Oscar Clinical Guideline: Vascepa (icosapent ethyl) (PG125, Ver. 2)

Vascepa (icosapent ethyl)

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.

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 2 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.

Omega-3 PUFAs, including Icosapent ethyl, are derived from cold-water fish and algae, and are also present in dietary supplements. The REDUCE-IT study provided evidence of a significant 25% reduction in major adverse cardiovascular events in patients taking Icosapent ethyl compared to placebo. Nonetheless, the use of the drug is associated with increased risks of serious bleeding and

hospitalizations for atrial fibrillation or flutter. Other less serious but commonly reported side effects include musculoskeletal pain, peripheral edema, gout, and constipation.

Hypertriglyceridemia is a condition marked by elevated levels of plasma triglycerides, which contribute to an increased cardiovascular risk. Severe hypertriglyceridemia, defined by a fasting triglyceride (TG) level of ≥500 mg/dL, further increases the risk of pancreatitis. Standard treatment options for severe hypertriglyceridemia include fibrates, niacin, and fish oils. Fibrates can reduce triglyceride levels by 30-50%, while omega-3 PUFAs can decrease fasting triglyceride concentrations by 20-50%.

Icosapent ethyl, known for primarily reducing serum triglyceride concentrations without raising LDL-C levels, is recommended at a dosage of 2 grams twice daily with food. However, it is still unclear if Icosapent ethyl can more effectively reduce the risk of coronary artery disease or pancreatitis than omega-3-acid ethyl esters (Lovaza) or omega-3 PUFAs from other sources, including fish.

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

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

"**Hypertriglyceridemia**" is a medical condition characterized by elevated triglyceride 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 **Vascepa (icosapent ethyl)** 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 patient 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 patients 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, or has adequately tried and failed maximally tolerated statin therapy**; *AND***
4. The member meets **ONE** of the following*:*
    a. Has established cardiovascular disease, defined as **ONE** of the following:
        i. Coronary artery disease (with ≥50% coronary artery stenosis, prior myocardial infarction, hospitalization for high-risk non-ST-segment elevation acute coronary syndrome, or prior ischemic stroke); ***or***
        ii. Cerebrovascular or carotid disease (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 (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 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 (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 (hsCRP) 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 (patients 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, Vascepa (icosapent ethyl) will be approved for 12 months.

Medical Necessity Criteria for Reauthorization:

Reauthorization for 12 months will be granted if **ALL** of the following criteria are met:

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 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

Vascepa (icosapent ethyl) 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)
- Use in patients under 18 years of age.
- Use as monotherapy without attempts at lifestyle modifications or without the presence of underlying risk factors.

References

1. "American College of Endocrinology Guidelines for the Management of Dyslipidemia and Prevention of Cardiovascular Disease." Endocrine Practice, vol. 23, no. Supplement 2, 2017, pp. S97-S115.
2. American Diabetes Association. "Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes - 2020." Diabetes Care, vol. 43, no. Supplement 1, 2020, pp. S111-S134.
3. AstraZeneca. "Update on Phase III STRENGTH Trial for Epanova in Mixed Dyslipidaemia." 30 Jan. 2020, http://bit.ly/2TPWtI5.
4. Ballantyne, C.M., et al. "Efficacy and Safety of Eicosapentaenoic Acid Ethyl Ester (AMR101) Therapy in Statin-Treated Patients with Persistent High Triglycerides (from the ANCHOR Study)." Am J Cardiol, vol. 110, 2012, p. 984.
5. Bays, H.E., et al. "Eicosapentaenoic Acid Ethyl Ester (AMR101) Therapy in Patients with Very High Triglyceride Levels (from the Multi-Center, Placebo-Controlled, Randomized, Double-Blind, 12-Week Study with an Open-Label Extension [MARINE] Trial)." Am J Cardiol, vol. 108, 2011, p. 682.
6. Bhatt, D.L., et al. "Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia." N Engl J Med, vol. 380, 2019, pp. 11-22.
7. Bhatt, D.L., et al. "Effects of Icosapent Ethyl on Total Ischemic Events: From REDUCE-IT." Journal of the American College of Cardiology, 22 Mar. 2019.
8. Jacobson, T.A., et al. "Effects of Eicosapentaenoic Acid and Docosahexaenoic Acid on Low-Density Lipoprotein Cholesterol and Other Lipids: A Review." J Clin Lipidol, vol. 6, 2012, p. 5.
9. Lovaza (Omega-3-Acid Ethyl Esters) [Prescribing Information]. Woodward Pharma Services LLC, 2021.

10. Mason, Preston R. "New Insights into Mechanisms of Action for Omega-3 Fatty Acids in Atherothrombotic Cardiovascular Disease." Curr Atheroscler Rep, vol. 21, no. 2, 2019, doi: 10.1007/s11883-019-0762-1.
11. Vascepa (Omega-3-Acid Ethyl Esters) [Prescribing Information]. Amarin Pharma Inc, 2019.
12. Yokoyama, M., et al. "Effects of Eicosapentaenoic Acid on Major Coronary Events in Hypercholesterolaemic Patients (JELIS): A Randomised Open-Label, Blinded Endpoint Analysis." Lancet, vol. 369, 2007, p. 1090.

Clinical Guideline Revision / History Information

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