Antihyperlipidemics - icosapent ethyl (Vascepa)

WA.PHAR.134 Effective Date: 2/1/2024

Related medical policies:

Policy Name	Indications
N/A	N/A

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: https://pharmacy.envolvehealth.com/content/dam/centene/envolve-pharmacy-solutions/pdfs/PDL/FORMULARY-CoordinatedCare_Washington.pdf

Medical necessity

Drug	Medical Necessity
icosapent ethyl (generic) icosapent ethyl (Vascepa)	**Icosapent ethyl** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Cardiovascular risk reduction with hypertriglyceridemia (adjunctive agent) icosapent ethyl (generic) icosapent ethyl (Vascepa)	Icosapent ethyl may be approved when all of the following criteria are met: 1. Patient is 18 of age or older; **AND** 2. Fasting triglyceride levels are greater than 150 mg/dl within the last 3 months; **AND** 3. Low-density lipoproteins cholesterol (LDL-C) is being controlled, demonstrated by one of the following: a. LDL-C is below 100 mg/dL within the last 3 months; **OR** b. Patient has been taking appropriate treatment to lower LDL-C, including a high-intensity statin (atorvastatin 40-

	80 mg daily or rosuvastatin 20-40mg daily), unless contraindicated or not tolerated, for at least 3 months; **AND** 4. Patient has established cardiovascular disease (e.g. coronary artery disease, previous stroke, previous myocardial infarction, or peripheral arterial disease); **OR** 5. Diabetes with at least **TWO** of the following risk factors: a. Age 50 years or older b. Cigarette smoking c. Hypertension (e.g. blood pressure ≥ 140/90mmHg or being treated with antihypertensive medication) d. HDL-C less than 40 mg/dL for males or less than 50 mg/dL for females e. A body mass index (BMI) of 30kg/m^2 or greater f. Creatinine clearance less than 60 mL/min g. High sensitivity C-reactive protein (Hs-CRP) greater than 3mg/L h. Retinopathy i. Micro or macroalbuminuria j. Ankle-brachial index (ABI) below <0.9; **AND** 6. Currently taking a high-intensity statin (atorvastatin 40-80 mg daily or rosuvastatin 20-40mg daily). a. If a high intensity statin cannot be tolerated, the provider attests the patient is taking the highest-tolerated dose. b. If a statin is contraindicated, provide clinical documentation as to why the patient is unable to take a statin; **AND** 7. The total dose is 4 grams per day If ALL criteria are met, the request will be authorized for **12 months.** **Criteria (Reauthorization)** Icosapent ethyl may be approved when all of the following criteria are met: 1. The patient continues to take a statin at the highest-tolerated dose, unless contraindicated or not tolerated; **AND** 2. The total dose is 4 grams per day If ALL criteria are met, the request will be authorized for **12 months.**
Severe hypertriglyceridemia icosapent ethyl (generic) icosapent ethyl (Vascepa)	Icosapent ethyl may be approved when all of the following criteria are met: 1. Patient is 18 of age or older; **AND** 2. Fasting triglyceride levels are greater than or equal to 500 mg/dl within the last 3 months; **AND**

	3. Provider attests icosapent ethyl will be used as an adjunct to diet modifications (e.g. low-fat diet, alcohol avoidance, and reduction in refined carbohydrates); **AND** 4. History of failure, contraindication, or intolerance to ALL (a, b, and c) of the below. Failure is defined as the inability to reduce fasting triglycerides to less than 500 mg/dl after 3 months of treatment. a. A statin at the highest tolerated dose; **AND** b. A fibrate medication (fenofibrate or gemfibrozil) **AND**; c. Omega-3-acid ethyl esters (must be a legend product) **AND;** 5. The total dose is 4 grams per day If ALL criteria are met, the request will be authorized for **12 months.**
	Criteria (Reauthorization) Icosapent ethyl may be approved when all of the following criteria are met: 1. Documentation is submitted demonstrating a decrease in triglyceride levels from baseline (prior to initiation of icosapent ethyl); **AND** 2. The total dose is 4 grams per day If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form
Vascepa	**Reduction in cardiovascular risk** **Severe hypertriglyceridemia**	2 grams twice daily	• 1 gram capsule • 0.5 gram capsule
Icosapent ethyl	**Reduction in cardiovascular risk** **Severe hypertriglyceridemia**	2 grams twice daily	• 1 gram capsules • 0.5 gram capsule

Background:

Hypertriglyceridemia is commonly defined as persistent fasting triglyceride levels greater than 150 mg/dL. While there is limited evidence that elevated triglycerides increase the risk of atherosclerotic cardiovascular disease (ASCVD) in isolation, patients with hypertriglyceridemia generally are at an increased ASCVD risk due to concomitant risk factors.[1] Additionally, severe hypertriglyceridemia (>500 mg/dL) increases the risk of pancreatitis. The 2018 American Heart Association (AHA) Guideline on the Management of Blood Cholesterol prioritizes management of co-occurring conditions (e.g. obesity, diabetes, chronic kidney disease) for moderate hypertriglyceridemia (175 – 499mg/dL). In the presence elevated ASCVD risk, the AHA guidelines also recommend a statin. In the setting of severe hypertriglyceridemia (>500 mg/dL) it is reasonable to initiate omega-3 fatty acids or a fibrate (e.g. fenofibrate or gemfibrozil).[1]

In 2019, after the AHA Guidelines were published, icosapent ethyl was approved by the FDA as an adjunct to a maximally tolerated statins in patients with triglyceride levels 150 mg/dL or greater to prevent cardiovascular events.[2] The REDUCE-IT trial was a phase 3, double-blind, randomized, trial involving over 8,000 participants.[3] All participants were at least 45 years, were treated with a statin, had TG levels between 150 and 500 mg/dL, and had established ASCVD or diabetes plus other ASVCD risk factors. Participants taking 4 grams daily of icosapent ethyl had a significantly reduced risk for the composite cardiovascular endpoint (time to cardiovascular death, myocardial infarction, stroke, coronary revascularization, or hospitalization for unstable angina) compared to placebo (HR 0.75, 95%CI 0.68-0.83). Over the median follow up period of 4.9 years, 17.2% of participants in the icosapent ethyl group met the composite primary outcome compared to 22% in the placebo group (number need to treat = 21).[3] Adverse reaction occurring more frequently than placebo included musculoskeletal pain, constipation, gout, atrial fibrillation, and peripheral edema.[2]

Icosapent ethyl is also approved for severe hypertriglyceridemia as an adjunct to diet.[2] A trial evaluated triglyceride levels of participants taking icosapent ethyl 4 grams daily (n=76) compared to placebo (n=75).[4] Participants had baseline triglyceride levels of 680mg/dL and 703 mg/dL in the treatment and placebo groups, respectively. After 12 weeks, icosapent ethyl reduced triglyceride levels by a median of 27%, while levels in the placebo group increased by 10%.[4] While statistically significant, it is unclear if the observed decrease in triglyceride levels result in improved outcomes, including reduced risk of ASCVD or pancreatitis. Additionally, icosapent ethyl has not shown superiority to other omega-3 ethyl esters related to reduction in triglycerides.[5] Adverse reactions included arthralgia and oropharyngeal pain.[2]

References

1. Grundy SM, Stone NJ, Bailey AL, et al. 2018 aha/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).
2. Vascepa [Prescribing Information]. Bridgewater, NJ: Amarin Pharma, Inc. September 2021
3. Bhatt DL, Steg PG, Miller M, et al. Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. N Engl J Med. 2019;380(1):11-22.
4. Amarin Pharma Inc. Evaluation of the Efficacy and Safety of Amr101 (Ethyl Icosapentate) in Patients with Fasting Triglyceride Levels ≥ 500 Mg/Dl and ≤ 2000 Mg/Dl. Available at: https://clinicaltrials.gov/ct2/show/results/NCT01047683
5. Maki KC, Bays HE, Ballantyne CM, et al. A head-to-head comparison of a free fatty acid formulation of omega-3 pentaenoic acids versus icosapent ethyl in adults with hypertriglyceridemia: the enhance-it study. J Am Heart Assoc. 2022;11(6):e024176.

6. 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. Journal of the American College of Cardiology. 2021;78(9):960-993.

History

Approved Date	Effective Date	Version	Action and Summary of Changes
8/16/2023	2/1/2024	39.50.00.AA-v1	Approved by DUR Board New policy created