reference no: 1679
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Clinical Commissioning Policy:

Lomitapide for treating homozygous familial hypercholesterolaemia (adults) [1679]

Summary

Lomitapide is recommended to be available as a routine commissioning treatment option for homozygous familial hypercholesterolaemia within the criteria set out in this document.

The policy is restricted to adults aged ≥18 years old[1] in line with the findings of the evidence review.

Committee discussion

Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed here: NHS England » Clinical Commissioning Policy: Lomitapide for treating homozygous familial hypercholesterolaemia (adults)

What we have decided

NHS England has carefully reviewed the evidence to treat homozygous familial hypercholesterolaemia with lomitapide. We have concluded that there is enough evidence to make the treatment available at this time as an alternative, but in the same position in the treatment pathway, to evinacumab.

The evidence review which informs this commissioning position can be accessed here: NHS England » Clinical Commissioning Policy: Lomitapide for treating homozygous familial hypercholesterolaemia (adults)

Links and updates to other policies

This document updates Clinical Commissioning Policy: Lomitapide for treating homozygous familial hypercholesterolaemia (adults) (2018)

This document relates to NICE guidance (CG71) on the identification and management of familial hypercholesterolaemia.

1 Post-pubescent children can access under the Commissioning Medicines for Children Policy. Pre-pubescent children are not covered by this policy given the unavailability of safety data in this age group and children not being included in the drug's marketing authorisation.

This document has been updated in line with NICE Technology Appraisal (TA1002) Evinacumab for treating homozygous familial hypercholesterolaemia in people 12 years and over to include evinacumab as an alternative to lomitapide.

Plain language summary

About homozygous familial hypercholesterolaemia (HoFH)

Familial hypercholesterolemia (FH) is an inherited disease that results in very high levels of harmful cholesterol (a type of fat made by the body). In people with FH, there are raised levels of low-density lipoprotein cholesterol (LDL-C), also known as ‘bad cholesterol’. FH is not caused by an unhealthy lifestyle but is passed from generation to generation through one or more 'faulty genes' that are responsible for making and removing cholesterol in the body.

People with the homozygous form of familial hypercholesterolemia (HoFH) have two faulty copies of these genes. The term HoFH includes HoFH, autosomal recessive hypercholesterolaemia, compound heterozygous familial hypercholesterolaemia and double heterozygous familial hypercholesterolaemia. About 90% of cases are caused by mutations in low density lipoprotein receptors (LDLR). Clinical features of HoFH include small yellow bumps caused by collections of cholesterol under the skin or tendons (xanthomas), greyish-white rings of cholesterol around the iris (corneal arcus), and aortic and supra-aortic valve disease. It puts people at risk of heart diseases much earlier in their lifetimes than compared with the general population, causing heart attacks, heart valve disease (where the valves in the heart become damaged by putting additional pressure on the heart) and strokes.

About current treatment

The NICE guideline on the identification and management of familial hypercholesterolaemia states that healthcare professionals should consider a clinical diagnosis of HoFH in adults with LDL-C greater than 13 mmol/l. It states statins are usually given as initial treatment for all adults with FH, in addition to dietary and lifestyle advice (smoking cessation, dietary manipulation, weight loss, and increased physical activity).

The NICE guidance does not contain any other recommendations for specific medicines that should be given in combination with a statin for people with HoFH; it instead states that prescribing of medicines for adults with HoFH should be undertaken within a specialist centre. Treatments that are used in clinical practice in addition to a statin for people with HoFH include ezetimibe, a bile acid sequestrant (resin), a fibrate, the PCSK-9 inhibitor evolocumab or evinacumab.

The NICE guideline also states that lipoprotein apheresis should be considered for people with HoFH, with the timing for the initiation of this depending on factors such as the person’s response to lipid- modifying drug therapy and presence of coronary heart disease. Finally, the NICE guideline states that liver transplantation should be considered as an option. Transplant is considered if disease progression occurs despite optimal treatment with lipid-lowering medication and lipoprotein apheresis. However, in clinical practice, it is a treatment of last resort, there is a shortage of organs, and the procedure is very rarely performed for people with HoFH because their need for a liver transplant is not prioritised above that of a patient with hepatic failure.

About lomitapide

Lomitapide is thought to block the action of a protein that releases LDL-C into the blood stream and absorbs LDL-C from the intestine. This decreases the amount of fat released into the blood and therefore reduces the level of cholesterol in the blood. The European public assessment report (EPAR) states that lomitapide represents a new class of drugs with a mechanism of action that differs from those of other classes of lipid-lowering medicines.

Lomitapide has a licence as an adjunct to a low-fat diet and other lipid-lowering medicinal products with or without low density lipoprotein (LDL) apheresis in adult patients with HoFH.

Lomitapide is an add-on to existing cholesterol lowering treatments, with dietary and lifestyle advice, and with or without lipoprotein apheresis. It is therefore given if the disease progresses despite these treatments and provides an additional treatment option before the consideration of liver transplant. If the addition of lomitapide controls the disease, then patients and their clinicians may be able to consider stopping or reducing the frequency of apheresis.

Epidemiology and needs assessment

The prevalence of HoFH is estimated to be 1 per 1 million population in the UK (France et al, 2016), although this may be an underestimate because of phenotypic variation (France et al., 2016). Based on actual patient numbers being treated in major apheresis centres, it is estimated that the prevalence of HoFH may be 1 in 670,000 adults in England.

Applying these prevalence rates to the England population aged 18 and over (approximately 45.7 million, ONS 2023), there are between 46 and 68 adult patients in England with HoFH. Based on prevalence rates and life expectancy, is it estimated there will be around 1 new case of HoFH every year.

It is not expected that all people with HoFH would start treatment with lomitapide, since some people will gain adequate control of their cholesterol levels using other treatments. In addition, it is a requirement in the licence for lomitapide that people must have a low fat diet (no more than 20% of their diet from fat) before and during treatment, and some people may have difficulty adhering to this.

Assuming the higher prevalence estimate (68 adults in England), it is estimated that 36 people would be eligible for treatment with lomitapide in NHS practice in England, based on the following assumptions for people with HoFH that is not controlled with existing treatments including lipoprotein apheresis:

- Approximately 22% (15 patients) of people with HoFH have disease that is LDLR negative (based on combining published data from registries in Spain, Sánchez-Hernández, 2016 and Alonso, 2016). LDLR negative disease does not respond to PCSK-9 inhibitors (France et al. 2016), therefore these patients may be eligible for lomitapide.

- The remaining 78% (53 patients) would use a PCSK-9 inhibitor.

- Approximately 30% of people would have disease that does not respond to treatment (Raal et al. 2017) (n=16) and therefore would be eligible for lomitapide.
- Of the 70% of people who do respond to a PCSK-9 inhibitor, approximately 50% would have disease that initially responds but does not reach the recommended LDL-C target (n=19) and therefore be eligible for lomitapide.
- The total number of people currently eligible for lomitapide would be 50. But of these 28% (based on the LOWER registry), would be unwilling or unable to commit to the low-fat diet required to take lomitapide, avoid alcohol, or because of co-morbidities resulting in liver toxicity concerns.
- Therefore it is estimated that 36 patients (72% of those eligible for lomitapide) will remain on it. It is estimated this figure will remain reasonably steady year on year, with any new cases offset by people stopping treatment because of lack of effectiveness, adverse events or death.

Implementation

Inclusion criteria

Lomitapide should only be considered if **ALL** of the following criteria are met:

- Patient has confirmed diagnosis of HoFH should be obtained using 1 of the following criteria:
    - Documented functional mutation(s) in both LDL receptor alleles or alleles known to affect LDL receptor functionality, OR;
    - Untreated LDL-C greater than 13 mmol/L
- HoFH is not adequately controlled by existing treatments (these should include ALL of the following medications (if they are clinically indicated and tolerated): statins, ezetimibe, bowel assisted sequestrants, evolocumab and lipoprotein apheresis (can be combined as appropriate).
- Patient is at high risk of cardiovascular events: where LDL-C is as follows (based on specific therapeutic targets for LDL-C lowering in HoFH set by HEART UK (France et al. 2016) and the European Atherosclerosis Society
    - >2.5mmol/L for adults with FH
    - >1.8mmol/L for adults with atherosclerotic cardiovascular disease.
- Patients should have a low fat diet prior to treatment with lomitapide (<20% energy from fat).

Exclusion criteria

Please review SmPC for guidance regarding exclusion criteria.

Starting criteria

A multidisciplinary team (MDT) made up of people including a physician specialised in lipids (lipidologist), specialist nurse/pharmacist practitioner and dietician should be responsible for prescribing lomitapide. The decision to initiate lomitapide should be as a result of shared decision making between patient and clinician.

Currently 8 centres provide lipoprotein apheresis in England. These centres should be responsible for prescribing lomitapide, monitoring and follow up of patients.

Stopping criteria

A decision to stop using lomitapide should be made by the treating clinician if:

- Lomitapide does not control disease (stop lomitapide treatment if LDL-C levels do not drop by 20% of pre-lomitapide levels) (efficacy is not demonstrated).
- The patient is unwilling or unable to adhere to a low fat diet (<20% of energy from fat).
- Where liver damage may be occurring as guided by the SmPC.

Monitoring

A multidisciplinary team (MDT), as indicated above, should be responsible for prescribing lomitapide, monitoring and follow up of patients.

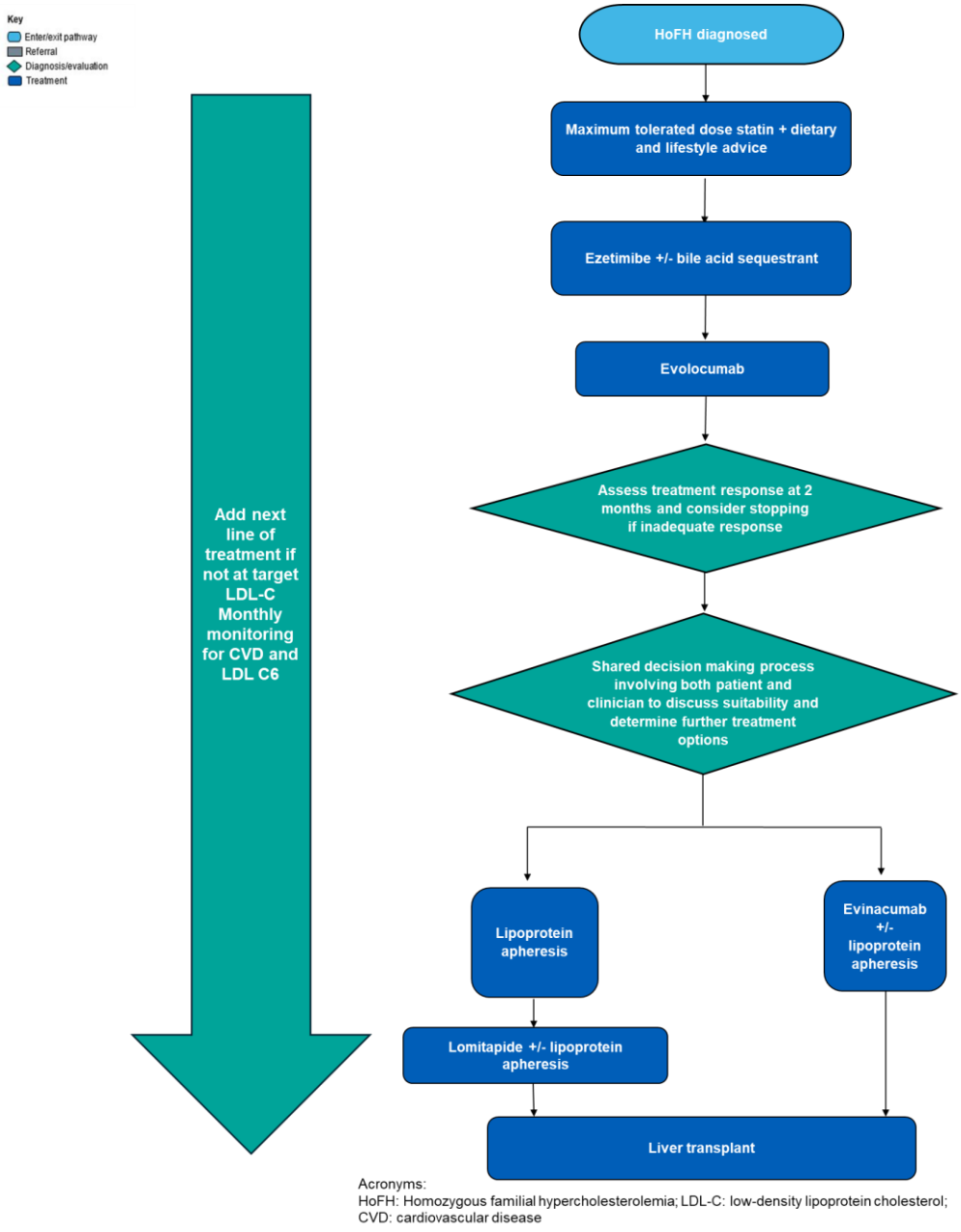
Please see the SmPC for full prescribing details. To minimise the risk of progressive liver disease, the SmPC for lomitapide requires that patients have their liver function tests monitored regularly. It also includes several special warnings and precautions for use related to liver abnormalities and liver monitoring, monitoring of liver function tests, dose modification based on elevated hepatic aminotransferases, hepatic steatosis and risk of progressive liver disease, monitoring for evidence of progressive liver disease, concomitant use of statins and reduced absorption of fat-soluble vitamins and serum fatty acids.

Patients should have a low fat diet during treatment with lomitapide (<20% energy from fat).

Dose

For lomitapide dosing information refer to SmPC.

Patient pathway



Governance arrangements

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Any provider organisation treating patients with this intervention is required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process.

Mechanism for funding

Lomitapide will be commissioned and funded by NHS England Specialised Commissioning under existing arrangements for the provision of service specification for Specialised Endocrine Services (Adult).

Audit requirements

Long-term safety and efficacy of lomitapide in patients with HoFH is being studied in the Lomitapide Observational Worldwide Evaluation Registry (LOWER) study (NCT02135705). This a long-term study in patients taking lomitapide to provide further data on its safety and effectiveness, including its side effects on the liver, stomach, gut, and cardiovascular system (to assess the progression of atherosclerosis). The study will also provide data on pregnancies in women taking the medicine, and on healthcare professionals' compliance with the recommendations to screen and monitor patients before and during treatment. All patients eligible for lomitapide must be registered on LOWER.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and

- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Atherosclerosis	The thickening and hardening of artery walls, which can cause partial or total blockages in the arteries.
Cholesterol	A type of fat known as a lipid that is carried in the blood. It is produced by the liver and can also be found in some foods. It is essential for several processes in the body but too much causes atherosclerosis, increasing the risk of cardiovascular events.
Hepatic steatosis	An accumulation of fat in the liver (also known as 'fatty liver').
Homozygous familial hypercholesterolemia	Familial hypercholesterolemia is an inherited disease that results in exceptionally high levels of low density lipoprotein cholesterol (LDL-C) from birth. The homozygous form of the disease is when there are 2 faulty copies of the genes responsible for cholesterol production and removal. The term HoFH includes HoFH, autosomal recessive hypercholesterolaemia (ARH), compound heterozygous familial hypercholesterolaemia and double heterozygous familial hypercholesterolaemia.
High density lipoprotein (HDL) cholesterol	Known as 'good' cholesterol because it absorbs cholesterol and transports it to the liver where it is removed from the body.
Lipoprotein	A protein in the body that carries cholesterol in the blood, to and from cells. They are particles made up of cholesterol and other lipids in the core surrounded by a single layer of phospholipid molecules. There are four main lipoproteins which can vary in size, content and density: chylomicrons, very low density lipoproteins (VLDL), low density lipoproteins (LDL) and high density lipoproteins (HDL).
Lipoprotein apheresis	This involves using a machine to filter the blood and remove low density lipoprotein cholesterol (and other atherogenic lipoproteins).
Low density lipoprotein (LDL) cholesterol	Known as 'bad' cholesterol because it has a tendency to deposit in the arteries. Over time this can cause a build-up of cholesterol, blood cells and other debris from the body. This causes plaque build-up which can thicken and block the artery, causing cardiovascular problems. LDL cholesterol makes up the majority of cholesterol in the body.

Non-HDL cholesterol	This is the sum of all ‘bad’ cholesterol, including LDL cholesterol. It is calculated by subtracting HDL cholesterol from total cholesterol.
Plaque	Fatty deposits that form inside the artery wall consisting of cholesterol, fatty substances, cellular waste products, calcium and fibrin. Over time plaque build-up hardens and thickens the artery wall, causing it to narrow, and causes partial and sometimes total blockages. This blocks oxygen and blood getting to cells and leads to cardiovascular problems.

References

References which inform this Clinical Policy are located within evidence summary.

France et al, 2016 France M, Rees A, Datta D et al. (2016) HEART UK statement on the management of homozygous familial hypercholesterolaemia in the United Kingdom. Atherosclerosis, 255 128-139.

Raal et al (2017) Long-term treatment with evolocumab added to conventional drug therapy, with or without apheresis, in patients with homozygous familial hypercholesterolaemia: an interim subset analysis of the open-label TAUSSIG study. Lancet Diabetes and Endocrinology. 5(4):280-290