NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Icosapent ethyl for reducing the risk of cardiovascular events due to hypertriglyceridemia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of icosapent ethyl within its marketing authorisation for preventing cardiovascular events due to elevated triglycerides.

Background

Hypertriglyceridemia is a form of dyslipidaemia characterised by high concentrations of triglycerides in the blood and is a risk factor for CVD[1]. Triglyceride levels can be raised due to either primary causes (an inherited genetic condition) or secondary causes (other influences on triglycerides such as diet, lifestyle and medical conditions such as kidney disease, non-alcoholic fatty liver disease, gout, obesity and type 2 diabetes)[2]. Some people with hypertriglyceridemia have normal levels of high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol. Others have mixed dyslipidaemia, defined as elevations in triglyceride and LDL cholesterol levels that are often accompanied by low levels of HDL cholesterol[3].

People with hypertriglyceridemia are at increased risk of cardiovascular disease (CVD) because of the build-up of fatty deposits in arteries (atherosclerosis) which can lead to angina, and an increased risk of blood clots, myocardial infarction and stroke[4]. It can be associated with damage to arteries in organs such as the brain, heart, kidneys and eyes. CVD is a common cause of death in England, accounting for approximately 136,317 deaths in 2018, and it is a major cause of disability and reduced quality of life[3].

NICE guideline CG181 recommends advising people at high risk of, or with, CVD to eat a cardioprotective diet, engage in physical activity and stop smoking. Statins are recommended for both primary prevention of CVD (in people with increased risk of CVD in whom lifestyle modification is ineffective or inappropriate) or secondary prevention of cardiovascular events in people with CVD. Fibrates, nicotinic acid, bile sequestrants and omega-3 fatty acids are not currently recommended for the primary or secondary prevention of CVD. There are around 6.1 million people living with CVD in England and around 6.5 million adults in England are currently taking lipid-lowering drugs such as statins[3].

The technology

Icosapent ethyl (Vascepa, Amarin Corporation) is an omega-3 fatty acid agent. Icosapent ethyl is thought to reduce hepatic very low-density lipoprotein triglyceride synthesis and secretion and enhance triglyceride clearance. It is administered orally.

Icosapent ethyl does not currently have a marketing authorisation in the UK. It has been studied in combination with statins in clinical trials in adults with established CVD or high risk for CVD and hypertriglyceridemia for the prevention of cardiovascular events.

Intervention(s)	Icosapent ethyl in combination with a statin
Population(s)	Adults with established cardiovascular disease or at high risk of cardiovascular disease with hypertriglyceridemia and on statin therapy

Comparators	• Statins:
	  o atorvastatin
	  o fluvastatin
	  o pravastatin
	  o rosuvastatin
	  o simvastatin
	• When statins are contraindicated or not tolerated:
	  o alirocumab
	  o evolocumab
	• For people with hypertriglyceridemia and primary hypercholesterolaemia:
	  o ezetimibe

Outcomes	The outcome measures to be considered include: • time to cardiovascular event (including myocardial infarction, stroke and unstable angina) • mortality • hospital admissions • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	If the evidence allows the following subgroups will be considered: • adults at high risk of cardiovascular disease (primary prevention) • adults with established cardiovascular disease (secondary prevention) Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (2016). NICE Technology Appraisal 394. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (2016). NICE Technology Appraisal 393. Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (2010). NICE Technology Appraisal 210. Appraisals in development: Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia NICE Technology Appraisals guidance [ID1647]. Expected publication date: July 2021 Bempedoic acid for treating primary hypercholesterolaemia or mixed dyslipidaemia NICE Technology Appraisals guidance [ID1515]. Publication date to be confirmed. Related Guidelines: Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease (2013). NICE clinical guideline 172. Update ongoing. Cardiovascular disease: risk assessment and reduction, including lipid modification (2014). NICE clinical guideline 181. Update due. Related Quality Standards: Cardiovascular risk assessment and lipid modification (2015). NICE quality standard 100. Secondary prevention after a myocardial infarction (2015). NICE quality standard 99. Related NICE Pathways: Cardiovascular disease prevention (2017) NICE pathway
Related National	NHS RightCare. Preventing CVD by managing the high-risk

Policy	conditions. Public Health England. Health matters: preventing cardiovascular disease (2019) Public Health England. Cardiovascular disease: getting serious about prevention (2016) Department of Health. Cardiovascular Disease Outcomes Strategy Improving outcomes for people with or at high risk of cardiovascular disease (2013) The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2.

Questions for consultation

Is it appropriate to refer to reducing cardiovascular events in the title? Is it more appropriate to refer to 'treating hypertriglyceridemia'?

Should the remit and population in the scope also include people with mixed dyslipidaemia?

Have all relevant comparators for icosapent ethyl been included in the scope? Which treatments are considered to be established clinical practice in the NHS for prevention of cardiovascular events?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom icosapent ethyl is expected to be more clinically effective and cost effective or other groups that should be examined separately? Specifically, is it appropriate to add people with mixed dyslipidaemia as a subgroup?

Where do you consider icosapent ethyl will fit into the existing NICE pathway, cardiovascular disease prevention?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which icosapent ethyl will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider icosapent ethyl to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of icosapent ethyl can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Yuan et al., Hypertriglyceridemia: its etiology, effects and treatment. CMAJ, 176 (8) 1113-1120; 2007

2. Heart UK; Triglycerides. Accessed August 2020

3. British Heart Foundation, England factsheet, July 2020. Access August 2020

4. Peng et al., Hypertriglyceridemia and atherosclerosis. Lipids in Health and Disease, 16: 233; 2017

