NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Evinacumab for treating homozygous familial hypercholesterolaemia in people aged 12 and over

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of evinacumab within its marketing authorisation for treating homozygous familial hypercholesterolaemia in people aged 12 and over.

Background

Familial hypercholesterolaemia (FH) is an inherited disorder where the liver is incapable of metabolising or removing excess low density lipoprotein (LDL) cholesterol[1] caused by a genetic defect. This can lead to very high LDL levels which increase the risk of premature cardiovascular disease (CVD). There are two forms of FH; heterozygous and homozygous. Homozygous FH (HoFH) is much less common than heterozygous FH and is more severe. In HoFH, the inherited gene mutations affecting LDL is from both parents (so the individual has two genetic mutations)[2].

NICE CG71 scope states that HoFH has an incidence of approximately one case per million. According to the 2018 mid-year population estimates, this would equate to 56 people with HoFH in England[3]. The Clinical Commissioning Policy for lomitapide estimates that the prevalence of HoFH is 1 in 670,000 adults in England. Applying this to the population aged 18 and over, there are between 43 and 66 adult patients in England with HoFH. Based on prevalence rates and life expectancy, there is an estimated 1 new case of HoFH every year[4].

The signs of HoFH are lumps and bumps around the knuckles or Achilles tendon (caused by cholesterol deposits), yellow cholesterol build-up around the eyes and eyelids, or a pale ring around the iris of the eye[5]. People with HoFH are at increased risk of CVD because long-term elevations of cholesterol accelerate the build-up of fatty deposits in the arteries (atherosclerosis). The narrowed arteries can cause diseases such as angina, myocardial infarction and stroke. CVD is a common cause of death in England, and it is a major cause of disability and reduced quality of life.

Managing familial hypercholesterolaemia involves dietary and lifestyle changes such as smoking cessation, weight loss and increased physical activity. NICE clinical guideline 71 recommends that in children and young people with HoFH, LDL-C concentration may be lowered by lipid-modifying drug therapy. It also states that prescribing of drug therapy for adults with HoFH should be undertaken within a specialist centre. Depending on a person's response to lipid-modifying drug therapy and the presence of coronary heart disease, healthcare professionals should consider offering LDL apheresis (a process similar to dialysis which removes LDL from the blood stream) for children/young people and adults with HoFH. Following treatment with lipid-modifying drug therapy and LDL apheresis, healthcare professionals should consider offering liver transplantation.

The technology

Evinacumab (Brand name unknown, Regeneron Pharmaceuticals) is a fully human monoclonal antibody to angiopoietin-like protein 3 (ANGPTL3). ANGPTL3 is produced in the liver and regulates levels of triglycerides, LDL-C, and high-density lipoprotein cholesterol in the blood. Evinacumab binds and inhibits ANGPTL3 and lowers cholesterol. It is administered intravenously.

Evinacumab does not currently have a marketing authorisation in the UK for any indication. It has been studied in a clinical trial compared with placebo in patients with homozygous familial hypercholesterolaemia aged 12 and over.

Intervention(s)	Evinacumab
Population(s)	People with homozygous familial hypercholesterolaemia aged 12 and over
Comparators	• Established clinical management without evinacumab (including but not limited to lomitapide, evolocumab and ezetimibe)
Outcomes	The outcome measures to be considered include: • plasma lipid and lipoprotein levels, including LDL-cholesterol, non-HDL cholesterol, apolipoprotein B and lipoprotein a • requirement of procedures including LDL apheresis and revascularisation • fatal and non-fatal cardiovascular events • mortality • 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: • Presence or risk of cardiovascular disease • People with statin intolerance • Severity of hypercholesterolaemia 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	**Appraisals in development (including suspended appraisals):** Bempedoic acid for treating primary hypercholesterolaemia or mixed dyslipidaemia. NICE technology appraisals guidance [ID1515]. Publication date to be confirmed. Mipomersen for the prevention of cardiovascular events in people with homozygous or severe heterozygous familial hypercholesterolemia. NICE technology appraisals guidance [ID524]. Suspended appraisal. **Related Guidelines:** Familial hypercholesterolaemia: identification and management (2008 updated 2019) NICE guideline CG71 **Related NICE Pathways:** Familial Hypercholesterolaemia (2013) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Clinical Commissioning Policy: Lomitapide for treating homozygous familial hypercholesterolaemia (adults) NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 7 section C Inherited Cardiac Condition Services Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for evinacumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for homozygous familial hypercholesterolaemia? Would evinacumab be used as an adjunct to other lipid-lowering therapy, or as a different line of therapy?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom evinacumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

What is the prevalence of HoFH in England and what data are there to support this?

Where do you consider evinacumab will fit into the existing NICE pathway, Familial Hypercholesterolaemia (2013)?

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 evinacumab 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 evinacumab 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 evinacumab 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 The FH Foundation. What is FH? (2019). Accessed February 2020.

2 National Organization for Rare Diseases. Familial Hypercholesterolemia (2019). Accessed March 2020.

3 Office for National Statistics. Population Estimates (2019). Accessed March 2020.

4 NHS England. Clinical Commissioning Policy: Lomitapide for treating homozygous familial hypercholesterolaemia (adults) (2018). Accessed April 2020.

5 British Heart Foundation. Heart Matters. Focus on: Familial hypercholesterolaemia. Accessed February 2020.