

## Background

Treatment of hypercholesterolaemia is in the [NHSE Long Term Plan](#). The aim is to decrease cardiovascular disease (CVD) events by 150,000 over the next 10 years. Information from Academic Health Science Network (AHSN) lipid webinar 14/10/21 ([www.weahsn.net](http://www.weahsn.net)):

- More than two thirds of high-risk CVD patients remain on only low or medium intensity statin monotherapy which achieves target LDL in only one third of cases<sup>1</sup>.
- 90% of symptoms attributed to statins are not due to statins (i.e. more perseverance with statins is needed)<sup>2</sup>. As well as reducing CVD events (MI & stroke), statin treatment dramatically reduces the risk of heart failure in later life. Patients who stop statin treatment after an MI suffer a 3-4 fold increase in mortality over 3-4 years.
- Optimising prescribed lipid lowering treatment AND adherence in a population of 500,000 would prevent 12,000 CVD events every year. This equates to one MI, stroke, or CV death prevented every two weeks in an average practice<sup>3</sup>.
- Familial Hypercholesterolaemia (FH) is a high priority because it is underdiagnosed, life-limiting if unrecognised, but readily treatable. If unrecognised 50% have CVD event by age 50 and only 50% live to retirement age. Life expectancy is normal with generic statins and healthy lifestyle. Only 5% currently diagnosed<sup>4</sup>. [NHS LTP](#) aim to increase this to 25% by 2025.

## Inclisiran (Leqvio®)

Inclisiran (Leqvio®) is the first of a new type of cholesterol-lowering treatment which uses RNA interference (RNAi) to boost the liver's ability to remove LDL-cholesterol from the blood. It is given by subcutaneous injection, either on its own or alongside statins or other cholesterol-lowering drugs.

[NICE TA733](#) (6<sup>th</sup> October 2021, FAST-TRACK TA<sup>5</sup>) recommends Inclisiran as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults. It is recommended only if:

**There is a history of any of the following cardiovascular events:**

- acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation)
- coronary or other arterial revascularisation procedures
- coronary heart disease
- ischaemic stroke or
- 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, and

**the company provides inclisiran according to the commercial arrangement (see next page).**

NHSE&I have committed to deliver inclisiran access via a population health management (PHM) approach identifying eligible patients across England. NHSE&I have requested several actions including an urgent request for area prescribing committees to accept inclisiran based on the positive NICE Final Appraisal Determination (FAD), making routine funding available within 30-days of the publication of NICE FAD, and permit primary care prescribing through the Accelerated Access Collaborative (AAC) and Commercial Medicines Directorate at NHSE. Due to the exceptionally rapid turnaround time, [BSW Area Prescribing Committee \(APC\)](#) have agreed to adopt the NICE recommendations, whilst work is on-going to provide further prescribing guidance and education for GPs supported by the AHSN.

Inclisiran has been added to [BSWformulary](#) with **GREEN TLS** as per the recommendation in [NICE TA733](#) (section 3.3) and NHSE/I ([letter](#) dated 22/9/21).

## Pricing structure and mechanism of supply for inclisiran

NHSE/I have set up a novel funding mechanism which supports prescribing of inclisiran in primary care and promotes a PHM approach to lipid management. The goal of the PHM approach is to implement a large-scale intervention, with patients proactively identified and their lipid management optimised in primary care. Support for primary care will be provided by the AHSN and a national primary care DES is expected for the new financial year (22/23) to have a focus on CVD prevention.

AAH UK will supply Inclisiran to primary care in England under a Solus distribution arrangement. AAH UK are expected to start selling Inclisiran into primary care from September 2021. Inclisiran will be available to order from AAH as agreed within the commercial agreement between Novartis and NHSE&I.

For further information about the new part VIIIIC category in the drug tariff for inclisiran and pricing, see: <https://psnc.org.uk/our-news/inclisiran-legvio-added-to-a-new-section-in-the-drug-tariff-part-viiiic/>

There is a strong disincentive in the local Health community for secondary care prescribing as it is significantly more expensive to secondary care. There is the expectation centrally that in-patients with CVD may receive an initial dose but a strong directive that outpatient services should not initiate or prescribe but should instead recommend this to primary care for initiation and long-term prescribing.

- Inclisiran should be prescribed in primary care as a **personally administered item**. Practices to purchase stock from wholesaler (AAH) and claim via the monthly submitted FP34D. Alternatively it may be prescribed on FP10.
- **Practices can buy inclisiran for £45 but the reimbursement price to primary care will be £55 if prescribed via the FP34D route.**

## Dose, frequency and titration<sup>5</sup>

- Inclisiran is administered as a subcutaneous injection into the abdomen, upper arm, or thigh. The recommended dose is 284 mg inclisiran loading dose at 0 months and 3 months, then long-term maintenance every 6 months. It is intended for administration by a Healthcare Professional, not the patient.

## Baseline and on-going investigations

Refer to AAC national guidance found on links below

## Treatment Pathway

**The AAC National Guidance for Lipid Management for Primary and Secondary Prevention of CVD has been updated (Dec 2021) and now includes inclisiran alongside other approved treatments:**

- high intensity statins (HISTs)
- ezetimibe for use as an adjunct when statin monotherapy is ineffective, or as monotherapy for those patients that are intolerant to statins (NICE TA385)
- PCSK9 inhibitors (alirocumab, evolocumab) for use either alone or in combination with statins or ezetimibe (NICE TA393, 394)
- Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia as an adjunct to diet in adults (NICE TA694)

The current pathways from AAC (approved by NICE and endorsed by BSW APC for local use) which include all the above drugs (apart from inclisiran) can be found here:

- [National Guidance for Lipid Management for Primary and Secondary Prevention of CVD](#)
- [Statin Intolerance Pathway](#)

## Adverse effects<sup>5</sup> (only most common are listed):

The only adverse reactions associated with inclisiran were adverse reactions at the injection site (8.2%). The manufacturer's [summary of product characteristics](#) (SPC) and the most current edition of the [British National Formulary](#) should be consulted for full information.

## Cautions and contra-indications<sup>5</sup> (see [SPC](#) or [BNF](#) for further information)

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients.

**Cautions:** Haemodialysis: The effect of haemodialysis on inclisiran pharmacokinetics has not been studied. Considering that inclisiran is eliminated renally, haemodialysis should not be performed for at least 72 hours after inclisiran dosing. Sodium content: Leqvio® contains less than 1 mmol sodium (23 mg) per dose, essentially “sodium-free”.

## Interactions<sup>5</sup>:

Inclisiran is not an inhibitor or inducer of cytochrome P450 enzymes or common drug transporters. Therefore, inclisiran is not expected to have clinically significant interactions with other medicinal products. Based on the limited data available, clinically meaningful interactions with atorvastatin, rosuvastatin or other statins are not expected.

## BSW Specialist contact information:

Lipid specialists	E-mail/address	Telephone
Dr Mayur Patel (GWH)	<a href="mailto:mayur.patel3@nhs.net">mayur.patel3@nhs.net</a>	
Dr Moya O'Doherty (RUH)	<a href="mailto:moya.o'doherty@nhs.net">moya.o'doherty@nhs.net</a>	
Dr Paul Downie/ Dr Niki Meston (SFT)	<a href="mailto:shc-tr.bioenquiries@nhs.net">shc-tr.bioenquiries@nhs.net</a>	01722 336262 ext 5427

**NOTE: GPs can use 'cinapsis' app to request consultant support with initiation from GWH and RUH**

Also, please be aware that the specialist listed above can deal with queries about this new lipid treatment as well as the NHS BSW CCG Medicines Optimisation team on [bswccg.formulary@nhs.net](mailto:bswccg.formulary@nhs.net) or [bswccg.prescribing@nhs.net](mailto:bswccg.prescribing@nhs.net)

## References:

1. Stock J K DA VINCI study: Change in approach to cholesterol management will be needed to reduce the implementation gap between guidelines and clinical practice in Europe. *Atherosclerosis* 2020;314:74 [https://www.atherosclerosis-journal.com/article/S0021-9150\(20\)30542-6/pdf](https://www.atherosclerosis-journal.com/article/S0021-9150(20)30542-6/pdf) (accessed 8/11/21)
2. N-of-1 trial of statin, placebo, or no treatment to assess side-effects. *NEJM* 2020;383:2182-2184 <https://www.nejm.org/doi/full/10.1056/NEJMc2031173> (Accessed 8/11/21)
3. Khunti K et al. Association of a Combined Measure of Adherence and Treatment Intensity With Cardiovascular Outcomes in Patients With Atherosclerosis or Other Cardiovascular Risk Factors Treated With Statins and/or Ezetimibe. *JAMA Netw Open* . : (8)1;2018e185554. doi:10.1001/jamanetworkopen.2018.5554 <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2717559> (Accessed 8/11/21)
4. AHSN lipid webinar 14<sup>th</sup> October 2021, Dr Graham Bayley, consultant chemical pathologist; ([www.weahsn.net](http://www.weahsn.net))
5. Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia. NICE TA733 6/10/21 (Accessed 5/11/21) [Overview | Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia | Guidance | NICE](#)
6. Summary of product characteristics Leqvio 284mg solution for injection in pre-filled syringe. (Accessed 5/11/21) <https://www.medicines.org.uk/emc/product/12039>

**Additional resources:** Heart UK -Tackling Cholesterol Together <https://www.heartuk.org.uk/tackling-cholesterol-together/home>

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