Omega-3 Fatty Acids

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Medical Necessity Criteria

Icosapent ethyl (Vascepa) is considered medically necessary when ALL of the following criteria are met:

- Age 18 years and older
- When used for ONE of the following indications:
  - **Hypertriglyceridemia** when ALL of the following criteria are met:
    - Triglycerides greater than or equal to 150 mg/dL
    - Documented failure / inadequate response, contraindication per FDA label, intolerance, or not a candidate for Omega-3-acid ethyl esters (generic Lovaza)
    - Documented failure / inadequate response, contraindication per FDA label, intolerance, or not a candidate for ONE of the following:
      - Fibrate (fenofibrate, fenofibrlic acid, gemfibrozil)
      - Niacin (immediate or extended-release)
      - Statin (for example, atorvastatin, rosuvastatin)
  - **Cardiovascular Event Risk Reduction** when ALL of the following criteria are met:
    - Triglycerides greater than or equal to 150 mg/dL
    - Use is adjunctive to maximally tolerated statin therapy unless contraindicated per FDA label or intolerant
    - EITHER of the following:
- Established cardiovascular disease (coronary artery disease, cerebrovascular disease, peripheral artery disease)
- Diabetes mellitus and 2 or more additional risk factors for cardiovascular disease [for example: age greater than or equal to 50 years of age; low high-density lipoprotein cholesterol (HDL-C) levels (for example, less than or equal to 40 mg/dL); renal dysfunction (creatinine clearance less than 60 mL/min); family history of premature coronary disease; presence of albuminuria; smoker (or recently quit); familial hypercholesterolemia; and increased weight (body mass index greater than 25 kg/m²)]

Initial and reauthorization is up to 12 months.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Icosapent ethyl (Vascepa) is considered experimental, investigational or unproven for ANY other use.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

*If you’re a Cigna provider, please log in to the Cigna for Health Care Professionals website and search for specific patients to view their covered medications.

**FDA Approved Indications**

**FDA Approved Indication**
Vascepa® (icosapent ethyl) is indicated:
- 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.

**Limitations of Use:**
The effect of Vascepa® on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

**Recommended Dosing**

**FDA Recommended Dosing**
The daily dose of Vascepa is 4 grams per day taken as either:
- four 0.5-gram capsules twice daily with food; or as
- two 1-gram capsules twice daily with food

Patients should be advised to swallow Vascepa capsules whole. Do not break open, crush, dissolve, or chew Vascepa.

**Drug Availability**
Vascepa capsules are supplied in the following dosage form strengths:
- 0.5 gram
- 1 gram
**Background**

**Professional Societies/Organizations**

**American Association of Clinical Endocrinologist/American College of Endocrinology (AACE/ACE)**

The AACE/ACE 2017 update of the guideline for the management of dyslipidemia and prevention of atherosclerosis update reports that omega-3 fatty acids lead to reduced TGs (-27% to -45%), total cholesterol (-7% to -10%), VLDL-C (-20% to -42%), apo B (-4%) and non-HDL-C (-8% to -14%) in individuals with severe hypertriglyceridemia. Also, that Vascepa decreases LDL-C levels by -5% whereas Lovaza can lead to increases in LDL-C levels. (Jellinger, 2018)

**Endocrine Society (EDS)**

The 2012 EDS clinical practice guideline regarding the evaluation and treatment of hypertriglyceridemia defines normal TG levels as < 150 mg/dL. Other classifications (with TG ranges), are as follows: mild hypertriglyceridemia (TGs between 150 to 199 mg/dL), moderate hypertriglyceridemia (TGs between 200 to 999 mg/dL) severe hypertriglyceridemia (TGs between 1,000 to 1,999 mg/dL), and very severe hypertriglyceridemia (TGs ≥ 2,000 mg/dL). For mild to moderate hypertriglyceridemia, lifestyle therapy, including dietary counseling, physical activity, and a program to achieve weight reduction for those who are overweight or obese, is recommended. For severe and very severe hypertriglyceridemia (TGs ≥ 1,000 mg/dL) a reduction of dietary fat and simple carbohydrate intake should be combined with medication therapy to reduce the risk of pancreatitis. A fibrate should be used first-line for the reduction of TGs in patients at risk for TG-induced pancreatitis. Fibrates, niacin, and omega-3 fatty acids should be used alone or in combination with a statin as treatment options for patients with moderate to severe TG levels. Statins should not be used as monotherapy for the treatment of severe or very severe hypertriglyceridemia. Statins may be utilized for the treatment of moderate hypertriglyceridemia when needed to modify CV risk. (Berglund, 2012)

**National Lipid Association (NLA)**

The 2015 NLA published recommendations for patient-centered management of dyslipidemia. The guidelines focus on categorizing patients at very high and high risk. Regarding LDL-C, patients at low, moderate, or high risk are recommended to obtain an LDL-C level < 100 mg/dL. Patients at very high risk are recommended to achieve an LDL-C level < 70 mg/dL. Patients with atherosclerotic cardiovascular disease (ASCVD) are included among the patients defined as being very high risk. Unless contraindicated, first-line drug therapy for the treatment of disorders involving dyslipidemia includes a moderate- or high-intensity statin. High-intensity statin therapy includes atorvastatin (40 to 80 mg daily) or rosvastatin (20 to 40 mg daily), which leads to an LDL-C reduction of ≥ 50%. Moderate-intensity statin therapy (atorvastatin 10 to 20 mg, fluvastatin 40 mg twice-daily, fluvastatin extended-release 80 mg, lovastatin 40 mg, Livalo 2 to 4 mg, pravastatin 40 to 80 mg, rosuvastatin 5 to 10 mg, and simvastatin 20 to 40 mg) will generally lower LDL-C by -30% to < -50%. The guidelines state that the most commonly used medications for elevated TGs include fibric acids, nicotinic acids, and high-dose long-chain omega-3 fatty acids. Also, it is mentioned that omega-3 fatty acids containing DHA may increase LDL-C levels. It is cited that omega-3 fatty acid medications can decrease TG levels by -19 to -44%. LDL-C levels may decrease (up to -6%) or increase (up to 25%) with omega-3 fatty acid products. (Jacobson, 2015)

**Off Label Uses**

AHFS Drug Information 2019 Edition supports no off-label uses of Vascepa.

**Comparative Studies**

There are no clinical studies comparing Vascepa with other therapeutic alternatives. While no head-to-head studies have been conducted with Vascepa (icosapent ethyl) and Lovaza (omega-3-acid ethyl ester), placebo-controlled demonstrated similar triglyceride lowering effects (-20% to 50%) in those with severe and moderate-to-severe hypertriglyceridemia. However, unlike Lovaza, Vascepa did not increase low-density cholesterol (LDL-C) levels. (Bays, 2011; Lovaza PI, 2019; Vascepa PI, 2017)
Generics
The FDA's generic drug approval process does not require the drug sponsor to repeat costly animal and clinical research on ingredients or dosage forms already approved for safety and effectiveness. Generic drugs must establish the following for approval:
• contain the same active ingredients as the innovator drug (inactive ingredients may vary)
• be identical in strength, dosage form, and route of administration
• have the same use indications
• be bioequivalent
• meet the same batch requirements for identity, strength, purity, and quality
• be manufactured under the same strict standards of FDA's good manufacturing practice regulations required for innovator products

A generic drug is the same as a brand-name drug in dosage, safety, strength, quality, the way it works, the way it is taken and the way it should be used. FDA requires generic drugs have the same high quality, strength, purity and stability as brand-name drugs. Not every brand-name drug has a generic drug. When new drugs are first made they have drug patents. Most drug patents are protected for 20 years. The patent, which protects the company that made the drug first, doesn't allow anyone else to make and sell the drug. When the patent expires, other drug companies can start selling a generic version of the drug. But, first, they must test the drug and the FDA must approve it.

References
1. AHFS Drug Information 2019

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