Kent Surrey Sussex Academic Health Science Network

Cardiovascular Disease Prevention

CVD Central: Resource Pack

To support Primary Care with the implementation of Inclisiran

September 2022

KSS AHSN CVD Central Team & Contacts

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Introduction

High cholesterol is a significant risk factor for developing heart and circulatory diseases. In addition to behaviour changes, there are a number of treatment options for high cholesterol.

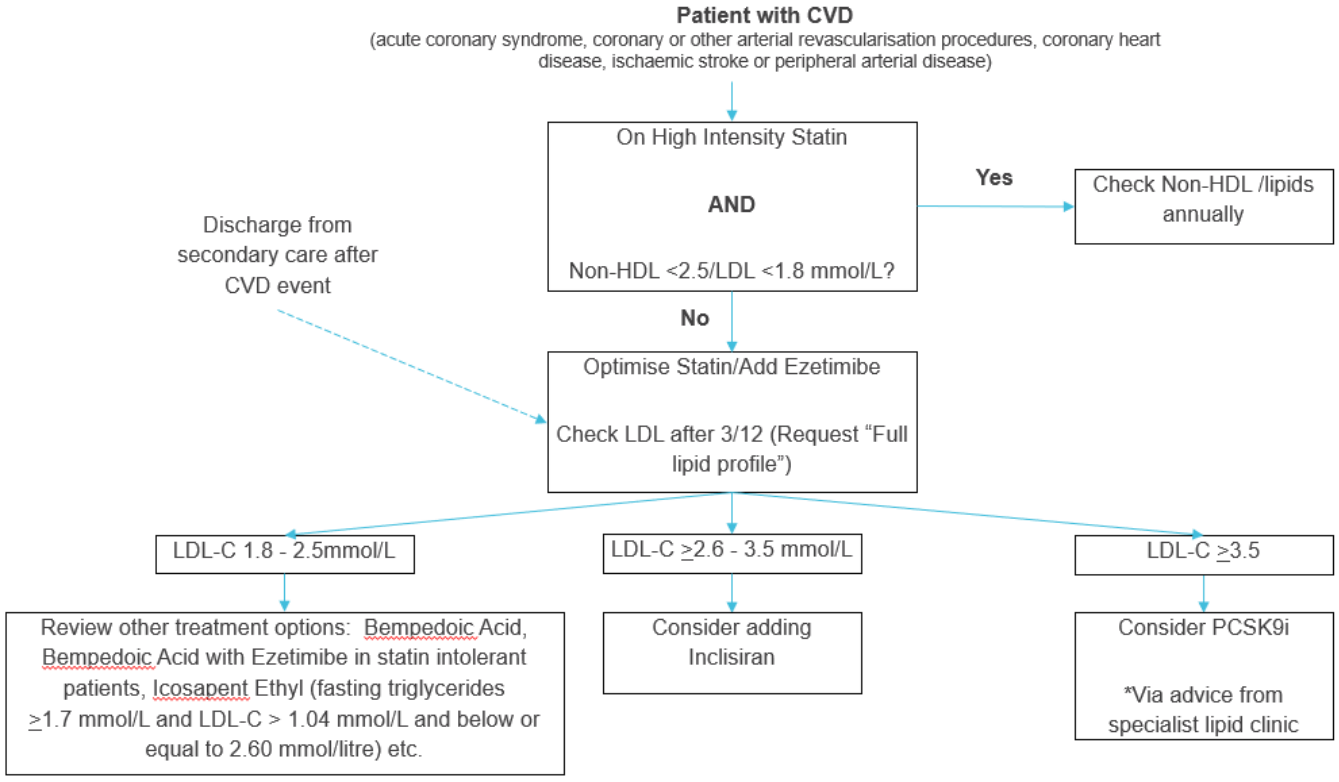
Lipid optimisation is an important aspect of CVD prevention and there are several new therapy options available if statins are not tolerated or effective in reducing cholesterol to target. These include Ezetimibe, Bempedoic Acid, PCSK9 inhibitors and Inclisiran (plus icosapent ethyl for hypertriglyceridaemia).

Inclisiran was added to the NICE endorsed lipid management pathway in October 2021 as a secondary prevention option for patients treated with a maximum tolerated dose of statins and LDL ≥2.6 mmol/L. The lipid management pathway can be found **here**

In October 2020, NHS England commissioned the AHSN Network to deliver a national lipid optimisation and FH programme. The ultimate aim of this three-year programme is to support the NHS Long Term Plan ambition of reducing cardiovascular deaths and disease. The AHSN Network, will work with clinical teams to identify and overcome barriers and realise the benefits of this new therapy, prescribed alongside other medicines in the lipid management pathway. AHSN teams will support local organisations with information and education to raise awareness of the treatment and its benefit for patients within the lipids management pathway.

This document aims to provide some guidance in relation to some of the operational questions and issues that may arise when looking to implement Inclisiran.

Example Inclisiran Pathway:



Frequently Asked Questions (FAQs):

General Information:

Q: What are the licencing details for Inclisiran?

A: Inclisiran (Leqvio®) is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia **(Page 4)**

Q: How do report a concern or incident relating to Inclisiran?

A: Side effects and incidents related to Inclisiran should reported to MHRA via the Yellow Card scheme here: Yellow Card **(Page 4)**

Eligible Patients:

Q: Which patients may be suitable for Inclisiran?

A: All patients with pre-existing ASCVD with last LDL-C of 2.6 mmol/L or higher **(Page 5)**

Q: How do I identify eligible patients?

A: They may be identified from an annual QOF review or by running searches such as Ardens **(Page 5)**

Q: How many patients are likely to be eligible and what will the impact on workload be?

A: From local case study and national analysis, 2 – 4 patients per 1000 population are likely to be eligible for Inclisiran **(Page 6)**

Q: Is there an order in which these patients should be assessed?

A: Although there is no specific order to assess patients, risk stratification for those with multiple CV events, CVD in multiple vascular beds, or those with very high non-HDL-C on maximal tolerated treatment would be appropriate **(Page 6)**

Ordering:

Q: How do I order Inclisiran?

A: To ensure practices receive the £10 per dose they should order Inclisiran direct from the wholesaler AAH by phoning 0344 561 8899 **(Page 8)**

Storage and Administration

Q: Are there any specific storage requirements for Inclisiran?

A: Inclisiran does not require any special storage conditions. It should not be frozen **(Page 9)**

Q: How should Inclisiran be administered?

A: The recommended dose is 284 mg Inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months **(Page 9)**

Resources & Evidence:

Q: Where can I find more information about Inclisiran for our clinical team?

A: Detailed information including NICE guidance, mode of action, administration and side effects are included later in this document **(Page 10)**

Q: Are there additional resources about Inclisiran for patients?

A: Additional information and links to resources are included later in this document **(Page 10)**

Q: Are there any additional resources to support practices in the use of this medicine?

A: Some areas (e.g. Sussex) provide additional payments via Locally Commissioned Service (LCS). Please check with your local PCN /ICB.

A: Kent Surrey and Sussex AHSN can provide further information and support to practices around the wider Lipid and FH pathway and Inclisiran implementation. Email us at: kssahsn.cvdprevention@nhs.net

General Information

Drug Details:

Drug Name: Inclisiran

Brand Name: Leqvio®

Drug Form: Solution for injection in pre-filled syringes

Drug Strength: 284 mg (equivalent to 300 mg inclisiran sodium)

Each pre-filled syringe contains inclisiran sodium equivalent to 284 mg inclisiran in 1.5 ml solution

Inclisiran is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin, or statin with other lipid lowering therapies, in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin, or
- alone or in combination with other lipid lowering therapies in patients who are statin intolerant, or for whom a statin is contraindicated.

Drug dose: The recommended dose is 284 mg inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months.

Intended Duration of Use: Long-term

Incident Reporting:

The MHRA runs the Yellow Card scheme, which collects and monitors information on suspected safety concerns involving healthcare products, such as, a side effect with a medicine. The scheme relies on voluntary reporting of problems by healthcare professionals and members of the public to enable issues to be identified that may not be known about.

To report an incident related to Inclisiran please visit: Yellow Card

If you are not able to submit a report via the website, please send an email with as much information as possible (excluding patient identifiable data) to yellow.card@mhra.gov.uk

Eligibility for Inclisiran:

Inclisiran is licensed for patients with existing **Atherosclerotic Cardiovascular Disease (ASCVD)**

This includes:

- Acute Coronary Syndrome (such as myocardial infarction, or unstable angina requiring hospitalisation)
- coronary or other arterial revascularisation procedures
- coronary heart disease
- ischaemic stroke
- peripheral arterial disease

AND

- low-density lipoprotein cholesterol (LDL-C) concentrations are persistently 2.6 mmol/l or more, despite maximum tolerated lipid-lowering therapy, that is:
    - maximum tolerated statins with or without other lipid-lowering therapies or,
    - other lipid-lowering therapies when statins are not tolerated or are contraindicated

Lipid Optimisation

It is slightly confusing that those patients requiring optimisation are not the same as those eligible for Inclisiran, so this is one recommended way of addressing this:

- If the last non-HDL-C is **<2.5 mmol/L** then the patient is to target and does not require further optimisation (as long as triglycerides also <1.7 mmol/L). Simply arrange an annual check for total cholesterol and non-HDL-C.
- If the last non-HDL-C is **≥ 2.5mmol/L** then review their notes to see if there have previous attempts to optimise lipid levels.
- Consider change to high intensity statins if not already taking (atorvastatin or rosuvastatin)
- Consider up-titration of high intensity statins if not already tried.
- Consider addition of ezetimibe 10mg if not already tried
- If despite this LDL-C remains at ≥2.6 mmol/L then consider Inclisiran.

Eligible patients may be identified during annual QOF or other LTC reviews.

Alternatively, patients may be identified by searches including EMIS, Ardens and System One **(Page 6)**

Identifying patients eligible for Inclisiran and planning for impact on clinical workload:

Searches:

Patients may be identified during annual QOF or other LTC review. Alternatively, they may be identified by computer searches.

- Ardens
- EMIS
- System One

Ardens Example:

Ardens: Conditions -> cardiovascular -> Alerts -> CVD -> ?Inclisiran indicated (CVD + LDL-C > 2.5)

Ardens searches have been updated to include a non-HDL proxy. This means that the Ardens search will now look for **CVD diagnosis + LDL-C >2.5 OR non-HDL >3.4 + maximum tolerated statins.**

The non-HDL proxy of 3.4 mmol/L is in line with European guidance which can be found here:

Section 4.6.1.3 non high density lipoprotein cholesterol - table 10: *2021 ESC Guidelines on cardiovascular disease prevention in clinical practice*

EMIS Example:

In EMIS search is in folder 5.1 – Conditions/Cardiovascular/CVD/Inclisiran

Example Case Study from a GP Practice on Expected Eligible Patients:

The average practice will identify 2 to 4 eligible patients per 1000 population. **For example in this case study,** the Ardens search was run in a practice of 11,500 patients with a CVD prevalence of 6% and only 39 eligible patients were identified (not all of whom may in reality be eligible for, or accepting of, further treatment).

The collaborative project between NHSE and Novartis assumes these patients will be assessed and the drug initiated within three years of the start of the project (November 2021).

In the above example that would mean 13 patients having an informed discussion with an appropriately trained and skilled clinician each year for 3 years. The first two doses are given 3 months apart and then every subsequent 6 months. It is expected that maybe as few as 22.5% of patients will start the treatment but workload is calculated in the event of 100% of patients accepting.

Example modelling of patient contact based on case study

Year 1:

13 informed discussions

39 doses given.

Year 2:

13 informed discussions

65 doses given

Year 3:

13 informed discussions

81 doses given.

Informed discussion appointments will be reduced by identifying unsuitable patients e.g. other life-limiting illnesses, the impact on nursing appointments could be much lower again depending on patient uptake. Each dose ordered is associated with £10 net income to the practice (NHS tariff cost £45, FP34D reimbursement £55).

Risk Stratification of Eligible Patients:

Practices may simply work through the list of eligible patients but if there is a concern about the workload, it may be worthwhile briefly reviewing the records to risk stratify patients.

Those at highest risk would be those with recurrent CV events, for instance admission with Acute Coronary Syndrome following Percutaneous Coronary Intervention (PCI) of Coronary Artery Bypass Graft (CABG).

Patients with ASCVD in multiple vascular beds, for instance coronary heart disease and stroke or stroke and peripheral arterial disease, will be considered at higher risk.

Another way of risk stratifying patients would be to start with those with the highest non-HDL-C despite maximal tolerated lipid lowering therapy.

Although the Ardens Inclisiran search only includes those who have ever been prescribed a statin, it would obviously be worthwhile including those who have always declined a statin or where a statin was never initiated because it was contraindicated.

How do I order Inclisiran?

Inclisiran initiation and management is intended to be carried out predominantly within the primary care setting where most patients with ASCVD are currently managed. However, it is possible to order in secondary care as per the guidelines below:

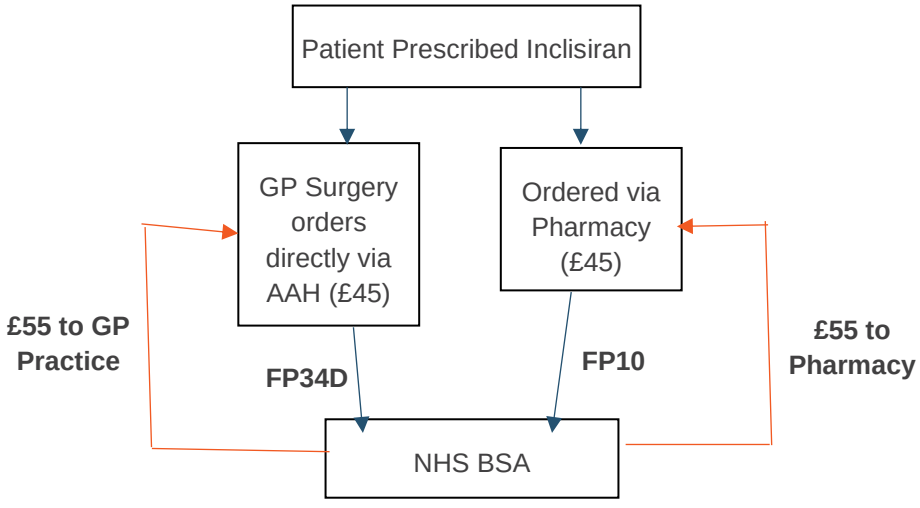
Primary Care:

- The preference is for Inclisiran to be ordered directly to the GP practice (£45 per pre-filled syringe) by calling the AAH customer care team on 0344 561 8899.
- Inclisiran should be administered by the GP practice and added to the FP34D submission to NHS BSA (done by the practice team at the end of each month). Typically, there would be no patient prescription charge via this method.
- The GP practice will be reimbursed at the NHS discounted drug tariff price of £55. The difference between the purchase price the NHS reimbursement price (i.e. £10) represents an injection administration and handling fee.
- Inclisiran can also be supplied by the FP10 route, with the patient bringing the injection to the surgery for administration. If issued via FP10, patients would pay the prescription charge, if they normally do so. A GP practice will not be paid this £10 fee if they obtain inclisiran from a pharmacy via the FP10 route.

AAH Accounts:

- To order Inclisiran directly from AAH, the GP practice will be required to create an account by following this link: https://www.aah.co.uk/s/opening-an-aah-account
- **IMPORTANT:** To prevent surcharges from being incurred by the practice, the practice must email AAH to state that they wish to make their account 'solus'. Once the account is marked as 'solus' no charges will be incurred.

The process below outlines the reimbursement process for doses of Inclisiran in primary care:



Secondary Care Ordering:

Preferred route (FP10HNC)

Prescriptions are funded from a central NHSE/I budget.

1. Eligible patients are identified by secondary care specialist in line with the NICE guidance;
2. Pre-filled syringes are ordered directly at the confidential contract price;
3. The usage is reported under Commissioned Service Category Code 21; a Blueteq form and the DrPLCM are completed and provided for reimbursement.

Stock can be ordered directly from the Novartis Customer Care Team (who can be contacted via telephone: 08457 419 442, fax: 08457 419 443 or email: commercial.team@novartis.com) using this code: EAN code 7613421044237.

It can also be supplied by FP10(HP) route (patients will need to collect the pack at a community pharmacy and get administered either at the hospital or by an appropriate primary care provider.)

Storage and Administration of Inclisiran

Storage:

- Inclisiran does not require any special storage conditions. It should not be frozen.
- Inclisiran has a 2-year shelf life.
- Inclisiran solution should be clear, colourless to pale yellow and essentially free of particulates. If the solution contains visible particulate matter, the solution should not be used.

Administration:

- The recommended dose is 284 mg inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months.
- Inclisiran is given by subcutaneous injection into the abdomen; alternative injection sites include the upper arm or thigh. Injections should not be given into areas of active skin disease or injury such as sunburns, skin rashes, inflammation, or skin infections.

Resources and Clinical Information

Inclisiran Patient Booklet:

A patient's guide to Inclisiran may be downloaded via the following link:

Inclisiran ▼ (LEQVIO®) Public Home | Novartis UK

HCP Inclisiran Portal:

For HCPs link to the Novartis Inclisiran portal page:

Inclisiran ▼ (Leqvio®) Resources | Novartis UK HCP Portal

NICE TA733: Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia:

NICE guidance can be found here: Inclisiran | Guidance | NICE

National Guidance for Lipid Management:

The national lipid management pathway, which includes Inclisiran can be found here:

NHS Accelerated Access Collaborative » Summary of national guidance for lipid management (england.nhs.uk)

Introducing Inclisiran to the Lipid Management Pathway:

Professor Ahmet Fuat MBChB PhD FRCGP FRCP (London) FRCP (Edinburgh) FPCCS PGDiP Cardiology, describes his experience of using the novel therapy Inclisiran for patients in North East and North Cumbria:

AHSN | Introducing Inclisiran into the Lipid Management Pathway - YouTube