

What medical societies have recognized icosapent ethyl (VASCEPA®/VAZKEPA) in their medical treatment guidelines or scientific statements?

A growing number of medical societies are recommending the usage of icosapent ethyl (VASCEPA®/VAZKEPA) in appropriate patients. In addition to recommending the use of icosapent ethyl, many of these guidelines emphasize that the positive clinical results of the REDUCE-IT® cardiovascular outcomes study should not be generalized to any product other than icosapent ethyl (i.e., the clinical results are unique to VASCEPA).

Medical societies that have updated their guidelines and/or issued scientific statements include:

North America

- American Diabetes Association (ADA)
- American Heart Association (AHA)
- American Stroke Association (ASA)
- National Lipid Association (NLA)
- American Association of Clinical Endocrinologists (AACE)
- American College of Endocrinology (ACE)
- Thrombosis Canada
- Endocrine Society (ENDO)
- Canadian Cardiovascular Society (CCS)

Europe

- European Society of Cardiology (ESC)
- European Atherosclerosis Society (EAS)

South America

- Brazilian Society of Cardiology (SBC)
- Colombian Association of Endocrinology, Diabetes and Metabolism, Colombian Society of Cardiology and Cardiovascular Surgery

Asia/Africa

- Japan Circulation Society (JCS)
- Chinese Society of Cardiology (CSC)
- Chinese Journal of Internal Medicine (a journal of the Chinese Medical Association [CMA])
- The Egyptian Heart Journal (the official journal of the Egyptian Society of Cardiology)

Below are more details regarding these guidelines and scientific statements (listed in chronological order):

- The American Diabetes Association updated their Standards of Medical Care in Diabetes in March of 2019 to recommend that icosapent ethyl be considered for patients with diabetes and

atherosclerotic cardiovascular disease or other cardiac risk factors on a statin with controlled LDL-C, but with elevated triglycerides (135-499 mg/dL) to reduce CV risk.

The findings were made with a level “A” grade of scientific evidence, which under ADA standards, reflects that REDUCE-IT was considered to be a large well-designed clinical trial. Generally, according to ADA, A-level recommendations have the best chance of improving outcomes when applied to the population to which they are appropriate.

- The American Diabetes Association is a United States-based nonprofit that seeks to prevent and cure diabetes and to improve the lives of all people affected by diabetes.¹ In May 2019, the Japan Circulation Society referenced REDUCE-IT and eicosapentaenoic acid in their publication of updated guidelines.²
- The American Heart Association issued a Scientific Advisory in August of 2019 recognizing that elevated triglycerides may be a causal factor for CVD; that dietary supplements are not recommended, nor FDA approved, to treat medical conditions; and that positive outcomes results were demonstrated in REDUCE-IT.

The AHA is the nation’s oldest and largest voluntary organization dedicated to fighting heart disease and stroke.³

- The European Society of Cardiology updated their patient treatment guidelines on September 1, 2019 to include icosapent ethyl (VASCEPA) to address high-risk cardiovascular patients with elevated triglycerides (135-499 mg/dL). They updated their guidelines jointly with the European Atherosclerosis Society (EAS). The classification is a Level B recommendation which reflects a relatively high weight of scientific evidence under ESC and EAS standards.

ESC is a not-for-profit medical society led by expert volunteers. They unite Member National Cardiac Societies, cardiovascular ESC sub-specialty communities, Affiliated Cardiac Societies, distinguished Fellows of the ESC and individual members from around the world.⁴

- The European Atherosclerosis Society joined ESC to jointly issue the above described patient treatment guidelines.

EAS was founded in 1964 with the aim of “advancing and exchanging knowledge concerning the causes, natural history, treatment and prevention of atherosclerotic disease.” For more than 50 years the Society’s expertise has been used to teach clinicians how to manage lipid disorders and how to prevent atherosclerosis.⁵

- The National Lipid Association issued a position statement on September 13, 2019 recommending icosapent ethyl (VASCEPA) for atherosclerotic cardiovascular disease (ASCVD) risk reduction in

high- and very-high-risk patients, 45 years of age or older with clinical ASCVD, or 50 years of age or older with type 2 diabetes requiring medication and with ≥ 1 additional risk factor, and fasting triglycerides of 135-499 mg/dL on maximally tolerated statin, with or without ezetimibe. The NLA recommendation was issued as a Class I, Level B-R (STRONG) recommendation, its highest designation, for icosapent ethyl.

The NLA is a leading professional society dedicated to enhancing the practice of lipid management in clinical medicine.⁶ The NLA's Board of Directors is comprised of leading experts who specialize in clinical lipidology.

- On February 3, 2020, a consensus statement by the American Association Of Clinical Endocrinologists (AACE) and American College Of Endocrinology (ACE) on the comprehensive management of type 2 diabetes was released.⁷ The AACE diabetes algorithm is a comprehensive management algorithm that covers lifestyle, obesity, prediabetes, lipids, hypertension and glucose management strategies. It is the most up-to-date and progressive management algorithm that now includes strategies based on all the newest cardiovascular (CV) outcomes trials in diabetes and related metabolic CV outcomes trials and incorporates the latest FDA-approved indications.

Strategies included in the 2020 AACE diabetes algorithm go beyond just managing and controlling CV risk factors to preventing the next CV events - morbidity and mortality in both patients with established ASCVD and those at high risk for cardiovascular disease (CVD).

The specific update regarding icosapent ethyl in the new guidance includes the following:

- Management of patients with established or high risk for CVD who have triglyceride levels between 135-499 mg/dL with EPA with proven benefits to prevent the next event
- In November of 2019, The Brazilian Society of Cardiology (SBC) released an Updated Cardiovascular Prevention Guideline.⁸ SBC has 12 scientific departments and 10 study groups, as well as an organization in 26 regional societies throughout Brazil.

SBC provided the following update regarding icosapent ethyl with a Level I, Grade B rating:

- Supplementation with an E-EPA (ethyl eicosapentaenoic acid) formulation (4 g/day) can be recommended for high-risk patients with elevated TG levels using statins, as it seems to reduce the risk for ischemic events, including CV death.

Data from these studies suggest that high doses of EPA (4 g) can be used in patients with prior CVD and who remain with elevated TG levels, despite taking statins to prevent CVD. However, there is no evidence for the use of lower doses and other formulations of omega-3 for CV prevention, both primary and secondary.

- In February of 2020, The Thrombosis Canada clinical guide on Stroke – Secondary Prevention was updated. This update mentions icosapent ethyl as a therapeutic approach to reduce the risk of recurrent vascular events in patients who have already suffered a stroke or TIA.⁹
 - The Thrombosis Canada clinical guides have been developed to assist clinicians with point of care decision making. They are not intended to be taken as guidelines. The Thrombosis Canada™ *Clinical Guides* are:
 - Developed voluntarily by Thrombosis Canada™ members, internationally recognized as experts
 - Peer reviewed by Thrombosis Canada clinical guide committee
 - Reviewed for applicability to primary care by members of the College of Family Physicians of Canada
 - Reflect recommendations of evidence-based clinical practice guidelines
 - Not supported financially by any external funders

- In February 2020, the Colombian Association of Endocrinology, Diabetes and Metabolism, Colombian Society of Cardiology and Cardiovascular Surgery published the Recommendations of the expert panel on the diagnostic pathophysiology and treatment of dyslipidemias in the adult population¹⁰
 - Issued post FDA approval in US and prior to application in Columbia
 - Referenced the REDUCE-IT results and the CV risk-lowering effects of IPE in joint dyslipidemia recommendations from the Colombian Association of Endocrinology, Diabetes & Metabolism and Colombian Society of Cardiology and Cardiovascular Surgery
 - Recommend pharmacological forms of omega-3 fatty acids (non-supplements) and in doses of 4 g/day (as described in the REDUCE-IT study, where icosapent ethyl was administered as 2 g every 12 hours)

- On April 13 of 2020, The American Heart Association issued a Scientific Statement on the Clinical Management of Stable Coronary Artery Disease in Patients with Type 2 Diabetes Mellitus.¹¹
 - Within this scientific statement AHA calls out icosapent ethyl as a consideration for further cardiovascular risk reduction when triglycerides remain elevated (>135 mg/dL) despite maximally tolerated statin based on the results of REDUCE-IT.

- In August 2020, ESC updated Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation.¹²
 - These guidelines reference the REDUCE-IT results in the Guidelines for the management of NSTEMI-ACS
 - Highlights use of very high doses of icosapent ethyl (2 g twice daily)
 - Refers to the icosapent ethyl Ila recommendation in 2019 ESC/EAS Guidelines for the management of dyslipidemias

- In October of 2020, The Endocrine Society (ENDO) published their Full Guideline: Lipid Management in Patients with Endocrine Disorders.¹³
 - Within this guideline, based upon the results of REDUCE-IT, ENDO recommends that IPE should be considered first-line therapy in patients on statin therapy with TGs >150 mg/dL and with either atherosclerotic cardiovascular disease or diabetes plus 2 additional risk factors
 - The guideline also conveys that CVD benefit seen in REDUCE-IT does not apply to other omega-3 fatty acids, particularly those with a mix of EPA and DHA.

- In December 2020, the Chinese Society of Cardiology (CSC) published their Guidelines for Primary Prevention of Cardiovascular Diseases in China.¹⁴
 - References use of IPE (as studied in REDUCE-IT)
 - If TG is >2.3 mmol/L in high-risk persons of ASCVD after receiving moderate-dose statin therapy, consider giving high-dose eicosapentaenoic acid ethyl ester (IPE) (2 g, twice daily) to further reduce the risk of ASCVD (Category IIa, Evidence Level B)

- In February 2021, the Egyptian Heart Journal published a practical guidance in lipid management. In this guidance, icosapent ethyl was listed as a consideration in patients with high TG levels (above 200 mg/dL). The recommendation states to exclude and treat secondary causes of HTG [TG levels > 200 mg/dL]. Patients with HTG and at high risk must receive a statin as a first-line treatment to reduce CVD risk. In high-risk (or above) patients with TG levels between 135 and 499 mg/dL despite statin treatment, n-3 PUFAs (icosapent ethyl 2 × 2g/day) should be considered in combination with a statin.¹⁵

- In March 2021, the Canadian Cardiovascular Society published their Guidelines for Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. In this guidance, icosapent ethyl was recommend for use to lower the risk of CV events in patients with ASCVD, or with diabetes and ≥1 CVD risk factors, who have an elevated fasting triglyceride level of 1.5-5.6 mmol/L despite treatment with maximally tolerated statin therapy (Strong Recommendation; High-Quality Evidence). In addition, the guidelines do not recommend the use of over-the-counter omega-3 polyunsaturated fatty acids supplements (marketed as natural health products in Canada) to reduce CVD risk (Strong Recommendation; High-Quality Evidence).¹⁶

- In May 2021, the Chinese Journal of Internal Medicine¹⁷ (one of the journals of the Chinese Medical Association) published *Expert consensus on diagnosis and treatment of diabetic patients with cardiovascular disease* which referenced IPE:
 - On the basis of strict lifestyle intervention and statin therapy, patients at high risk/extremely high risk for CVD tend to use high-dose ethyl eicosapentaenoate (also

known as icosapent ethyl) (2 g, twice daily) to further reduce the risk for CVD if TG >2.3 mmol/L.

- In May 2021, the American Heart Association (AHA)/American Stroke Association (ASA) published the *2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack*¹⁸. This guideline was reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons; endorsed by the Society of Vascular and Interventional Neurology; and the American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.
 - This stroke guideline from the AHA/ASA contains the following recommendations:
 - *In patients with ischemic stroke or TIA, with fasting triglycerides 135 to 499 mg/dL and LDL-C of 41 to 100 mg/dL, on moderate- or high-intensity statin therapy, with HbA1c <10%, and with no history of pancreatitis, AF, or severe heart failure, treatment with icosapent ethyl (IPE) 2 g twice a day is reasonable to reduce risk of recurrent stroke.*
 - This guideline also recognized the potential mechanism of CV risk reduction with IPE as well as differences between IPE/EPA as compared to DHA, another omega-3 fatty acid, with the following language:
 - *Because triglyceride levels were similar, higher EPA levels may account for the results seen in REDUCE-IT. In addition, the differing effects of EPA and DHA on membrane stabilization may contribute to the lack of effect with EPA/DHA compared with EPA alone or IPE.*

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