Clinical Policy: Icosapent Ethyl (Vascepa)

Reference Number: CP.CPA.357
Effective Date: 03.01.23
Last Review Date: 02.24
Line of Business: Commercial

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Icosapent ethyl (Vascepa®) is an ethyl ester of eicosapentaenoic acid (EPA).

FDA Approved Indication(s)

Vascepa is indicated:

- As 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 (CVD) 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

Limitation(s) of use: The effect of Vascepa on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Vascepa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hypertriglyceridemia without ASCVD (must meet all)**:**

1. Diagnosis of hypertriglyceridemia;
2. Age ≥ 18 years;
3. Fasting TG ≥ 500 mg/dL (lab must be dated within 90 days);
4. Failure of a ≥ 3 consecutive month trial of fibrate therapy in the last 6 months at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of omega-3-acid ethyl esters (generic Lovaza®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed (a and b):
   a. 4 g per day;
   b. 4 capsules per day.

Approval duration: 6 months

B. Reduction of Cardiovascular Disease Risk (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Atherosclerotic cardiovascular disease (ASCVD) as evidenced by a history of any one of the following conditions (i-vii):
      i. Acute coronary syndromes;
      ii. Clinically significant coronary heart disease (CHD) diagnosed by invasive or noninvasive testing (such as coronary angiography, stress test using treadmill, stress echocardiography, or nuclear imaging);
      iii. Coronary or other arterial revascularization;
      iv. Myocardial infarction;
      v. Peripheral arterial disease presumed to be of atherosclerotic origin;
      vi. Stable or unstable angina;
      vii. Stroke or transient ischemic attack (TIA);
   b. Diabetes with ≥ 2 CVD risk factors (*see Appendix G*);
2. Age ≥ 45 years;
3. Documentation of both of the following (labs must be dated within 90 days) (a and b):
   a. Fasting TG between 150-499 mg/dL;
   b. Low-density lipoprotein cholesterol (LDL-C) between 41-100 mg/dL;
4. For members on statin therapy, both of the following (a and b):
   a. Vascepa is prescribed in conjunction with a statin at the maximally tolerated dose;
   b. Member has been adherent for at least the last 4 months to maximally tolerated doses of one of the following statin regimens (i, ii, or iii):
      i. A high intensity statin (*see Appendix D*);
      ii. A moderate intensity statin (*see Appendix D*), and member has one of the following (a or b):
         a) Intolerance to two high intensity statins;
         b) A statin risk factor (*see Appendix E*);
      iii. A low intensity statin, and member has one of the following (a or b):
         a) Intolerance to one high and one moderate intensity statins;
         b) A statin risk factor (*see Appendix E*) and history of intolerance to two moderate intensity statins;
5. For members not on statin therapy, member meets one of the following (a or b):
   a. Statin therapy is contraindicated per Appendix F;
   b. For members who are statin intolerant, both of the following (i and ii):
      i. Member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin);
      ii. Member meets one of the following (a or b):
         a) Member has documented statin risk factors (*see Appendix E*);
         b) Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (1 and 2):
            1) Documentation of intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
            2) Documentation of re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);

6. Dose does not exceed (a and b):
   a. 4 g per day;
   b. 4 capsules per day.

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

II. Continued Therapy

A. Hypertriglyceridemia without ASCVD (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Initial re-authorization: 20% reduction in TG levels from baseline;
   b. Subsequent re-authorizations: continued reduction or maintenance in reduction of TG levels from baseline;
3. If request is for a dose increase, new dose does not exceed (a and b):
   a. 4 g per day;
   b. 4 capsules per day.

Approval duration: 12 months

B. Reduction of Cardiovascular Disease Risk (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. Member is responding positively to therapy as evidenced by no increase in TG and LDL-C levels from baseline;
3. If statin tolerant, documentation of adherence to a statin at the maximally tolerated dose;
4. If request is for a dose increase, new dose does not exceed (a and b):
   a. 4 g per day;
   b. 4 capsules per day.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation Key

ASCVD: atherosclerotic cardiovascular disease
CVD: cardiovascular disease
EPA: eicosapentaenoic acid
FDA: Food and Drug Administration
LDL-C: low-density lipoprotein cholesterol
SAMS: statin-associated muscle symptoms
TG: triglyceride

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fenofibrate (TriCor®)	HyperTG without ASCVD: 48-145 mg PO QD	145 mg/day
gemfibrozil (Lopid®)	HyperTG without ASCVD: 600 mg PO BID	1,200 mg/day
omega-3-acid ethyl esters (Lovaza®)	HyperTG without ASCVD: 4 g PO QD or 2 g PO BID	4 g/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity (e.g., anaphylactic reaction) to Vascepa or any of its components
- Boxed warning(s): none reported

Appendix D: High and Moderate Intensity Daily Statin Therapy for Adults

High Intensity Statin Therapy ***Daily dose shown to lower LDL-C, on average, by approximately ≥ 50%***
• Atorvastatin 40-80 mg • Rosuvastatin 20-40 mg
Moderate Intensity Statin Therapy ***Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%***
• Atorvastatin 10-20 mg • Fluvastatin XL 80 mg • Fluvastatin 40 mg BID • Lovastatin 40 mg • Pitavastatin 1-4 mg • Pravastatin 40-80 mg • Rosuvastatin 5-10 mg • Simvastatin 20-40 mg
Low Intensity Statin Therapy ***Daily dose shown to lower LDL-C, on average, by < 30%***
• Simvastatin 10 mg • Pravastatin 10-20 mg • Lovastatin 20 mg • Fluvastatin 20-40 mg

Appendix E: Statin Risk Factors

Statin Risk Factors
• Multiple or serious comorbidities, including impaired renal or hepatic function • Unexplained alanine transaminase (ALT) elevations > 3 times upper limit of normal, or active liver disease • Concomitant use of drugs adversely affecting statin metabolism • Age > 75 years, or history of hemorrhagic stroke • Asian ancestry

Appendix F: Statin Contraindications

Statins
• Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy) • Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment

Statins
• Pregnancy*, actively trying to become pregnant, or nursing • Immune-mediated hypersensitivity to the HMG-CoA reductase inhibitor drug class (statins) as evidenced by an allergic reaction occurring with at least TWO different statins

**In July 2021, the FDA requested removal of the contraindication against use of statins in pregnant women. Because the benefits of statins may include prevention of serious or potentially fatal events in a small group of very high-risk pregnant patients, contraindicating these drugs in all pregnant women is not appropriate. https://www.fda.gov/safety/medical-product-safety-information/statins-drug-safety-communication-fda-requests-removal-strongest-warning-against-using-cholesterol*

Appendix G: Risk Factors for CVD (2021 ADA and 2013 AHA Guidelines)

- Men and women ≥ 50 years of age
- Cigarette smoker or stopped smoking within 3 months
- Hypertension (blood pressure ≥ 140 mmHg systolic OR ≥ 90 mmHg diastolic) or on antihypertensive medication
- HDL-C ≤ 40 mg/dL for men or ≤ 50 mg/dL for women
- Renal dysfunction: creatinine clearance (CrCL) > 30 and < 60 mL/min or chronic kidney disease
- Micro- or macroalbuminuria
  - Microalbuminuria: either a positive micral or other strip test (may be obtained from medical records), an albumin/creatinine ratio ≥ 2.5 mg/mmol, or an albumin excretion rate on timed collection ≥ 20 mg/min all on at least two successive occasions
  - Macroalbuminuria: Albustix or other dipstick evidence of gross proteinuria, an albumin/creatinine ratio ≥ 25 mg/mmol, or an albumin excretion rate on timed collection ≥ 200 mg/min all on at least two successive occasions
- Obesity/overweight
- Dyslipidemia
- Family history of premature coronary disease

Appendix H: General Information

- The diagnosis of SAMS is often made based on clinical criteria. Typical SAMS include muscle pain and aching (myalgia), cramps, and weakness. Symptoms are usually bilateral and involve large muscle groups, including the thigh, buttock, back, and shoulder girdle musculature. In contrast, cramping is usually unilateral and may involve small muscles of the hands and feet. Symptoms may be more frequent in physically active patients. Symptoms often appear early after starting stain therapy or after an increase in dose and usually resolve or start to dissipate within weeks after cessation of therapy, although it may take several months for symptoms to resolve completely. Persistence of symptoms for more than 2 months after drug cessation should prompt a search for other causes or for underlying muscle disease possibly provoked by statin therapy. The reappearance of symptoms with statin rechallenge and their disappearance with drug cessation offers the best evidence that the symptoms are truly SAMS.
- Pravastatin, fluvastatin, and rosuvastatin are hydrophilic statins which have been reported to confer fewer adverse drug reactions than lipophilic statins.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hypertriglyceridemia without ASCVD	2 g PO BID	4 g/day
Reduction of CVD risk		

VI. Product Availability

Capsules: 0.5 g, 1 g

VII. References

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4. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract 2017;23(Suppl 2):1-87.
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15. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline from the American Heart Association/American Stroke Association. Stroke. 2021; 52: e354-e467.
16. Warden BA, Guyton JR, Kovacs AC, et al. Assessment and management of statin-associated muscle symptoms (SAMS): A clinical perspective from the National Lipid Association. Published September 9, 2022. Available at: https://www.lipid.org/nla/clinical-perspective-assessment-management-statin-associated-muscle-symptoms-sams. Accessed October 18, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policy CP.PMN.187; no significant changes; removed redirections to generic icosapent ethyl for brand Vascepa requests; references reviewed and updated.	12.15.22	02.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	11.07.23	02.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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