Effective Date: 04/2024
Last Approval/Version:04/2024
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Policy Number: C25231-A

Omega-3 Fatty Acids - IL Medicaid Only

PRODUCTS AFFECTED

Lovaza (omega-3-acid ethyl esters), Omega-3-acid Ethyl Esters (generic) capsules, Omega-3-acid Ethyl Esters Cap 1 GM, Vascepa (icosapent ethyl) capsule, icosapent ethyl (generic) capsules

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hypertriglyceridemia and cardiovascular (CV) risk reduction

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. HYPERTRIGLYCERIDEMIA:
1. Documentation of severe elevated triglyceride (TG) levels (≥500 mg/dL)

AND

2. Prescriber attests low-density lipoprotein cholesterol (LDL-C) levels have been evaluated and are being treated appropriately
   AND
3. Documentation member has experienced a failure of or an intolerance (i.e., sensitivity, drug allergy, or adverse effect) to treatment with at least two formulary statins (e.g., simvastatin, lovastatin)
   AND
4. Prescriber attests that appropriate lifestyle modifications have been implemented, including an appropriate diet, exercise, and weight loss in obese members

B. CARDIOVASCULAR RISK REDUCTION:

1. Documentation of baseline elevated triglyceride (TG) levels (≥150 mg/dL)
   AND
2. Clinical documentation of a therapeutic failure on, intolerance to, or contraindication to high-intensity statin therapy met by ONE (1) of the following:
   (a) Adherent* on a maximally tolerated high-intensity statin therapy (daily dose of atorvastatin 40-80 mg or rosuvastatin 20 to 40mg) AND inability to achieve and maintain a triglyceride level <150mg/dL, with a combination of medications, diet, and exercise
   *NOTE: Adherence is defined as at least 85% of the time as confirmed by claims history for at least 180 days OR attestation from the prescriber.
   OR
   (b) Member has ANY of the following contraindication(s) to statin therapy [ONE]: (i)Hypersensitivity to statins or any component of the product, active liver disease (confirmed with labs) or CK levels (defined as >10 times the upper limit of normal [ULN]), unexplained persistent elevation of hepatic transaminases [greater than 3 times the upper limit of normal (ULN) occurring on 2 or more occasions], women who are pregnant or may become pregnant or breastfeeding
   AND
3. Prescriber attests that appropriate lifestyle modifications have been implemented, including an appropriate diet, exercise, and weight loss in obese members
   AND
4. Documentation of ONE of the following: (a) OR (b)
   (a) Member is≥45 years AND
   (i) Documented CAD (at least one of the following primary criteria must be satisfied): Documented multivessel CAD (≥50% stenosis in ≥2 major epicardial coronary arteries, with or without antecedent revascularization) OR documented prior myocardial infarction (MI) OR
   Hospitalization for high-risk NSTE-ACS (with objective evidence of ischemia: ST-segment deviation or biomarker positivity)
   OR
   (ii) Documented cerebrovascular or carotid disease (at least one of the following primary criteria must be satisfied): Documented prior ischemic stroke OR Symptomatic carotid artery disease with ≥50% carotid arterial stenosis OR asymptomatic carotid artery disease with ≥70% carotid arterial stenosis per angiography orduplex ultrasound OR history of carotid revascularization (catheter-based orsurgical)
   OR
   (iii) Documented PAD (at least one of the following primary criteria must be satisfied): ABI <0.9 with symptoms of intermittent claudication OR history of aortoiliac orperipheral arterial intervention (catheter-based or surgical)
   OR
   (b) Diabetes mellitus (type 1 or type 2) requiring treatment with medication AND one of the following at Visit 1 (additional risk factor for cardiovascular disease [CVD]):
   (i) Men ≥55 years of age and women ≥65 years of age
   OR
   (ii) Cigarette smoker or stopped smoking within 3 months

OR
(iii) Hypertension (BP ≥140 mm Hg systolic OR ≥90 mm Hg diastolic) or on antihypertensive medication
OR
(iv) HDL-C ≤40 mg/dL for men or ≤50 mg/dL for women
OR
(v) hsCRP >3.00 mg/L (0.3 mg/dL)
OR
(vi) Renal dysfunction: CrCl >30 and <60 mL/min
OR
(vii) Retinopathy, defined as any of the following: non-proliferative retinopathy, pre-proliferative retinopathy, proliferative retinopathy, maculopathy, advanced diabetic eye disease, or a history of photocoagulation
OR
(viii) Micro- or macroalbuminuria

CONTINUATION OF THERAPY:
A. ALL INDICATIONS:
1. Documentation that member's condition has nor progressed or worsened on therapy
   AND
2. Adherence to therapy at least 85% of the time as confirmed by claims history OR attestation from the prescriber
   AND
3. Triglyceride level is within the normal limits or has dropped at least by 50%

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
None

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Max of 4 grams per day

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Antihyperlipidemic

FDA-APPROVED USES:
VASCEPA 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

LOVAZA is indicated:
- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Limitations of Use: The effect of LOVAZA on the risk for pancreatitis has not been determined. The effect of LOVAZA on cardiovascular mortality and morbidity has not been determined

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Lovaza (omega-3-acid ethyl esters) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet before receiving Lovaza and should continue this diet during treatment with Lovaza. Laboratory studies should be done to ascertain that the lipid levels are consistently abnormal before instituting Lovaza therapy. Every attempt should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed if possible, prior to consideration of TG-lowering drug therapy.

Vascepa (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adultpatients with severe (≥500 mg/dL) hypertriglyceridemia. Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving Vascepa and should continue this diet and exercise regimen with Vascepa. Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.

In REDUCE-IT, a randomized trial designed to evaluate the effect of fish oil therapy on CVD outcomes in patients with hypertriglyceridemia, a highly purified fish oil (icosapent ethyl) was effective.In this trial, over 8000patients with elevated triglyceride levels (fasting 135 to 499 mg/Dl [1.52 to 5.63 mmol/L]), on statin, and with either established CVD or diabetes plus other cardiovascular risk factors were randomly assigned to supplementation with icosapent ethyl 4 g daily or mineral oil. Icosapent ethyl reduced the risk of the primary combined CVD endpoint of cardiovascular death, nonfatal MI, nonfatal stroke, coronary revascularization, or unstable angina (17.2 versus 22.0 percent, hazard ratio0.75, 95% CI 0.68-0.83) after median follow-up of 4.9 years. From baseline to one year, the median triglyceride level decreased 18 percent in the treatment group and increased 2.2 percent in the control group, and LDL-C levels increased in both groups (treatment group 3.1 percent, control group 10.2 percent). At two years, C-reactive protein levels decreased by 13.9 percent in the treatment group and increased by 32.2 percent in the control group. A subsequently published prespecified analysis showed that the reduction occurred for both first and

subsequent (i.e., total) ischemic events.

Limitations of the REDUCE-IT trial include concerns that mineral oil may have caused the increases in atherogenic lipoproteins and C-reactive proteins in the control group and thus did not function as a true placebo. These adverse effects of mineral oil may have raised the risk of cardiovascular events in the control group and may partially account for the favorable risk reduction observed in the treatment group. If so, the true cardiovascular effect of icosapent ethyl may be less than observed in the trial. Another concern is that ratesof new- onset atrial fibrillation were significantly higher in the treatment group (5.3 versus 3.9 percent). Further investigations to explain the mechanisms for the reduction in cardiovascular events with icosapent ethyl are warranted, considering that the modest reductions in fasting triglycerides are unlikely to account for the magnitude of benefit. It isalso unknown whether other omega-3 preparations or doses would be similarly effective.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Omega-3 Fatty Acids are considered experimental/investigational and therefore will follow the Molina Healthcare, Inc. off-label policy.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Lovaza capsule 1GM
Omega-3-acid Ethyl Esters capsule 1GM
Vascepa capsule 0.5GM
Vascepa capsule 1GM
Icosapent Ethyl capsule 1GM
Icosapent Ethyl capsule 0.5GM

REFERENCES

1. Illinois Medicaid Preferred Drug List, Effective 01/01/2024.
2. Lovaza (omega-3-acid ethyl esters) [prescribing information]. Wixom, MI: Woodward Pharma Services LLC; February 2021.
3. Vascepa [package insert]. Bedminster, NJ: Arnarin Pharma Inc.; December 2022.
4. Omega-3 fatty acids [prescribing information]. Tempe, AZ: Century HealthCare Inc; July 2018.
5. Virani SS, Morris PB, Agarwala A, et al. 2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients With Persistent Hypertriglyceridemia: A Report of theAmerican College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2021; 78:960.
6. Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med 2019; 380:11.
7. Bhatt DL, Steg PG, Miller M, et al. Effects of Icosapent Ethyl on Total Ischemic Events: From

REDUCE-IT. J Am Coll Cardiol 2019; 73:2791.

SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- Notable revisions: Required Medical Information Continuation of therapy References	04/2024
Established tracking in new format	Q2/2023