Drug Coverage Policy

Effective Date.....8/1/2024
Coverage Policy Number.....IP0051
Policy Title.....Omega-3 Fatty Acid Products

Hyperlipidemia – Omega-3 Fatty Acid Products

- Vascepa® (icosapent ethyl capsules – Amarin, generic)

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, Certificate 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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

OVERVIEW
Vascepa, an ethyl ester of EPA, is indicated for **hypertriglyceridemia** (severe, triglyceride [TG] levels ≥ 500 mg/dL), to reduce TG levels as an adjunct to diet in adults.[1,2]

Vascepa is also indicated to **reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina** requiring hospitalization in adults with elevated TG levels (≥ 150 mg/dL) and either established cardiovascular (CV) disease or diabetes mellitus with two or more additional risk factors for CV disease, as an adjunct to maximally tolerated statin therapy.[2,3]

Vascepa has been studied in patients with TG levels ≥ 200 mg/dL and < 500 mg/dL and who have persistently high TGs despite treatment with statin therapy and proper dietary modifications.[4,5] In short-term trials lasting 6 to 12 weeks in duration, the addition of omega-3 fatty acid therapy led to further reductions in TG levels.

Guidelines/Scientific Statements
Several guidelines are available that discuss the management of elevated TG levels and have incorporated omega-3 fatty acid products.[6-11] Highlights from a few guidelines are below.

- The American College of Cardiology Expert Consensus Decision Pathway on the Management of Atherosclerotic Cardiovascular Disease (ASCVD) Risk Reduction in Patients with Persistent Hypertriglyceridemia (2021) recommends Vascepa in a variety of clinical scenarios in patients with persistent fasting hypertriglyceridemia (150 to 499 mg/dL).[6] Also, Vascepa is recommended in several circumstances in which patients have very elevated TG levels (≥ 500 mg/dL).
- The American Diabetes Association Standards of Care (2024) state that Vascepa should be considered to reduce CV risk for patients with ASCVD or other CV risk factors who are on a statin with controlled low-density lipoprotein cholesterol levels but with elevated TG levels (135 to 499 mg/dL).[10]
- The National Lipid Association (NLA) published a scientific statement regarding Vascepa (2019).[11] Based on the REDUCE-IT trial, the NLA position is that for patients ≥ 45 years of age with clinical ASCVD, or ≥ 50 years of age with diabetes mellitus requiring medication plus at least one additional risk factor, with fasting TG levels of 135 to 499 mg/dL on high-intensity or maximally tolerated statin therapy (with or without ezetimibe), treatment with Vascepa is recommended for ASCVD risk reduction (Class I evidence rating).

Medical Necessity Criteria

Icosapent ethyl capsules (Vascepa, generics) are considered medically necessary when ONE of the following is met (1, 2, or 3):

FDA-Approved Indication

1. **Cardiovascular Risk Reduction in a Patient with Elevated Triglycerides.** Approve for 1 year if the patient meets all of the following (A, B, C, and D):
   A) Patient meets one of the following (i or ii):
      i. Patient has established cardiovascular disease; OR
      Note: Examples of cardiovascular disease include a previous myocardial infarction; a history of an acute coronary syndrome event; angina (stable or unstable); past history of stroke or transient ischemic attack; peripheral arterial disease; or the patient has undergone a coronary or other arterial revascularization procedure in the past (e.g., coronary artery bypass graft, percutaneous coronary intervention, angioplasty, coronary stent procedure); OR
      ii. Patient meets both of the following (a and b):
         a) Patient has diabetes; AND
         b) According to the prescriber, patient has at least two additional risk factors for cardiovascular disease.

Note: Examples of risk factors for cardiovascular disease include hypertension; low high-density lipoprotein cholesterol levels (e.g., ≤ 40 mg/dL); renal dysfunction (creatinine clearance < 60 mL/min); family history of premature coronary disease; presence of albuminuria; current cigarette smoking; familial hypercholesterolemia; and increased weight (body mass index greater than 25 kg/m^2); AND

B) Prior to initiation of therapy, the patient had a fasting baseline triglyceride level ≥ 150 mg/dL; AND

C) Patient meets one of the following (i or ii):
- **i.** Patient is receiving statin therapy; OR
- **ii.** According to the prescriber the patient cannot tolerate statin therapy.

D) Preferred product criteria is met for the product(s) as listed in the below table [Individual and Family Plans only]:

2. **Hypertriglyceridemia with Triglyceride Levels ≥ 500 mg/dL.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Prior to initiation of therapy, the patient had a fasting baseline triglyceride level ≥ 500 mg/dL; AND
   - **B)** Patient has tried, or is currently receiving, one of the following products: niacin (immediate-release or extended-release), a fibrate, or a statin.
     Note: Examples of fibrates include gemfibrozil, fenofibrate, and fenofibric acid. Examples of statins include atorvastatin, rosuvastatin, simvastatin, pravastatin, lovastatin, fluvastatin, and Livalo (pitavastatin tablets). Also, a patient who requests Vascepa may potentially be reviewed under the criteria for Cardiovascular Risk Reduction in a Patient with Elevated Triglycerides.
   - **C)** Preferred product criteria is met for the product(s) as listed in the below table [Individual and Family Plans only]:

Other Uses with Supportive Evidence

3. **Hypertriglyceridemia with Triglyceride Levels of 150 mg/dL to < 500 mg/dL.** Approve for 1 year if the patient meets the following (A, B, and C):
   - **A)** Prior to initiation of therapy, the patient had a fasting baseline triglyceride level of 150 mg/dL to < 500 mg/dL; AND
   - **B)** Patient has tried, or is currently receiving, one of the following products: niacin (immediate-release or extended-release), a fibrate, or a statin.
     Note: Examples of fibrates include gemfibrozil, fenofibrate, and fenofibric acid. Examples of statins include atorvastatin, rosuvastatin, simvastatin, pravastatin, lovastatin, fluvastatin, and Livalo (pitavastatin tablets). Also, a patient who requests Vascepa may potentially be reviewed under the criteria for Cardiovascular Risk Reduction in Patients with Elevated Triglycerides.
   - **C)** Preferred product criteria is met for the product(s) as listed in the below table [Individual and Family Plans only]:

Individual and Family Plans:

Product	Criteria
Vascepa (icosapent ethyl capsules)	The patient has tried the bioequivalent generic product, **icosapent ethyl capsules,** AND cannot take due to a formulation difference in the inactive ingredient(s) [for example, difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction. [may require prior authorization]

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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Lovaza® capsules [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; September 2020.
2. Vascepa® capsules [prescribing information]. Bridgewater, NJ: Amarin; September 2021.
3. Bhatt DL, Steg G, Miller M, et al, for the REDUCE-IT Investigators. Cardiovascular risk reduction with isosapent ethyl for hypertriglyceridemia. *N Engl J Med*. 2019;380(1):11-22.
4. Ballantyne CM, Bays HE, Kastelein JJ, et al. Efficacy and safety of eicosapentaenoic acid ethyl ester (AMR 101) therapy in statin-treated patients with persistent high triglycerides (from the ANCHOR) study. *Am J Cardiol*. 2012;110(7):984-992.
5. Davidson MH, Stein EA, Bays HE, et al, for the COMBination of prescription Omega-3 with Simvastatin (COMBOS) investigators. Efficacy and tolerability of adding prescription omega-3 fatty acids 4 g/d to simvastatin 40 mg/d in hypertriglyceridemic patients: an 8-week, randomized, double-blind, placebo-controlled study. *Clin Ther*. 2007;29(7):1354-1367.
6. Virani SS, Morris PB, Kris-Etherton PM. 2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD risk reduction in patients with persistent hypertriglyceridemia. *J Am Coll Cardiol*. 2021;78(9):960-993. Accessed on January 24, 2023.
7. Handelsman Y, Jellinger PS, Guerin CK, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the management of dyslipidemia and prevention of cardiovascular disease algorithm – 2020 executive summary. *Endocrine Pract*. 2020;26(10):1196-1224.
8. Newman CB, Blaha NJ, Boord JB, et al. Lipid management in patients with endocrine disorders: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2020;105(12):3613-3682.
9. Grundy SM, Stone NJ, Bailey AL, et al. ACC/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-e1143.
10. American Diabetes Association. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes – 2024. *Diabetes Care*. 2024;47(Suppl 1):S179-S218.
11. Orringer CE, Jacobson TA, Maki KC. National Lipid Association Scientific Statement on the use of icosapent ethyl in statin-treated patients with elevated triglycerides and high or very-high ASCVD risk. *J Clin Lipidol*. 2019;13(6):860-872.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** policy title to Hyperlipidemia – Omega-3 Fatty Acid Products; previously was Omega-3 Fatty Acid Products **Cardiovascular Risk Reduction in a Patient with Elevated Triglycerides:** Added examples of cardiovascular disease to a Note for those with established cardiovascular disease; Added examples of risk factors for cardiovascular disease to a Note for those with diabetes. **Hypertriglyceridemia with Triglyceride Levels ≥ 500 mg/dL and Hypertriglyceridemia with Triglyceride Levels of 150 mg/dL to < 500 mg/dL.** Updated the previous indication of Hypertriglyceridemia with Triglyceride (TG) Levels greater than or equal to 150 mg/dL to clearly differentiate between the FDA-Approved Indication versus the Other Uses with Supportive Evidence indication for Vascepa; Added examples of fibrates and statin products.	8/1/2024

The policy effective date is in force until updated or retired.