Icosapent ethyl (Vascepa)

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 (≥ 150 mg/dL) and
    - established cardiovascular disease; or
    - diabetes mellitus and two (2) or more additional risk factors for cardiovascular disease (e.g., men ≥55 years, women ≥65 years, cigarette smoker or stopped in the last 3 months, hypertension or on antihypertensives, HDL-C ≤40 for men and HDL-C ≤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 (≥ 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.

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

"High-sensitvity 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.

"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.

Medical Necessity Criteria for Initial Authorization

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

For the treatment of severe hypertriglyceridemia with triglyceride level 500 mg/dL or above:

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 ≥500 mg/dL; *AND*
3. The member is unable to use, or has adequately tried and failed maximally tolerated statin OR fibrate therapy; *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; *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 risk reduction of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in members with elevated triglyceride levels:

1. The member is 18 years of age or older; *AND*
2. The member has documented pre-treatment (baseline) triglyceride level of ≥150 mg/dL; *AND*
3. The member is unable to use, has adequately tried and failed, or is currently on maximally tolerated statin therapy; *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., ≥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 ≥50% carotid arterial stenosis with symptomatic CAD OR ≥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 ≥55 years of age *or* women ≥65 years of age; *and/or*

ii. Cigarette smoker or stopped smoking within the past 3 months; *and/or*

iii. Hypertension (blood pressure [BP] ≥140 mmHg systolic OR ≥90 mmHg diastolic, *or* taking antihypertensive medication); *and/or*

iv. HDL-C ≤40 mg/dL for men or ≤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.

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

Medical Necessity Criteria for Reauthorization

<u>Reauthorization for up to 12 months will be granted if ALL of the following criteria are met:</u>

1. The member still meets the applicable initial 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.

Experimental or Investigational / Not Medically Necessary

Icosapent ethyl (Vascepa) for any other indication is considered not medically necessary by the Plan, as this is deemed to be experimental, investigational, or unproven. 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
- 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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