Oscar Clinical Guideline: Omega-3-acid ethyl esters (Lovaza) (PG005, Ver. 6)

Omega-3-acid ethyl esters (Lovaza)

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

Omega-3-acid ethyl esters (Lovaza) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (greater than or equal to 500 mg/dL) hypertriglyceridemia. Omega-3-ethyl esters contain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). 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%.

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 levels between 150 mg/dL and 499 mg/dL are considered to have moderate hypertriglyceridemia. Severe hypertriglyceridemia is defined as having a fasting TG level greater than or equal to (≥) 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. Adding Vascepa [icosapent ethyl] can further reduce cardiovascular risk.

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

"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

The Plan considers **omega-3-acid ethyl esters (Lovaza)** medically necessary when **ALL** of the following criteria are met for the following indication:

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 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 (including reason for treatment failure)**; *AND***
4. The requesting provider submits documentation or attestation indicating nutritionist or provider education about lifestyle modifications (dietary changes and exercise) has been performed and that the patient has been on and will continue an appropriate lipid-lowering diet and exercise regimen***; AND***
5. Chart documentation and supporting labwork are provided for review to substantiate the above listed requirements.

If the above prior authorization criteria is met, Lovaza (omega-3-acid ethyl esters) will be approved for 12 months.

Medical Necessity Criteria for Reauthorization:

Reauthorization for 12 months will be granted if the member meets **ALL** of the following criteria:

1. The member still meets the applicable initial criteria; ***AND***
2. The member has a documented therapeutic response to the requested therapy as evidenced by recent lab work (dated within the last 3 months) and clinical chart documentation showing **ONE** of the following:
    a. The member has shown a reduction in triglyceride (TG) levels since starting the requested medication; ***or***
    b. The member has reached and maintained their triglyceride (TG) level goal; ***AND***
3. The member maintains adherence to the prescribed dosing regimen as evidenced by pharmacy claims record.

Experimental or Investigational / Not Medically Necessary

Omega-3-acid ethyl esters (Lovaza) for any other indication are considered not medically necessary by the Plan, as this is deemed to be experimental, investigational, or unproven.

Appendix

Prevention of Cardiovascular Events

The inclusion of omega-3-acid ethyl esters (Lovaza) for the prevention of cardiovascular events is not supported at this time due to several key factors:

1. The effectiveness of marine- and plant-derived omega-3 fatty acids in preventing cardiovascular events remains uncertain. While some studies suggest a potential risk reduction in cardiovascular events and mortality related to coronary heart disease (CHD) with higher omega-3 fatty acid intake, the available evidence lacks consistency and conclusive results. Therefore, it is challenging to establish clear criteria for the use of Lovaza in preventing cardiovascular events.
2. Current guidelines from the American Heart Association/American College of Cardiology (AHA/ACC) prioritize lifestyle modifications, including dietary changes and exercise, as the primary approach for reducing cardiovascular risk. For patients with clinical atherosclerotic cardiovascular disease (ASCVD) or diabetes mellitus, statin therapy is the recommended treatment alongside lifestyle modifications to lower LDL cholesterol, a significant contributor to ASCVD. The guidelines also suggest considering other established therapies such as ezetimibe and PCSK9 inhibitors in specific cases. However, omega-3-acid ethyl esters (Lovaza), specifically, is not recommended by the guidelines for primary or secondary prevention of cardiovascular events.

3. While a cardiovascular outcomes study showed a reduction in ASCVD risk with an omega-3 fatty acid preparation containing EPA in statin-treated patients with hypertriglyceridemia and established ASCVD or high risk of ASCVD, it is crucial to note that this evidence cannot be applied universally to other omega-3 fatty acid preparations that contain a mixture of EPA and DHA. Different types of omega-3 fatty acids may have distinct effects on lipids and lipoproteins, making it challenging to generalize the findings to medications like omega-3-acid ethyl esters (Lovaza).

Review of Clinical Trials:

Clinical trials evaluating omega-3 fatty acids have yielded mixed results. Low-dose mixtures of EPA and DHA did not significantly reduce cardiovascular endpoints in recent trials such as ASCEND, VITAL, and OMEMI. The JELIS trial demonstrated a reduction in major coronary events with EPA, but concerns were raised about its trial design. The REDUCE-IT trial, using high-dose icosapent ethyl (IPE), showed a significant reduction in cardiovascular events. However, the STRENGTH trial with omega-3 carboxylic acids did not demonstrate cardiovascular benefits. Differences in trial design, patient populations, formulations of omega-3 fatty acids, and placebo comparators may contribute to these varying outcomes.

Potential Limitations and Considerations:

- *The use of mineral oil as a placebo in the REDUCE-IT trial has raised questions about its impact on LDL cholesterol and inflammatory markers, potentially influencing the observed cardiovascular benefits.*
- *Additionally, increased incidences of atrial fibrillation have consistently been observed in active treatment groups across recent omega-3 therapy trials.*

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Clinical Guideline Revision / History Information

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