Icosapent Ethyl (Vascepa®) for Reducing CV Risk
Criteria for Use
March 2021

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at the *PBM INTERnet* or *PBM INTRAnet* site for further information.

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive icosapent ethyl.

- ☐ Contraindication: History of hypersensitivity to icosapent ethyl or to any of its components[1]
- ☐ Not on a statin or unable to tolerate statins
- ☐ Severe NYHA Class IV congestive heart failure
- ☐ Severe renal insufficiency (e.g., creatinine clearance <30 mL/min) or on dialysis
- ☐ Severe comorbid non-cardiovascular condition(s) expected to limit life expectancy to ≤2 years
- ☐ Uncontrolled or poorly controlled diabetes (e.g., HGB A1C ≥ 10 %)

NYHA-New York Heart Association

[1]Patients with hypersensitivity to fish and/or shellfish were excluded from the REDUCE-IT trial. Those with known hypersensitivity to fish and/or shellfish should be informed about the potential for allergic reactions and to discontinue icosapent and seek medical attention if any reactions occur.

Inclusion Criteria

The answers to all of the following must be fulfilled in order to meet criteria.

- ☐ ≥ 45 years of age with established cardiovascular disease*
- ☐ Receiving a moderate to high dose statin (or maximally tolerated statin) and LDL is between 41 mg/dL and 100 mg/dL. **Statin doses should be maximized (as tolerated) prior to adding icosapent ethyl.**
- ☐ Fasting triglyceride level of ≥ 150 mg/dL

Secondary causes of hypertriglyceridemia have been considered and managed as appropriate before considering addition of icosapent ethyl (See supplementary information for examples)

Lifestyle and dietary changes have been discussed with the patient (See supplementary information)

*Cardiovascular disease: history of acute coronary syndrome (ACS), myocardial infarction, ischemic stroke and/or symptomatic peripheral arterial disease (PAD)

A statistically higher incidence of hospitalization for atrial fibrillation or flutter and trend towards a higher risk of serious bleeding events was reported in the icosapent ethyl versus placebo-mineral oil group.

Severe Hypertriglyceridemia

Evidence does not support a greater triglyceride lowering response between various fish oil products and icosapent ethyl. Therefore, use of icosapent is restricted to patients meeting criteria for reducing cardiovascular risk.

For patients with severe hypertriglyceridemia ≥ 500 mg/dL, who do not meet CFU for reducing CV risk, refer to the Omega-3-Acid Ethyl Esters (Lovaza and Lovaza generics) CFU.

Supplementary Information

- In the REDUCE-IT trial, high risk patients treated for secondary prevention consisted of approximately 70% of the study population while high risk patients (diabetic patients with at least one CV risk factor) treated for primary prevention consisted of 30% of the population. In a prespecified subgroup analysis between patients with and without CV disease, patients with CV disease had a statistically significant reduction in the primary (HR 0.73, 0.65-0.81) and key secondary endpoint (HR 0.72, 0.63-0.82) vs. placebo. In patients without established CV disease, no statistically significant reduction in the primary (HR 0.88, 0.7-1.10) or key secondary endpoint (HR 0.81, 0.62-1.06) vs. placebo was observed. In testing for statistical differences between subgroups, the p-value for interaction indicated statistical differences in the primary composite outcome between those with and those without CV disease.
- In May 2013, a protocol amendment was made to increase the triglyceride eligibility criterion from ≥ 150 mg/dL with 10% allowance for variability to ≥ 200 mg/dL with no allowance for variability. The manufacturer indicated the change was made to increase enrollment of patients with triglyceride levels of at least 200 mg/dL. The median triglyceride level (interquartile range-IQR) at baseline was 216 mg/dL.
- In the REDUCE-IT trial, a statistically higher incidence of hospitalization for atrial fibrillation or flutter was reported in the icosapent ethyl group versus placebo-mineral oil (3.1% vs. 2.1%, p=0.004, respectively). A nonsignificant trend towards a higher risk of serious bleeding events was also reported with icosapent ethyl vs. placebo (2.7% vs. 2.1%, p=0.06, respectively).
- In the REDUCE-IT trial, patients on other omega-3 fatty acids (OM-3 FA), dietary supplements containing OM-3 FA, niacin or fibrates were excluded unless they had stopped these medications for at least 28 days. In patients who are receiving niacin, fibrates or other OM-3 FA or supplements containing OM-3 FA for reducing elevated triglyceride levels, consider stopping them and rechecking a fasting triglyceride level after 1-3 months to determine if patient is eligible based upon their repeat fasting triglyceride value.
- Secondary causes of hypertriglyceridemia may include (list not all-inclusive): hypothyroidism, uncontrolled diabetes, nephrotic syndrome, alcohol abuse, obesity, metabolic syndrome and medications (e.g., tamoxifen, oral estrogens, systemic corticosteroids, thiazide diuretics, protease inhibitors, non-cardioselective beta-blockers [except carvedilol], clozapine, olanzapine, etc.). Secondary causes should be managed as appropriate [treating hypothyroidism, improving glycemic control, weight loss, limiting alcohol intake, etc.] while considering the balance of risk vs. benefit of continuing medications that may be contributing to triglyceride elevation.
- Lifestyle and dietary changes should be encouraged as part of good clinical care including adoption of a healthy diet, weight loss in obese patients, aerobic exercise, smoking cessation, limiting alcohol intake, etc.
- Moderate (high) dose statins: Simvastatin 20-40 mg, atorvastatin 10-20 (40-80) mg, rosuvastatin 5-10 (20-40) mg, pravastatin 40-80 mg.
- Adherence to treatment with icosapent ethyl 2 grams twice daily, along with statins +/- ezetimibe, should be emphasized with patients. If capsule size is a problem for some patients, icosapent ethyl is available in 500 mg capsules (4 caps twice daily)

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