Health Innovation Kent Surrey Sussex

Cardiovascular Disease Prevention

CVD Central: Resource Pack

To support Primary Care with the implementation of Inclisiran

September 2024

Health Innovation KSS – CVD Prevention Team compiled this resource document. created September 2022, updated December 2022 and September 2024. V2

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Join our new FutureNHS CVD Central Community of Practice - you will be able to find the recordings and full copy of the slides from a range of topics from CVD webinars

Introduction

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

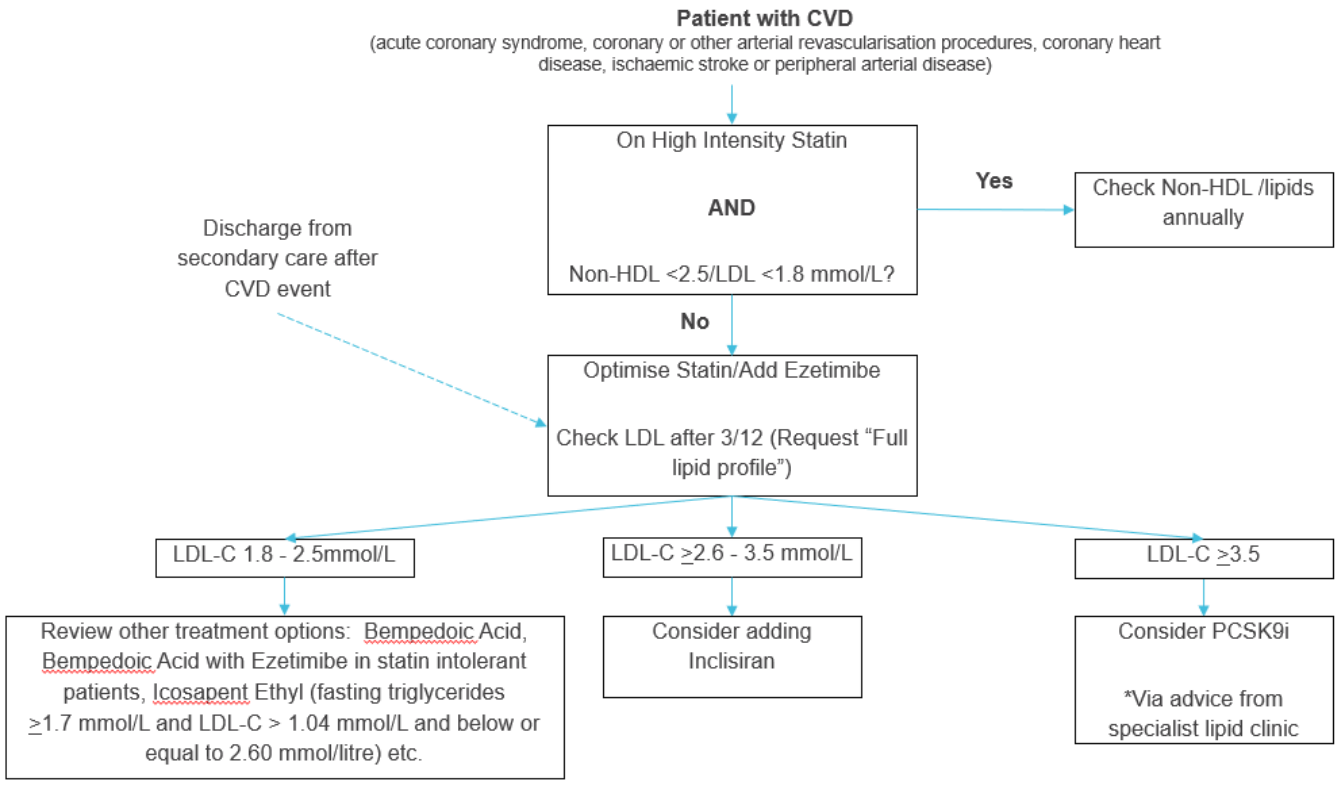
Lipid optimisation is an important aspect of CVD prevention and there are several new therapy options available if statins are not tolerated or effective in reducing cholesterol to target. These include Ezetimibe, Bempedoic Acid, PCSK9 inhibitors and Inclisiran (plus icosapent ethyl for hypertriglyceridaemia).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

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. Inclisiran should be delivered as part of a **lipid management pathway,** in support of improving CVD prevention in England which has been recognised as a priority reflected by the introduction of two new lipid management incentives into QOF [1]

Inclisiran is an effective LDL-C lowering therapy that can help primary care practices achieve QOF cholesterol targets recommend by NICE as a treatment option for high-risk patients with sub-optimal lipid management[5]. It's given by injection every three to six months.

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:



Quality Outcome Framework (QOF) 2024/25

High cholesterol is one of the most significant risk factors for CVD. Globally, a third of ischaemic heart disease is attributable to high cholesterol. It is estimated to account for 7.1% of deaths and 3.7% of disability-adjusted life years (DALYS) in England.

With a heightened focus on the role of cholesterol within secondary prevention QOF has two cholesterol indicators (worth 30 points~£36m), within the Quality Outcomes Framework 2024/25 (england.nhs.uk)

- **CHOL003.** Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, Stroke/TIA or Chronic Kidney Disease Register who are currently prescribed a statin, or where a statin is declined or clinically unsuitable, another lipid-lowering therapy
- **CHOL004.** Percentage of patients on the QOF Coronary Heart Disease (CHD), Peripheral Arterial Disease (PAD), or Stroke/ Transient Ischaemic Attack (TIA) Register, who have a recording of LDL (Low-density Lipoprotein) cholesterol in the preceding 12 months that is 2.0 mmol/L or lower or where LDL cholesterol is not recorded a recording of non-HDL (High-density Lipoprotein) cholesterol in the preceding 12 months that is 2.6 mmol/L or lower

CHOL003 (Based on NICE 2022 menu ID: NM212)

CHOL003 Rationale:

1) The aim of this indicator is to ensure that all patients with established cardiovascular disease, defined as Coronary Heart Disease, Peripheral Arterial Disease, Stroke/TIA or Chronic Kidney Disease receive treatment to reduce cholesterol in line with NICE guidelines, summarised here: https://www.england.nhs.uk/aac/publication/summary-of-national-guidance-for-lipid-management/

2) Treatment with a statin is recommended as first line therapy for the secondary prevention of CVD . Options recommended by NICE when a statin is declined or clinically unsuitable due to contraindications or intolerance include:

   a) Ezetimibe, with the addition of bempedoic acid if a sufficient fall in cholesterol is not achieved with ezetimibe monotherapy.

   b) PCSK9 inhibitors for people with an LDL persistently above 3.5 or 4.0 mmol/L depending on their CVD risk profile.

   c) Inclisiran for people with an LDL persistently 2.6mmol/L or above.

   iii. Where a statin is declined or clinically unsuitable due to contraindications or intolerance, these treatments will be included as a ‘success’.

CHOL004 (NICE 2023 menu ID: NM252)

CHOL004 Rationale:

1) The purpose of the indicator is to introduce an interim outcome measure for the use of lipid lowering treatments outlined in CHOL001, for patients with established cardiovascular disease. This aims to ensure that all patients with established cardiovascular disease, defined as Coronary Heart Disease, Peripheral Arterial Disease, or Stroke/TIA are considered for intensification of therapy where there is an insufficient reduction in cholesterol with first line therapy, usually a statin.

2) The aim of managing LDL cholesterol to 2.0 mmol/L or lower or non-HDL cholesterol to 2.6 mmol/L or lower is aligned with the NICE guideline NG238 for Cardiovascular disease: risk assessment and reduction, including lipid modification. The full guideline can be found here: https://www.nice.org.uk/guidance/ng238

3) Where there is an insufficient reduction in cholesterol, treatment should be intensified in line with NICE guidance which is summarised here: https://www.england.nhs.uk/aac/publication/summary-of-national-guidance-for-lipid-management/

4) Patients may be considered for the addition of ezetimibe or injectable therapies in line with the NICE inclusion criteria for the individual agents – for example, for inclisiran, patients must have an LDL≥ 2.6mmol/L and for the use of PCSK9i(mabs), an LDL cholesterol > 3.5 or 4mmol/L depending on their risk profile. Where statin intolerance exists and ezetimibe monotherapy is ineffective, the addition of bempedoic acid may be considered in line with the statin intolerance pathway: https://www.england.nhs.uk/aac/publication/statinintolerance-pathway

For those working in clinical practice, it may be useful to create yourself a handy 'lipids management folder' by **printing** out the documents from the 3 links below, so you can refer to them when you see patients for lipid management in your clinic. To note the lipid clinic referral form is available on all NHS Sussex and Kent & Medway GP clinical systems (Emis and SystmOne) via Ardens templates:

Documents to print (3 links below):

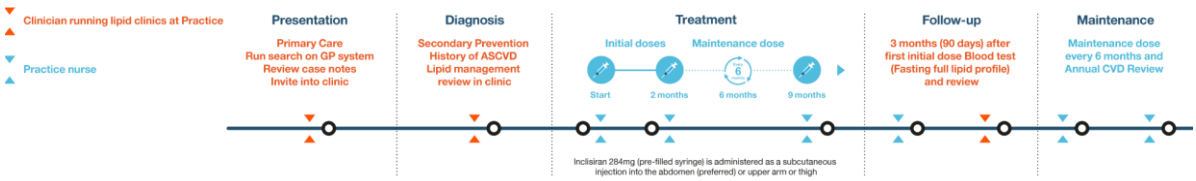
1. National Lipid Management Pathway
2. Lipid Clinic Referral Form
3. Inclisiran Pathways

Implementing Inclisiran in a GP Practice setting

Inclisiran Pathways – for GP Practice MDT Team

The **Inclisiran Pathways** were created for practices, to set out the eligibility criteria and guidance for the MDT Team to refer to at the GP Practice. The pathways will hopefully help practices to set up a system for patients through MDT working from Inclisiran initiation to follow up.

InclisiranPathway: Secondary Prevention 1



Inclisiran is licensed for patients with existing **Atherosclerotic Cardiovascular Disease (ASCVD)** with history of any of the CVD events below:

ELIGIBLE CVD PATIENTS:

- ACS (MI or unstable angina needing hospitalisation)
- Coronary or other arterial revascularisation procedures
- Coronary heart disease
- Ischaemic stroke or
- Peripheral arterial disease,

and

- LDL-C persistently >2.6 mmol/l, despite max. tolerated lipid - lowering therapy: statins with or without other therapies or, other therapies when statins are not tolerated.

Inclisiran is indicated in adults:

- 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.

Inclisiran FACTS:

- Drug undetectable within 48 hours (t1/2 9 hrs, no accumulation)
- LDL reduction apparent within 14 days; in 90 days up to 52% further reduction in LDL-C levels, in addition to maximum oral therapy.
- No known side effects (injection site mild and transient)
- No known drug interactions
- No data on pregnancy, breast feeding, severe hepatic impairment

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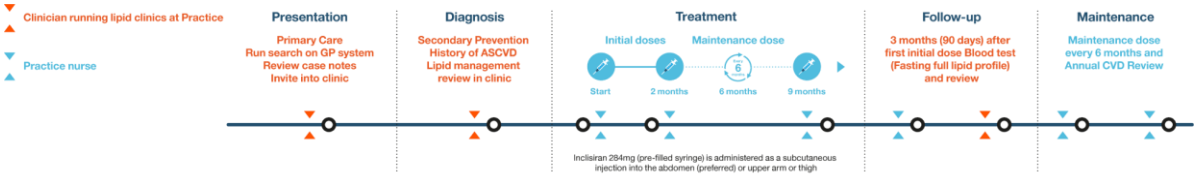
Inclisiran Pathway and Practice pathway x 2 slides created by Jen Bayly on behalf of NHS Sussex and HI KSS (September 2023). Email contact: jennifer.bayly@nhs.net

Inclisiran: Practice pathway 2

Inclisiran initiation and management is intended to be carried out predominantly within the primary care setting wher most patients with ASCVD are currently managed



Inclisiran Consultation: Clinician running lipid clinics Primary Care Pathway

PC 1: Run search on GP system for eligible patients.
PC 2: Review patient case notes to check CVD history and if eligible
PC 3: Invite patient/s in for a lipid management review
PC 4: At consultation discuss prevention, risk factors, lipid level results, lifestyle and lipid lowering therapy options as per eligibility.
PC 5: Provide verbal and also written information on Inclisiran and discuss how the medicine works, the aim to reduce LDL -C levels, the administration, side effects, follow up blood tests and review, etc. Printable CVD Central - Summary of Inclisiran Patient Information May 2023
PC 6: For CVD assessment: check sitting and standing BP readings, pulse rate, pulse rhythm
PC 7: Agree preferred treatment option with patient, advise of next steps
PC 8: Write initial first dose Inclisiran prescription and print for the nurse or lead who orders it from AAH via the GP practice AAH account.

Inclisiran ordering and administering: Practice Nurse Practice Pathway

PP 1: Order Inclisiran injection from AAH to the GP practice
PP 2: Invite patient in to administer first dose injection
PP 3: Advise patient next initial dose is in 3 months, order next dose, invite patient in to administer second initial dose
PP 4: Complete blood form for **Fasting** lipids (full lipid profile) and book in patient for fasting blood test 3 months (90 days) after first initial dose. (can be on same day as second dose (preferred), or days before, or after second initial dose)
PP 5: Book patient in for review of lipid management with lipid clinician
1 week after blood test
PP 6: Commence routine 6 monthly maintenance doses and annual CVD review plus bloods (including **Non-Fasting** full lipid profile)

- Inclisiran Implementation and FAQs Resource Pack to support Primary Care available to download directly from: CVD Central Website

Storage / Shelf-life

- No special storage conditions (do not freeze)
- Shelf-life = 3 years.

As Inclisiran is classed as an MHRA black triangle ▼drug, any suspected adverse reactions should be reported via the **Yellow card scheme**

Missed doses

- Planned dose missed by **less than 3 months**: Administer Inclisiran and continue as per original dosing schedule
- Planned dose missed by **more than 3 months**: Start new dosing schedule i.e., initial dose, second dose at 3 months, followed by a dose every 6 months.

Fasting blood test: Patient advice

On the day (prior) to having the fasting lipids blood test

Can have:

- Water
- Medicines
- Tea without sugar or milk
- **Avoid having any fat or sugar**

Cardiovascular Disease Prevention

Inclisiran Pathway and Practice pathway x 2 slides created by Jen Bayly on behalf of NHS Sussex and HI KSS (September 2023). Email contact: jennifer.bayly@nhs.net

Cardiovascular Disease Prevention

FAQs: Inclisiran for the optimisation of Lipids in secondary prevention of Atherosclerotic Cardiovascular Disease

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 for optimisation and what will the impact on workload be?

A: From local 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 £5 per dose reimbursement they should order Inclisiran direct from the wholesaler AAH, directly to the GP practice (£45 per pre-filled syringe) by ordering Inclisiran directly from the AAH account the GP Practice has set up. **(Page 8)** (note: reimbursement amount reduced to £5 from the 1st April 2023 with the introduction of the new QOF targets.

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 10)**

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 11)**

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 10)**

Q: Are there additional resources about Inclisiran for patients?

A: Additional information and links to resources are included later in this document **(Page 11)**

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: Health Innovation KSS 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

Resources & Evidence:

Clinical trial data demonstrates it leads to a further 50-60% reduction in LDL cholesterol. Whilst, there is limited long-term data for Inclisiran yet, The Orion3 published in January 2023 provides further reassurance**. Link here: Orion 3 Lancet Jan 2023**

The data in ORION-8 represents the largest long-term safety and efficacy follow-up trial with LEQVIO to date:

ORION-8 is a 3-year open-label extension study from the pivotal trials, including 3,274 eligible patients with ASCVD, ASCVD risk equivalent or HeFH who completed either the Phase 2 ORION-3 study or one of the three Phase 3 studies (ORION-9, ORION-10 or ORION-11).ORION-8 pre-specified lipid goals: ASCVD <1.8 mmol/L (<70 mg/dL); ASCVD risk equivalent <2.6 mmol/L (<100 mg/dL).[3] With over 12,000 patient-years exposure and >20,000 injections, the safety profile of LEQVIO® remains consistent, with no new safety signals identified.

There is overwhelming evidence of the benefit of LDL cholesterol reduction and lowering LDL cholesterol is irrefutably associated with a reduced risk of further cardiovascular events.

Inclisiran is now considered normal clinical practice and has an established position in national, NICE, and local lipid pathways. Therefore, the potential risk in prescribing Inclisiran for an individual GP should be minimal.

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 **<2.6 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 **≥ 2.6mmol/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: Population reporting > Ardens > 4.10 conditions-cardiovascular (v18.8) > medication - Inclisiran

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).

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

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 £5 net income to the practice (NHS tariff cost £45, FP34D reimbursement £50).

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.

A systematic approach to the identification of people who will benefit from lipid optimisation is recommended; this will also identify those individuals who will benefit from novel therapies such as Inclisiran.

Identify patient cohort

The UCLPartners CVD Proactive Care Frameworks provide a platform for optimising clinical care and self-care for people with these high-risk conditions, supporting primary care teams to do things differently and at scale. such as:

- enable practices to prioritise clinical activity by stratifying patients who are at the highest risk
- deploy the wider workforce to reduce the workload for GPs
- improve the personalised care offer for patients.

They are free and can be downloaded directly into a practices clinical system and help identify the individuals who would benefit from a review and possible referral.

The following slide packs include pathways and resources to support clinicians treating patients with single or multiple cardiovascular conditions.

• Atrial Fibrillation

• Heart Failure

• Hypertension

• Lipid management including Familial Hypercholesterolaemia

• Type 2 Diabetes

The frameworks include:

1. Comprehensive **search tools** to risk stratify patients – built for EMIS and SystmOne
2. **Pathways** that prioritise patients for follow up, support remote delivery of care, and identify what elements of LTC care can be delivered by staff such as Health Care Assistants and link workers.
3. **Scripts and protocols** to guide Health Care Assistants and others in their consultations.
4. **Training** for staff to deliver education, self-management support and brief interventions. Training includes health coaching and motivational interviewing.
5. **Digital and other resources** that support remote management and self-management

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:

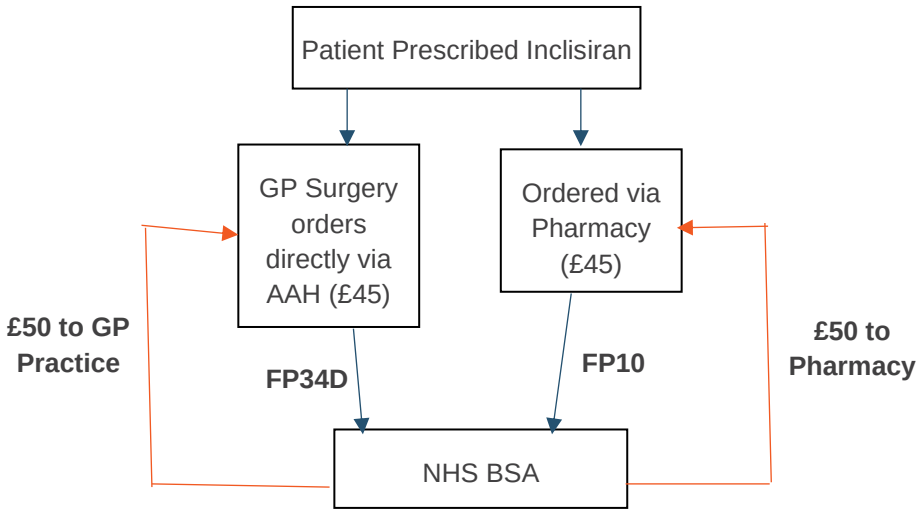
- The preference is for Inclisiran to be ordered directly to the GP practice (£45 per pre-filled syringe) by ordering Inclisiran directly from the AAH account the GP Practice has set up.
- **AAH Accounts:** To get set up with an account with AAH the GP practice will be required to create an account by 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.
- It is recommended the best route to contact AAH is via the practice online account or by email. If necessary though the AAH customer care team are available on 0344 561 8899.
- NHS England fund inclisiran centrally from a national NHS budget (funding and supply of inclisiran) in order that local finances are not a barrier to access
- Inclisiran is available in general practice as a personally administered item reimbursed via an FP10 prescription and is listed in the Drug Tariff at a Reimbursed Amount of £50 (from 01 April 2023) per injection (the £45 Nominal Charge plus £5) (**note:** reimbursement amount reduced from £10 to £5 from the 1st April 2023 with the introduction of the new QOF targets)
- The GP practice will be reimbursed at the NHS discounted drug tariff price of £50. The difference between the purchase price the NHS reimbursement price (i.e. £5) represents an injection administration and handling fee.
- 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.
- Inclisiran, as an injectable (not a vaccine), is considered a personally administered item. Depending on whether your practice is a dispensing or non-dispensing practice you may be required to use a different version of the FP34 when submitting a claim to NHS BSA. The table below outlines, which form to use:

Type of dispensing contractor	Type of item dispensed	Form to send	Form colour
Appliance contractor	Medical appliance	FP34A	Green
All dispensing contractors	Private controlled	FP34PCD	White
Dispensing doctor	Any item allowed on an FP10	FP34D Submission Document	Pink

Dispensing doctor	High volume personally administered vaccine item	FP34D Appendix form (together with FP34D Submission Document)	Pink
GP who is not a dispensing doctor	A personally administered item (such as a vitamin B12 injection)	FP34PD Submission	Peach
GP who is not a dispensing doctor	High volume personally administered vaccine item	FP34PD Appendix form (together with the FP34PD Submission Document)	Peach
Pharmacists	Any allowed item on an FP10	Account Identifier Document (FP34C submitted digitally on MYS)	White

IMPORTANT: 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 £5 fee if they obtain inclisiran from a pharmacy via the FP10 route.

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



Secondary Care Ordering:

NHS trusts can also prescribe and recharge the cost of inclisiran to NHS England which means there should not be a cost barrier to patient access to inclisiran in secondary care.
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.

Warnings and precautions before giving Leqvio: - for patients receiving dialysis – with severe liver disease - severe kidney disease.

You must not give Leqvio - if patient is allergic to inclisiran or any of the other ingredients of this medicine (listed below in what inclisiran contains).

What Inclisiran contains

- The active substance is inclisiran.
- Each pre-filled syringe contains inclisiran sodium equivalent to 284 mg inclisiran in 1.5 ml solution.
- Each ml contains inclisiran sodium equivalent to 189 mg inclisiran.
- The other ingredients are water for injections, sodium hydroxide (see section 2 “Leqvio contains sodium”) and concentrated phosphoric acid.

Resources and Clinical Information

Inclisiran Patient Booklet:

"A patient's guide to Inclisiran (Leqvio®)" produced by Novartis, April 2022, download via the following link: https://www.health.novartis.co.uk/resources-and-training/cardio-metabolic/product/inclisiran-resources/#dwell

Package leaflet – information for the patient, download via this 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 NICE-endorsed national lipid management pathway, which includes Inclisiran can be found here: National Lipid Management Pathway

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

Health Innovation KSS hosted two learning webinars on Inclisiran to support Primary Care

Discussing how Inclisiran fits within the **NICE Lipid Management pathway,** some of the operational considerations and shared examples of patients who would benefit from Inclisiran treatment. You can find the links to the October session below:

- 6th October 2022 - Click **here** to view the recording.
- Click **here** to access the slides

Patient-focused resources from HEART UK:

- **HEART UK** have produced a helpful animation, which may be beneficial to share with your patients, to better understand their cholesterol.
- They also have a helpful diet quiz - All quizzes - HEART UK
- **Heart UK:** www.heartuk.org.uk/
- **Heart UK -** Tackling Cholesterol Together gives a very useful holistic overview/training/education/resources on managing cholesterol. Link here: Tackling Cholesterol Together (heartuk.org.uk)

Inclisiran for managing high cholesterol: A guide for patients.

There are several tablets now available to lower cholesterol levels in the blood, including statins (e.g., atorvastatin, rosuvastatin, and pravastatin), ezetimibe and bempedoic acid.

If you can't take any of these medicines, or your cholesterol levels are still too high when you're taking them, your healthcare professional might talk to you about considering medicines which are injected, either instead of tablets or in addition to them.

Inclisiran (brand name Leqvio®) is one of the injectable medicines currently available for lowering cholesterol levels.

How inclisiran works:

Low density lipoprotein (LDL) is a substance in the body which carries cholesterol from the liver to cells that need it. LDL is sometimes known as "bad" cholesterol because high levels lead to fatty build-up inside the arteries, which increases the risk of heart disease (also known as cardiovascular disease, or CVD).

Inclisiran lowers the levels of a type of protein called PCSK9 in the cells of the liver, and by doing this increases the number of LDL-receptors. These receptors act as "dump trucks" to help get rid of LDL ("bad") cholesterol from the blood stream so that they can be broken down in the liver.

The less LDL cholesterol in the bloodstream, the lower your risk of major adverse cardiovascular events.

What inclisiran is used for:

Inclisiran is used in addition to your cholesterol-lowering diet if you are an adult with a high cholesterol level in your blood (primary hypercholesterolaemia, including heterozygous familial and non-familial, or mixed dyslipidaemia).

Inclisiran is given: - together with a statin (a type of medicine that treats high cholesterol), sometimes combined with another cholesterol-lowering treatment if the maximum dose of the statin does not work well enough, or - alone or together with other cholesterol-lowering medicines when statins do not work well or cannot be used.

How is inclisiran given?

Inclisiran is given as an injection under the skin and will be administered by your healthcare professional.

When you start treatment, you will be given a single injection, followed by another injection 3 months later. After these first two injections, inclisiran will be given every 6 months.

Treatment with inclisiran is intended to be long-term so will continue indefinitely unless you and your healthcare professional decide there is a reason to stop. It should also be taken alongside

any other cholesterol-lowering medicines that you are currently taking. Do not stop your statin or other cholesterol-lowering tablet unless you have been told to do so.

Important information

Inclisiran is a new-in-class drug, so it acts in a different way from all the other cholesterol-lowering drugs. It has its effect by reducing the gene expression of the PCSK9 protein. By reducing the expression of the PCSK9 protein, you have more LDL receptors to help remove LDL-C from your blood stream.

Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common (may affect up to 1 in 10 people)

• Injection site reactions, such as pain, redness, or rash.

Reporting of side effects If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in the package information leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine

Where can I find more information?

The following resources are available online to download and access electronic versions, or your GP practice may send them to you in a link by text message, they are also available to order for free in hard copies.

Inclisiran patient information:

This summary guide was adapted from **"A patient's guide to Inclisiran (Leqvio®)"** produced by Novartis, April 2022. This full document can be found at: https://www.health.novartis.co.uk/resources-and-training/cardio-metabolic/product/inclisiran-resources/#dwell

Package information leaflet for patients: Leqvio, INN-inclisiran (medicines.org.uk)

Further information on how cholesterol increases the risk of heart disease and how it can be managed can be found on these websites:

- Heart UK: The cholesterol charity www.heartuk.org.uk
- NHS Health A to Z www.nhs.uk/conditions/high-cholesterol/
- British Heart Foundation www.bhf.org.uk/informationsupport/risk-factors/high-cholesterol

HEART UK have produced a helpful animation, for patients, to better understand their cholesterol. They also have a helpful diet quiz - All quizzes - HEART UK