Vascepa Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
04-01-2024	10-01-2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Vascepa® (icosapent ethyl)* Capsule	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 (greater than or equal to 150 mg/dL) and • Established cardiovascular disease or • Diabetes mellitus and 2 or more additional risk factors for cardiovascular disease Adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (greater than or equal to 500 mg/dL) hypertriglyceridemia. Limitations of Use: the effect of Vascepa on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.	*generic available	1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Efficacy	Vascepa was studied in the REDUCE-IT phase 3b multinational, randomized, double blind, placebo-controlled trial comparing icosapent ethyl (4 grams daily) to placebo in 8,179 adult patients. REDUCE-IT enrolled men or women at least 45 years of age with established cardiovascular disease (71%) or at least 50 years of age with diabetes mellitus and one additional risk factor (29%). Randomization required fasting triglycerides (TG) of at least 150 mg/dL to 499 mg/dL and LDL-C of 41 mg/dL to 100 mg/dL with a stable statin (for at least 4 weeks prior to qualifying measurements).(1,3) Due to the intraindividual variability of TG levels, the initial protocol allowed for a 10% lower TG level from the target lower limit, which permitted patients to be enrolled if they had a TG level of at least 135 mg/dL.(2) Patients with established cardiovascular disease (CVD) had a documented history of coronary artery disease, cerebrovascular or carotid disease, or peripheral artery disease.(1,3) Risk factors for CVD in the second group of patients included:(3) • Men at least 55 year of age and women at least 65 years of age • Cigarette smoker or stopped smoking within 3 months • Hypertension (greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic) or on antihypertensive medication • HDL-C less than or equal to 40 mg/dL for men or less than or equal to 50 mg/dL for women • High-sensitivity C-reactive protein (hsCRP) greater than 3.00 mg/L

	• Renal dysfunction (CrCl greater than 30 and less than 60 mL/min) • Retinopathy defined as any of the following: nonproliferative retinopathy, preproliferative retinopathy, proliferative retinopathy, maculopathy, advanced diabetic eye disease, or a history of photocoagulation • Micro- or macroalbuminuria • An ankle-brachial index (ABI) of less than 0.9 without symptoms of intermittent claudication The primary efficacy endpoint was a composite of CV death, nonfatal myocardial infarction (MI) (including silent MI), nonfatal stroke, coronary revascularization, or unstable angina in a time-to-event analysis. The key secondary endpoint is a composite of CV death, nonfatal MI, or nonfatal stroke in a time-to-event analysis. Additional individual or composite endpoints include: composite of CV death or nonfatal MI; fatal or nonfatal MI; emergency or urgent coronary revascularization; CV death; hospitalization for unstable angina; fatal or nonfatal stroke; a composite of death from any cause, nonfatal MI, or nonfatal stroke; and death from any cause. A primary end-point event occurred in 17.2% of the patients in the icosapent ethyl group, as compared with 22.0% of the patients in the placebo group (hazard ratio, 0.75; 95% confidence interval [CI], 0.68 to 0.83; P less than 0.001). The corresponding rates of the key secondary endpoint were 11.2% and 14.8% (hazard ratio, 0.74; 95% CI, 0.65 to 0.83; P less than 0.001). The rates of additional ischemic end points, as assessed according to a prespecified hierarchical schema, were significantly lower in the icosapent ethyl group than in the placebo group, including the rate of fatal or non-fatal MI (6.1% vs. 8.7%), emergency or urgent coronary revascularization (5.3% vs. 7.8%), cardiovascular death (4.3% vs. 5.2%), hospitalization for unstable angina (2.6% vs. 3.8%), and fatal or nonfatal stroke (2.4% vs. 3.3%).(1) The American Heart Association (AHA) released an advisory statement identifying icosapent ethyl is the first non–LDL-focused lipid therapy to demonstrate CV benefit and should be considered first-line therapy for patients with diabetes mellitus type 2 and coronary artery disease whose TG remain elevated (>135 mg/dL) despite maximally tolerated statin and lifestyle changes.(5) The American Diabetes Association (ADA) gives icosapent ethyl an "A" level recommendation in patients with atherosclerotic CVD or other CV risk factors on a statin with controlled LDL-C but elevated triglycerides (135–499 mg/dL) noting the addition of icosapent ethyl can be considered to reduce CV risk.(4) The National Lipid Association (NLA) released an advisory statement saying their position for high-risk and very-high-risk patients with TG 135-499 mg/dL on high-intensity or maximally tolerated statin therapy (±ezetimibe), treatment with icosapent ethyl is recommended for ASCVD risk reduction (evidence rating: class I; evidence level: B-R [strong]). The NLA participated in the development of the 2018 American Heart Association/American College of Cardiology/Multisociety Guideline on the Management of Blood Cholesterol, which reaffirmed that lifestyle changes and statin treatment are therapeutic cornerstones for atherosclerotic cardiovascular disease (ASCVD) risk reduction. It updated prior recommendations to incorporate newer data demonstrating ASCVD risk reduction with ezetimibe and proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors as adjuncts to statin therapy for patients at high and very-high ASCVD risk. The 2018 Guideline was finalized shortly before full results were available from the REDUCE-IT trial. REDUCE-IT served as the primary basis for the NLA's review of evidence for the use of icosapent ethyl for ASCVD risk reduction.(6)
Safety	Vascepa is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to Vascepa or any of its components.(1)

REFERENCES

Number	Reference
1	Vascepa prescribing information. Amarin Pharma, Inc. September 2021.
2	Bhatt, D. L., Steg, P. G., Miller, M., Brinton, E. A., Jacobson, T. A., Ketchum, S. B., Doyle, R. T., Juliano, R. A., Jiao, L., Granowitz, C., Tardif, J.-C., & Ballantyne, C. M. (2019). Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. New England Journal of Medicine, 380(1), 11–22. https://doi.org/10.1056/nejmoa1812792
3	Bhatt, D. L., Steg, Ph. G., Brinton, E. A., Jacobson, T. A., Miller, M., Tardif, J.-C., Ketchum, S. B., Doyle, R. T., Murphy, S. A., Soni, P. N., Braeckman, R. A., Juliano, R. A., & Ballantyne, C. M. (2017). Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial. Clinical Cardiology, 40(3), 138–148. https://doi.org/10.1002/clc.22692
4	American Diabetes Association. Addendum 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes-2021. (2021). Diabetes Care, 44 (Suppl. 1), S125–S150. https://doi.org/10.2337/dc21-ad09a
5	Arnold, S. V., Bhatt, D. L., Barsness, G. W., Beatty, A. L., Deedwania, P. C., Inzucchi, S. E., Kosiborod, M., Leiter, L. A., Lipska, K. J., Newman, J. D., & Welty, F. K. (2020). Clinical Management of Stable Coronary Artery Disease in Patients with Type 2 Diabetes Mellitus: A scientific statement from the American Heart Association. Circulation, 141, e779–e806. https://doi.org/10.1161/cir.0000000000000766
6	Orringer, C. E., Jacobson, T. A., & Maki, K. C. (2019). National Lipid Association Scientific Statement on the use of icosapent ethyl in statin-treated patients with elevated triglycerides and high or very-high ASCVD risk. Journal of Clinical Lipidology, 13(6), 860–872. https://doi.org/10.1016/j.jacl.2019.10.014

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Vascepa	icosapent ethyl cap	0.5 GM ; 1 GM	M ; N ; O ; Y	O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Vascepa	Icosapent Ethyl Cap 0.5 GM	0.5 GM	240	Capsules	30	DAYS			
Vascepa	Icosapent Ethyl Cap 1 GM	1 GM	120	Capsules	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vascepa	icosapent ethyl cap	0.5 GM ; 1 GM	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vascepa	Icosapent Ethyl Cap 0.5 GM	0.5 GM	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Vascepa	Icosapent Ethyl Cap 1 GM	1 GM	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PREFERRED AGENTS

Disease State	Disease Name	Drug Name	Preferred Level	# of Prereq Necessary	Required Prereq Levels	Required Preferred Level 1 Agent	Required Preferred Age Limit	Required Preferred Age Limit Units
Vascepa								
Vascepa		Vascepa	1		0			
Vascepa		icosapent ethyl	2	1	1			

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	(see below)

Target Agent(s)	Preferred Target Agent(s)
Target and preferred agents - to be determined by client	Target and preferred agents - to be determined by client
icosapent ethyl*	Vascepa

*generic available

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The patient has a pre-treatment triglyceride (TG) level of greater than or equal to 500 mg/dL **OR**
   B. The patient is using the requested agent to reduce the risk of myocardial infarction, stroke, coronary revascularization, or unstable angina requiring hospitalization AND ALL of the following:
      1. ONE of the following:
         A. The patient is on maximally tolerated statin therapy **OR**
         B. The patient has an intolerance or hypersensitivity to statin therapy **OR**
         C. The patient has an FDA labeled contraindication to ALL statins **AND**
      2. The patient's triglyceride (TG) level is greater than or equal to 135 mg/dL **AND**
      3. ONE of the following:
         A. The patient has established cardiovascular disease **OR**
         B. The patient has diabetes mellitus AND 2 or more additional risk factors for cardiovascular disease (e.g., hypertension, premature family history, chronic kidney disease) **OR**

Module	Clinical Criteria for Approval
	C. The patient has another FDA approved indication for the requested agent and route of administration **OR** D. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. If the client has preferred agent(s), then ONE of the following: A. The requested agent is a preferred agent **OR** B. The patient has an intolerance or hypersensitivity to the preferred agent(s) that is not expected to occur with the non-preferred agent **OR** C. The patient has an FDA labeled contraindication to the preferred agent(s) that is not expected to occur with the non-preferred agent **OR** D. The patient's medication history includes use of a preferred agent **OR** E. BOTH of the following: 1. The prescriber has stated that the patient has tried a preferred agent **AND** 2. The preferred agent was discontinued due to lack of effectiveness or an adverse event **OR** F. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** G. The prescriber has provided documentation that the preferred agent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. If the client has preferred agent(s), then ONE of the following: A. The requested agent is a preferred agent **OR** B. The patient has an intolerance or hypersensitivity to the preferred agent(s) that is not expected to occur with the non-preferred agent **OR** C. The patient has an FDA labeled contraindication to the preferred agent(s) that is not expected to occur with the non-preferred agent **OR** D. The patient's medication history includes use of a preferred agent **OR** E. BOTH of the following:

Module	Clinical Criteria for Approval
	1. The prescriber has stated that the patient has tried a preferred agent **AND** 2. The preferred agent was discontinued due to lack of effectiveness or an adverse event **OR** F. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** G. The prescriber has provided documentation that the preferred agent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: 12 months