesis that Pure EPA VASCEPA 4 g/d can provide additional CV risk reduction benefit on top of LDL-C control in studied patients²
- REDUCE-IT results cannot be generalized to earlier generation therapies including fenofibrate, fish oil, or omega-3 mixture products that contain DHA²

Additional updates on REDUCE-IT study results are planned in a peer-reviewed publication and presentation of REDUCE-IT results will occur at the late-breaker session at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018 in Chicago, Illinois.

As with any topline CV outcomes trial result, further REDUCE-IT data assessment and data release will yield additional useful information to inform greater understanding of study outcome.

Please see accompanying full Prescribing Information for VASCEPA or go to www.vascepahcp.com.
Amarin thanks the clinicians and patients who participated in the VASCEPA clinical studies.

In statin-treated adults with well-controlled LDL-C and other CV risk factors, including persistent elevated TG*

**REDUCE-IT™ TOPLINE RESULTS:**
**ADDING VASCEPA® 4 g/d SHOWED AN APPROXIMATELY 25% RRR IN CV EVENTS**

**PRIMARY ENDPOINT MET²:**
- Showed approximately 25% reduction in MACE, *P* value <0.001 (highly statistically significant)²
- This result was supported by robust demonstrations of efficacy across multiple secondary endpoints²
- VASCEPA was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labelling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups²
- Dosed at 4 g/d—2 g BID with food³
- As with any topline CV outcomes trial result, further REDUCE-IT data assessment and data release will yield additional useful information to inform greater understanding of study outcome

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RRR=relative risk reduction.

*LDL-C 41–100 mg/dL, TG 150–499 mg/dL. The median baseline LDL-C was 75 mg/dL and median baseline TG was 216 mg/dL.

†As compared to placebo in the intent-to-treat population.

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