NHS
Pan Mersey
Area Prescribing Committee

ICOSAPENT ETHYL capsules (Vazkepa® ▼) with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides

The Pan Mersey Area Prescribing Committee recommends the prescribing of ICOSAPENT ETHYL capsules (Vazkepa® ▼) with statin therapy, for reducing the risk of cardiovascular events in people with raised triglycerides in accordance with NICE TA805.

GREEN

NICE technology appraisal (TA) 805 (13 July 2022) recommends icosapent ethyl as an option for reducing the risk of cardiovascular (CV) events in adults. It is recommended if they have a high risk of CV events and raised fasting triglycerides (1.7 mmol/litre or above) and are taking statins, but only if they have:

- established CV disease (secondary prevention), defined as a history of any of the following:
  - acute coronary syndrome (such as myocardial infarction [MI] or unstable angina needing hospitalisation)
  - coronary or other arterial revascularisation procedures
  - coronary heart disease
  - ischaemic stroke
  - peripheral arterial disease, **and**
- low-density lipoprotein cholesterol (LDL-C) levels above 1.04 mmol/litre and below or equal to 2.60 mmol/litre.[1]

Costing information

Based on the NICE Resource Impact Report for NICE TA805, the estimated cost of implementing this guidance is £12,000 per 100,000 population in 2022/23, rising to £51,000 per 100,000 population by 2026/27 when it is assumed that steady state has been reached.[2]

NICE states that icosapent ethyl is unlikely to be cost effective for primary prevention of cardiovascular events, so it is not recommended for this indication.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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Effectiveness

Icosapent ethyl is a stable ethyl ester of the omega-3 fatty acid, eicosapentaenoic acid (EPA). The mechanisms of action contributing to reduction of CV events with icosapent ethyl are not completely understood. The mechanisms are likely to include improved lipoprotein profile with reduction of triglyceride-rich lipoproteins, anti-inflammatory, and antioxidant effects, reduction of macrophage accumulation, improved endothelial function, increased fibrous cap thickness/stability, and antiplatelet effects.[3]

The company provided clinical evidence to NICE from REDUCE-IT, a randomised trial comparing icosapent ethyl with a mineral oil placebo. The trial included people who had statins with or without ezetimibe, fasting triglyceride levels of 1.53 mmol/litre or more and below 5.64 mmol/L, and LDL-C levels of more than 1.04 mmol/L to 2.60 mmol/L. In the trial, 8,179 people were randomised and 71% were in the secondary prevention group. The primary end-point was time from randomisation to the first occurrence of any component of the major adverse CV event (MACE) composite outcome. This comprised CV death, nonfatal MI, nonfatal stroke, coronary revascularisation and unstable angina.[3] A primary end-point event occurred in 17.2% of the patients in the icosapent ethyl group, 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<0.001), an absolute between-group difference of 4.8 percentage points (95% CI, 3.1 to 6.5). The number needed to treat [NNT] to avoid one primary end-point event was 21 (95% CI, 15 to 33) over a median follow-up of 4.9 years.[4]

The NICE committee concluded that REDUCE-IT may not fully represent NHS clinical practice, which increases uncertainty about the generalisability of the results, but evidence from REDUCE-IT suggests that icosapent ethyl reduces the risk of CV events, compared with placebo, in people with raised fasting triglycerides (1.7 mmol/litre or above) who are taking statins. The trial only included people with LDL-C levels above 1.04 mmol/litre and below or equal to 2.60 mmol/litre [1]

Safety[3]

Contraindicated in hypersensitivity to the active substance, soya or to any of the excipients.

Icosapent ethyl is obtained from the oil of fish. Icosapent ethyl should be used with caution in patients with known hypersensitivity to fish and/or shellfish.

The most frequently reported adverse reactions associated with icosapent ethyl were bleeding (11.8%), peripheral oedema (7.8%), atrial fibrillation (5.8%), constipation (5.4%), musculoskeletal pain (4.3%), gout (4.3%) and rash (3.0%).

See SPC for full safety information.

Cost

Icosapent ethyl costs £144.21 per pack of 120 capsules.[5] The annual treatment cost per patient is £1,755.

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NICE states that the cost-effectiveness estimates for icosapent ethyl are uncertain. Icosapent ethyl is unlikely to be cost effective for primary prevention, so it is not recommended. However, the most likely cost-effectiveness estimates for secondary prevention are within what NICE normally considers an acceptable use of NHS resources so icosapent ethyl is recommended for secondary prevention in people with LDL-C levels above 1.04 mmol/L and below or equal to 2.60 mmol/L.[1]

Patient factors[3]

No dose adjustment is necessary based on age, renal impairment or hepatic impairment.

There is no relevant use of icosapent ethyl in children aged <18 years of age.

Use in pregnancy should be avoided unless the benefit of use outweighs the potential risk to the foetus.

It is not known whether icosapent ethyl is excreted in human milk and a risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from icosapent ethyl therapy considering the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Prescribing information

- The recommended daily oral dose is four capsules taken as two 998 mg capsules twice daily.[3]
- Icosapent ethyl should be taken with or following a meal.[3]
- To ensure the full intended dose is received, patients should be advised to swallow the capsules whole and not to break, crush, dissolve, or chew them.[3]
- If a dose is missed, patients should take it as soon as they remember. However, if one daily dose is missed, the next dose should not be doubled.[3]
- Patients must be taking a statin in order to have treatment with icosapent ethyl. People who cannot have statins are not covered by icosapent ethyl's marketing authorisation, therefore NICE were unable to make any recommendations in this area.[1]

Implementation notes

- Patients, particularly those with a relevant medical history, should be monitored for clinical evidence of atrial fibrillation or atrial flutter (e.g., dyspnoea, palpitations, syncope/dizziness, chest discomfort, change in blood pressure, or irregular pulse). Electrocardiographic evaluation should be performed when clinically indicated.[3]
- In patients with hepatic impairment, ALT and AST should be monitored as clinically indicated before the start of treatment and at appropriate intervals during treatment.[3]
- Treatment with icosapent ethyl has been associated with an increased incidence of bleeding. Patients taking icosapent ethyl with antithrombotic agents (such as aspirin or anticoagulants) may be at increased risk of bleeding and should be monitored periodically. [3]
- Refer to NHS England lipid management pathway for advice regarding when to refer patients for specialist advice.

References

1. National Institute for Health and Care Excellence. Technology appraisal guidance 805: Icosapent ethyl with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides, 13 July 2022. Accessed 05 August 2022.
2. National Institute for Health and Care Excellence. Technology appraisal guidance 805: Resource impact report: Icosapent ethyl with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides, 13 July 2022. Accessed 05 August 2022.
3. Amarin Pharmaceuticals Ireland Limited. Summary of Product Characteristics; Vazkepa, 26 April 2022. Accessed 05 July 2022.
4. Bhatt D, Steg G, Miller M et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med 2019; 380:11-22. Accessed online 28 August 2022.
5. NHS Business Services Authority. Dictionary of Medicine and Devices (dm+d Browser). Accessed 05 August 2022.