

CVD Central: Resource Pack

**To support Primary Care
with the implementation of
Inclisiran**

May 2023

KSS AHSN CVD Central Team

- Please contact us via email with any queries or for support relating to the CVD Central Project:
- Email: kssahsn.cvdprevention@nhs.net

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.

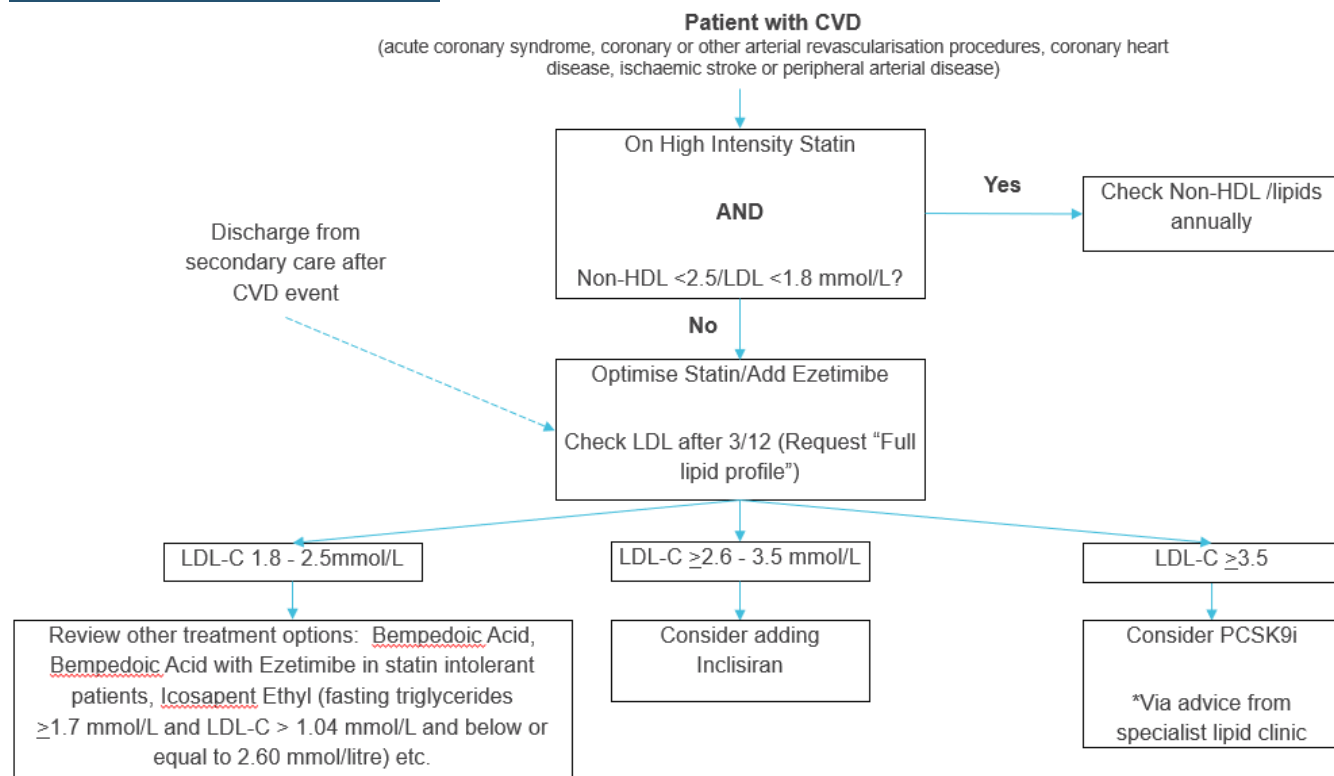
Lipid optimisation is an important aspect of CVD prevention and there are several new therapy options available if statins are not tolerated or effective in reducing cholesterol to target. These include Ezetimibe, Bempedoic Acid, PCSK9 inhibitors and Inclisiran (plus icosapent ethyl for hypertriglyceridaemia). 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 QOF¹

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 management⁵. 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:



1. Quality and Outcomes Framework guidance for 2023/24. Available at <https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00289-quality-and-outcomes-framework-guidance-for-2023-24.pdf> (Accessed 4th April 2023)

Quality Outcome Framework (QOF) 2023/24

This year reflects a heightened focus on the role of cholesterol within secondary prevention with two new cholesterol indicators (worth 30 points~£36m), added to the [2023/2024 Quality Outcome Framework \(QOF\)](#)¹ (published 30 March 2023):

- 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 therapy¹
- Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, or Stroke/TIA Register, who have a recording of non-HDL cholesterol in the preceding 12 months that is lower than 2.5 mmol/L, or where non-HDL cholesterol is not recorded a recording of LDL cholesterol in the preceding 12 months that is lower than 1.8 mmol/L¹

Raising awareness that LDL-C management for secondary prevention is a clinical priority for patients and the NHS, as recognised by the 2023/2024 QOF which will contribute to reducing the number of CVD events in England. Demonstrating support for primary care and recognising the challenges it faces, whilst championing lipid management among NHSE and National Clinical Leadership.

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](#))

1. Quality and Outcomes Framework guidance for 2023/24. Available at <https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00289-quality-and-outcomes-framework-guidance-for-2023-24.pdf> (Accessed 4th April 2023)

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: 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](#))

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 11](#))

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: 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

Clinical trial data demonstrates it leads to a further 50-60% reduction in LDL cholesterol. Whilst, there are no long-term data for Inclisiran yet, there is overwhelming evidence of the benefit of LDL cholesterol reduction. Lowering LDL cholesterol is irrefutably associated with a reduced risk of further cardiovascular events.

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: 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) or 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. The UCLPartners Proactive Care Frameworks for Lipid Optimisation can be used to support risk stratification and clinical prioritisation. These searches can be deployed into EMIS and are accessible via the following link: <https://s31836.pcdn.co/wp-content/uploads/CHOLESTEROL-FINAL-V6.pdf>

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:

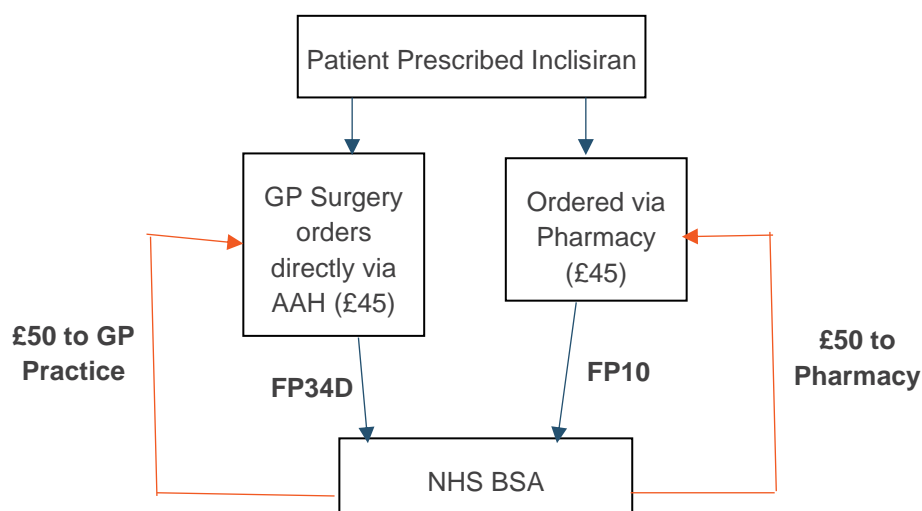
- The preference is for Inclisiran to be ordered directly to the GP practice (£45 per pre-filled syringe) by ordering Inclisiran directly from the AAH account the GP Practice has set up.
- **AAH Accounts:** To get set up with an account with AAH the GP practice will be required to create an account by 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 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](#)

KSS AHSN 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

CVD Central free resources

CVD Central free resources are available to any organisation in the country to support detection of high risk conditions (A,B,C) and are now on the KSS AHSN website. **You can order, download the resources direct from:** [CVD Central website](#)

Tackling Cholesterol Together is a comprehensive and varied education programme for healthcare professionals delivered in partnership between The AHSN Network, HEART UK and the NHS Accelerated Access Collaborative (AAC).

All available resources, webinars can be found on the Tackling Cholesterol Together homepage at: <https://www.heartuk.org.uk/tackling-cholesterol-together/home>

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, simvastatin 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 \(medicines.org.uk\)](https://www.medicines.org.uk/leqvio)

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/information-support/risk-factors/high-cholesterol

Heart UK: the diet checklist is now live at <https://www.heartuk.org.uk/primary-care-resource-centre/diet-checklist>.