NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Obicetrapib and obicetrapib–ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of obicetrapib monotherapy within its marketing authorisation for treating primary hypercholesterolaemia or mixed dyslipidaemia.

To appraise the clinical and cost effectiveness of obicetrapib–ezetimibe (fixed dose combination) within its marketing authorisation for treating primary hypercholesterolaemia or mixed dyslipidaemia.

Background

Hypercholesterolaemia is the presence of high levels of cholesterol, typically low-density lipoprotein (LDL) cholesterol, in the blood. Primary hypercholesterolaemia may be caused by a genetic defect (familial), or by the interaction of several genes with dietary and other factors (non-familial). There are 2 types of familial hypercholesterolaemia (FH): homozygous and heterozygous. In heterozygous FH, the inherited gene mutations are from a single parent. This is the more common type of FH. Mixed dyslipidaemia is defined as elevations in LDL cholesterol and triglyceride levels that are often accompanied by low levels of high-density lipoprotein (HDL) cholesterol.

People with hypercholesterolaemia or mixed dyslipidaemia are at increased risk of cardiovascular disease (CVD). This is because long-term elevations of cholesterol accelerate the build-up of fatty deposits in the arteries (atherosclerosis). This can result in angina, heart attacks and stroke. CVD causes around a quarter of all deaths in England, equating to around 140,000 deaths per year.[1] It is also a major cause of disability and reduced quality of life.

Managing primary hypercholesterolaemia and mixed dyslipidaemia involves dietary and lifestyle changes such as smoking cessation, weight loss and increased physical activity. In addition to dietary and lifestyle changes, statins are an important first-line treatment used to to lower cholesterol. NICE guidelines CG71 and NG238, and the NHS national guidance for lipid management provide further details on managing hypercholesterolaemia.

- NICE technology appraisal (TA) 385 recommends ezetimibe as an option for treating primary (heterozygous-familial or non-familial) hypercholesterolaemia, as monotherapy when statins are contraindicated or not tolerated, and in combination with statins when initial statin therapy does not provide appropriate control of LDL cholesterol.
- TA733 recommends inclisiran as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults, if there is a history of cardiovascular events and if LDL cholesterol concentrations are persistently

2.6 mmol/l or more, despite maximally tolerated statins with or without other lipid-lowering therapies, or other lipid-lowering therapies when statins are not tolerated or contraindicated.

- TA393 and TA394 recommend alirocumab and evolocumab as options for treating primary hypercholesterolaemia (heterozygous-familial or non-familial) and mixed dyslipidaemia if LDL cholesterol concentrations are persistently above the specified thresholds despite maximally tolerated lipid-lowering therapy.
- TA694 recommends bempedoic acid with ezetimibe as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults, if statins are contraindicated or not tolerated and ezetimibe alone does not control LDL cholesterol well enough.
- TA805 recommends icosapent ethyl with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides, established cardiovascular disease and LDL cholesterol levels above 1.04 mmol/litre and below or equal to 2.60 mmol/litre.

For some people, LDL cholesterol levels may remain above treatment goals despite maximally tolerated lipid-lowering therapy.

The technologies

Obicetrapib (Menarini) and obicetrapib–ezetimibe (Menarini) do not currently have marketing authorisations in the UK for primary hypercholesterolaemia or mixed dyslipidaemia. They have been studied in clinical trials compared with placebo in adults with heterozygous familial hypercholesterolemia or with a history of atherosclerotic CVD, or both. People in the trials were having maximally tolerated lipid-modifying therapy.

Interventions	• Obicetrapib monotherapy with maximally tolerated lipid-lowering therapy, as an adjunct to diet • Obicetrapib–ezetimibe fixed dose combination with maximally tolerated lipid-lowering therapy, as an adjunct to diet
Population	Adults with primary hypercholesterolaemia (heterozygous familial or non-familial) or mixed dyslipidaemia, with or without a history of atherosclerotic CVD, who are on lipid-lowering therapies that did not lower their LDL cholesterol well enough

Subgroups	• Primary hypercholesterolaemia
	  ○ Heterozygous familial
	  ○ Non-familial
	• Mixed dyslipidaemia
	• History of atherosclerotic CVD

Comparators	Maximally tolerated lipid-lowering therapy alone, or in combinations, including: • statins • ezetimibe – as monotherapy when statins are contraindicated or not tolerated and in combination with statins when initial statin therapy does not provide appropriate control of LDL cholesterol • inclisiran – if there is a history of cardiovascular events and if LDL cholesterol concentrations are persistently 2.6 mmol/l or more, despite maximally tolerated statins with or without other lipid-lowering therapies, or other lipid-lowering therapies when statins are not tolerated or contraindicated • alirocumab – if LDL cholesterol concentrations are persistently above the specified thresholds according to NICE TA393 despite maximally tolerated lipid-lowering therapy • evolocumab – if LDL cholesterol concentrations are persistently above the specified thresholds according to NICE TA394 despite maximally tolerated lipid-lowering therapy • bempedoic acid with ezetimibe – if statins are contraindicated or not tolerated, and ezetimibe alone does not control LDL cholesterol well enough • icosapent ethyl – in combination with statins in people with raised triglycerides, established cardiovascular disease and LDL cholesterol levels above 1.04 mmol/litre and below or equal to 2.60 mmol/litre • obicetrapib monotherapy (subject to NICE evaluation) • obicetrapib–ezetimibe fixed dose combination (subject to NICE evaluation)

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
	• triglyceride levels
	• fatal and non-fatal cardiovascular events, including but not limited to:
	  ○ cardiovascular death
	  ○ myocardial infarction
	  ○ stroke
	  ○ non-elective coronary revascularization
	• 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. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	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	**Related technology appraisals:** Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia (2021) NICE technology appraisal guidance 733. Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia (2021) NICE technology appraisal guidance 694. Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (2016) NICE technology appraisal guidance 393. Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (2016) NICE technology appraisal guidance 394. Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia (2016) NICE technology appraisal guidance 385. **Related NICE guidelines:** Familial hypercholesterolaemia: identification and management (2008 updated 2019) NICE guideline CG71 Cardiovascular disease: risk assessment and reduction, including lipid modification (2023) NICE guideline NG238 **Related quality standards:** Cardiovascular risk assessment and lipid modification. NICE quality standard.

References

1. British Heart Foundation. England Cardiovascular Disease Factsheet. Accessed September 2025.