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Clinical Guideline

Guideline Number: PG005, Ver. 1

Omega-3 Dyslipidemic Agents

Lovaza (omega-3-acid ethyl esters)
Vascepa (icosapent ethyl)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Oscar may delegate utilization management decisions of certain services to third-party delegates who may develop and adopt their own clinical criteria.

The clinical guidelines are applicable to all commercial plans. Services are subject to the terms, conditions, limitations of a member's plan contracts, state laws, and federal laws. Please reference the member's plan contracts (e.g., Certificate/Evidence of Coverage, Summary/Schedule of Benefits) or contact Oscar at 855-672-2755 to confirm coverage and benefit conditions.

Summary

Omega-3-acid ethyl esters (Lovaza) and icosapent ethyl (Vascepa) are FDA-approved for patients with severe hypertriglyceridemia. Icosapent ethyl is also FDA-approved as adjunct treatment for cardiovascular event prevention. Hypertriglyceridemia occurs when the body has a higher than normal level of triglyceride (a type of lipid). It is usually discovered after performing a routine test for different lipid levels in the body. Causes of high lipid levels (or high cholesterol) include high-fat diet, lack of physical exercise, and medical conditions such as diabetes, hypothyroidism (a condition in which the body does not make enough thyroid hormone), liver disease, and other conditions. People with triglyceride level between 150 mg/dL and 499 mg/dL are considered to have moderate hypertriglyceridemia. Severe hypertriglyceridemia is defined as having a fasting TG level ≥ 500 mg/dL. People with hypertriglyceridemia can have a higher risk of heart attacks, strokes, inflammation in the pancreas, and other health problems.

Hypertriglyceridemia treatment options include lifestyle and dietary changes, and medications such as statins (such as atorvastatin, simvastatin, lovastatin, pravastatin, rosuvastatin, and fluvastatin), fibrates (fenofibrate, fenofibric acid, and gemfibrozil) and fish oil supplements (omega-3-acid ethyl esters and icosapent ethyl).

Fibrate therapy can reduce triglyceride level by as much as 50% or more. Patients may receive a fibrate alone or in combination with a statin. Potential side effects of fibrates and statins may include myalgia (muscle pain), abdominal pain, skin reactions, and abnormal liver test results.

Omega-3-acid ethyl esters (Lovaza) are FDA-indicated as add-on therapy to diet for hypertriglyceridemia.

Icosapent ethyl (Vascepa) has the following FDA indications:

1) As add-on therapy to diet for severe hypertriglyceridemia (greater than or equal to 500 mg/dL)
2) As add-on therapy to statins to reduce the risk of heart attack, stroke and certain types of heart issues requiring hospitalization in adults with elevated triglyceride level (greater than or equal to 150 mg/dL) and
    a) Has established cardiovascular disease or
    b) Diabetes and 2 or more additional risk factors for cardiovascular disease.

Omega-3-ethyl esters contain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Icosapent ethyl contains EPA and has a different lipid-lowering profile from that of omega-3-acid ethyl esters. Omega-3-acid ethyl esters can reduce triglycerides by more than 50%, but may also increase low-density cholesterol (LDL-C) by 30 to 49%. While icosapent ethyl did not significantly change LDL-C in clinical studies (~2% compared to baseline), it has a less effect on triglycerides (~30%) compared to omega-3-ethyl esters. Clinical studies (e.g. REDUCE-IT clinical trial) showed that in patients with either established cardiovascular disease or diabetes plus other cardiovascular risk factors who achieved well-controlled LDL-C on a statin therapy but still had moderately elevated triglycerides (135-499 mg/dL), adding icosapent ethyl can be considered to reduce cardiovascular risk.

Potential side effects of omega-3-acid ethyl esters may include abdominal discomfort, nausea, vomiting, and skin rash. Potential side effects of icosapent ethyl include bleeding, irregular heart rhythm, muscle/joint pain, gout, swelling of the hands, legs, or feet, and constipation. Both medications also have possible allergic reactions in patients who have allergy to fish or shellfish.

Definitions

"Lipids" are several types of fats found in the body. They are essential for the body to make hormones, vitamin D, and substances that help with digestion.

"Triglycerides" are a type of lipid in the body.

"Hypertriglyceridemia" is a condition in which triglyceride levels are elevated.

Medical Necessity Criteria for Initial Authorization

Oscar covers omega-3-acid ethyl esters (Lovaza) when ALL of the following criteria are met for the following indication:

<u>Severe hypertriglyceridemia with triglyceride level 500 mg/dL or above:</u>

1. The patient is 18 years of age or older; *and*
2. Has documented severe hypertriglyceridemia with pre-treatment (baseline) triglyceride level of ≥500 mg/dL; *and*

3. Has a documented trial and failure or intolerance with maximally tolerated statin OR fibrate therapy (including reason for treatment failure); *and*
4. Documentation of nutritionist or provider education about lifestyle modifications (dietary changes and exercise), and documentation that the patient has been on and will continue an appropriate lipid-lowering diet and exercise regimen.

Oscar covers icosapent ethyl (Vascepa) when ALL of the following criteria are met for the following indications:

Severe hypertriglyceridemia with triglyceride level 500 mg/dL or above:

1. The patient is 18 years of age or older; *and*
2. Has documented severe hypertriglyceridemia with pre-treatment (baseline) triglyceride level of ≥500 mg/dL; *and*
3. Has a documented trial and failure or intolerance with maximally tolerated statin OR fibrate therapy (including reason for treatment failure); *and*
4. Has a documented trial and failure or intolerance with Lovaza 4 g/day for a minimum of 3 months (including reason for treatment failure); *and*
5. Documentation that the patient has been on and will continue an appropriate lipid-lowering diet and exercise regimen.

Risk reduction of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in patients with elevated triglyceride level:

1. The patient is 18 years of age or older; *and*
2. Has documented pre-treatment (baseline) triglyceride level of ≥150 mg/dL; *and*
3. Has a documented trial and failure or intolerance with maximally tolerated statin therapy (including reason for treatment failure); *and*
4. The patient meets *(a) or (b) below:*
    a. Documentation that the patient 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 or catheter-based or surgical aorto-iliac or peripheral arterial intervention).
    b. Documentation that the patient 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;
ii. Cigarette smoker or stopped smoking within the past 3 months;
iii. Hypertension (BP ≥140 mmHg systolic OR ≥90 mmHg diastolic, *or* taking antihypertensive medication);
iv. HDL-C ≤40 mg/dL for men or ≤50 mg/dL for women
v. High-sensitivity C-reactive protein (hsCRP) level >3.00 mg/L (0.3 mg/dL);
vi. Renal dysfunction: Creatinine clearance (CrCL) >30 and <60 mL/min;
vii. Retinopathy, maculopathy, advanced diabetic eye disease, or history of photocoagulation;
viii. Microalbuminuria or macroalbuminuria;
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).

If the above prior authorization criteria is met, the requested medication will be approved for 12 months

Medical Necessity Criteria for Reauthorization:

All prior authorization renewals will be reviewed on a case-by-case basis to determine if continuation of therapy is medically necessary. Prior Authorization may be extended based on the diagnosis, documentation of the response to therapy, updated/current triglyceride levels, and pharmacy claims record.

Table 1: Dosage information

Drug	Indication	Initial dose	Alternate dose	Additional Considerations
Omega-3-ethyl esters (Lovaza)	Hypertriglyceridemia, severe (triglyceride (≥ 500 mg/dL)	4 grams PO divided qd-bid with food		
Icosapent ethyl (Vascepa)	Hypertriglyceridemia, severe (triglyceride (≥ 500 mg/dL)	2 grams PO bid with food	The daily dose of icosapent ethyl is 4 grams/day, taken as either: (a) four 0.5-gram capsules twice daily with food; or (b) as two 1-gram capsules twice daily with food.	

Experimental or Investigational / Not Medically Necessary

Omega-3-acid ethyl esters and icosapent ethyl for any other indication are *not covered* by Oscar as it is considered experimental, investigational, or unproven.

References

1. Lovaza [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 4/2019.
2. Vascepa [package insert]. Bridgewater, NJ: Amarin Pharma, Inc.; 12/2019.
3. Bhatt DL, Steg G, Miller M, et al. Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. N Engl J Med 2019; 380:11-22.
4. American Diabetes Association. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes - 2020. Diabetes Care 2020 Jan; 43(Supplement 1): S111-S134.

Clinical Guideline Revision / History Information

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