

## Icosapent ethyl (Vascepa)

### Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

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### Summary

Icosapent ethyl (Vascepa), an ethyl ester of eicosapentaenoic acid (EPA), is an FDA-approved:

- 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 ( $\geq 150$  mg/dL) and

- established cardiovascular disease; or
- diabetes mellitus and two (2) or more additional risk factors for cardiovascular disease (e.g., men  $\geq 55$  years, women  $\geq 65$  years, cigarette smoker or stopped in the last 3 months, hypertension or on antihypertensives, HDL-C  $\leq 40$  for men and HDL-C  $\leq 50$  for women, High-sensitivity C-reactive protein [Hs-CRP]  $> 3.00$  mg/L, renal impairment, retinopathy, micro- or macro-albuminuria, ankle-brachial index [ABI]  $< 0.9$ ).
- As an adjunct to diet to reduce TG levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia.

The REDUCE-IT trial demonstrated a significant 25% reduction in major adverse cardiovascular events (MACE) in those treated with icosapent ethyl (Vascepa) compared to placebo, in those with and without diabetes. This landmark study forms the basis for its use in cardiovascular risk reduction. The 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline and other expert consensus statements, including those from the National Lipid Association (NLA) and the American Diabetes Association (ADA), recommend icosapent ethyl for ASCVD risk reduction in high-risk individuals with elevated triglycerides, consistent with the REDUCE-IT trial population. Members taking icosapent ethyl (Vascepa) should also adhere to lifestyle modifications, including a lipid-lowering diet and regular exercise, as these remain foundational components of cardiovascular risk reduction.

It is important to note that the cardiovascular benefits observed in the REDUCE-IT trial are specific to icosapent ethyl (Vascepa) and should not be generalized to other omega-3 fatty acid preparations, such as omega-3-acid ethyl esters (e.g., Lovaza) or dietary supplements containing a mixture of EPA and docosahexaenoic acid (DHA). Unlike icosapent ethyl (Vascepa), DHA-containing products may increase low-density lipoprotein cholesterol (LDL-C) levels, and no cardiovascular outcome benefits have been demonstrated for these products.

The ACC/AHA guidelines should be reviewed for the most current recommendations. Please refer to the ACC website at <https://www.acc.org/guidelines> for more information.

## Definitions

“ASCVD” refers to atherosclerotic cardiovascular disease.

“Cardiovascular Disease (CVD)” refers to conditions affecting the heart and blood vessels, often associated with atherosclerotic plaque buildup.

“Cholesterol” is a type of fat molecule that is essential for building cell membranes and producing hormones, but high levels of cholesterol in the blood can increase the risk of cardiovascular disease.

“Documentation” refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or

- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"High-intensity statin" is a statin with LDL-lowering capacity of 50% or greater.

"High-sensitivity C-reactive protein (Hs-CRP)" refers to a blood test that measures C-reactive protein, which is a marker of inflammation. It is commonly used to assess one's cardiovascular risk.

"Hypertriglyceridemia" is a medical condition characterized by elevated triglyceride levels.

"Low-density lipoprotein cholesterol (LDL-C)" is a type of cholesterol that is often referred to as "bad" cholesterol because high levels of LDL-C can increase the risk of cardiovascular disease. Statins and other medications are often used to lower LDL-C levels.

"Lipids" are diverse types of fats found in the body. They are crucial for the body's synthesis of hormones, vitamin D, and substances that aid digestion.

"Omega-3 Polyunsaturated Fatty Acids (PUFAs)" are a type of fat beneficial for heart health, found in certain types of fish, algae, and supplements.

"[s]" indicates state mandates may apply.

"Statin" refers to medications that lower cholesterol levels in the blood, which are often prescribed to prevent cardiovascular disease.

"Triglycerides" are a specific type of lipid present in the body.

## Clinical Indications

### Medical Necessity Criteria for Initial Clinical Review

#### Initial Indication-Specific Criteria

#### For the treatment of severe hypertriglyceridemia

The Plan considers ~~icosapent ethyl (Vascepa)~~ medically necessary when ALL of the following criteria are met for the applicable indication listed below:

1. The member is 18 years of age or older; *AND*
2. The member has documented diagnosis of severe hypertriglyceridemia with a pre-treatment (baseline) triglyceride level of  $\geq 500$  mg/dL; *AND*
3. The member is unable to use, or has adequately tried and failed maximally tolerated statin OR fibrate therapy;<sup>[s]</sup> *AND*

4. The member is unable to use, or has adequately tried and failed Omega-3-acid ethyl esters (Lovaza) 4 g/day for a minimum of 3 months;<sup>§</sup> *AND*
5. The provider submits documentation or attestation that the member will continue a lipid-lowering diet and exercise regimen; *AND*
6. Chart documentation and pre-treatment (baseline) laboratory test results are provided for review to substantiate the above requirements.

For cardiovascular risk reduction in established cardiovascular disease or high risk for cardiovascular disease

The Plan considers icosapent ethyl (Vascepa) medically necessary when ALL of the following criteria are met for the applicable indication listed below:

1. The member is 18 years of age or older; *AND*
2. The member has documented pre-treatment (baseline) triglyceride level of  $\geq 150$  mg/dL; *AND*
3. The member is unable to use, has adequately tried and failed, or is currently on maximally tolerated statin therapy;<sup>§</sup> *AND*
4. The member meets ONE (1) of the following:
  - a. Has established cardiovascular disease, defined as ONE (1) of the following:
    - i. Coronary artery disease (i.e.,  $\geq 50\%$  coronary artery stenosis, prior myocardial infarction, or hospitalization for high-risk non-ST-segment elevation acute coronary syndrome); *or*
    - ii. Cerebrovascular or carotid disease (i.e., prior ischemic stroke, angiography or ultrasound showing  $\geq 50\%$  carotid arterial stenosis with symptomatic CAD OR  $\geq 70\%$  carotid arterial stenosis with asymptomatic CAD, or history of carotid revascularization); *or*
    - iii. Peripheral arterial disease (i.e, ankle-brachial index  $< 0.9$  with symptoms of intermittent claudication, or history of catheter-based or surgical aorto-iliac or peripheral arterial intervention); *OR*
  - b. Has diabetes mellitus with TWO (2) or more additional risk factors for cardiovascular disease defined below:
    - i. Men  $\geq 55$  years of age *or* women  $\geq 65$  years of age; *and/or*
    - ii. Cigarette smoker or stopped smoking within the past 3 months; *and/or*
    - iii. Hypertension (blood pressure [BP]  $\geq 140$  mmHg systolic OR  $\geq 90$  mmHg diastolic, *or* taking antihypertensive medication); *and/or*
    - iv. HDL-C  $\leq 40$  mg/dL for men or  $\leq 50$  mg/dL for women; *and/or*
    - v. High-sensitivity C-reactive protein (Hs-CRP) level  $> 3.00$  mg/L (0.3 mg/dL); *and/or*
    - vi. Renal dysfunction: Creatinine clearance (CrCL)  $> 30$  and  $< 60$  mL/min; *and/or*
    - vii. Retinopathy, maculopathy, advanced diabetic eye disease, or history of photocoagulation; *and/or*
    - viii. Microalbuminuria or macroalbuminuria; *and/or*

- ix. Ankle-brachial index <0.9 *without* symptoms of intermittent claudication (members with ankle-brachial index <0.9 *with* intermittent claudication are discussed under (a) above); *AND*
5. Chart documentation and pre-treatment (baseline) laboratory test results are provided for review to substantiate the above requirements.

If the above prior authorization criteria is met, icosapent ethyl (Vascepa) will be approved for up to 12 months.<sup>[5]</sup>

#### *Continued Care*

#### Medical Necessity Criteria for Subsequent Clinical Review

##### Subsequent Medical Necessity Criteria

The Plan considers icosapent ethyl (Vascepa) medically necessary when ALL of the following criteria are met for the applicable indication listed below:

1. The member still meets the applicable Initial Indication-Specific Criteria; *AND*
2. The member has a documented therapeutic response to the requested therapy as shown by recent laboratory test results (dated within the last 3 months) and clinical chart documentation showing ONE (1) of the following:
  - a. Either a reduction in triglyceride (TG) levels since starting the requested medication; *or*
  - b. Achievement and maintenance of their triglyceride (TG) level goal; *AND*
3. The member adheres to the prescribed dosing regimen as evidenced by pharmacy claims records.

If the above prior authorization criteria is met, icosapent ethyl (Vascepa) will be approved for up to 12 months.<sup>[5]</sup>

#### Experimental or Investigational / Not Medically Necessary<sup>[5]</sup>

Icosapent ethyl (Vascepa) for any other indication is considered not medically necessary by the Plan, as this is deemed to be experimental, investigational, unproven, or not medically necessary. Non-covered indications include, but are not limited to, the following:

- Treatment of moderate hypertriglyceridemia (fasting or nonfasting triglyceride concentrations of 175–499 mg/dL), in the absence of established ASCVD. Icosapent ethyl (Vascepa) has been only shown to be effective in those with severe hypertriglyceridemia (triglyceride levels  $\geq$  500 mg/dl) or moderate hypertriglyceridemia in those with established ASCVD or at high risk for ASCVD.
- Use in members under 18 years of age. Icosapent ethyl (Vascepa) has not been studied in a pediatric population.

- Use as monotherapy without attempts at lifestyle modifications or without the presence of underlying risk factors. Icosapent ethyl (Vascepa) was studied in those who were actively receiving statin therapy and as an adjunct to a diet aimed at lowering triglyceride levels.

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#### Clinical Guideline Revision / History Information

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