NHS BSW CCG Primary care guidance for the treatment of primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia with inclisiran

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

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):

- 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[1].
- 90% of symptoms attributed to statins are not due to statins (i.e. more perseverance with statins is needed)[2]. 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[3].
- 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[4]. NHS Long Term Plan 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 (6th October 2021, FAST-TRACK TA[5]) 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).

Inclisiran has been added to BSWformulary with GREEN TLS

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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 funding has changed from April 2023 and further information about this can be found here: NHSE Summary information on the funding and supply of inclisiran (Leqvio®).
AAH UK will supply Inclisiran to primary care in England under a Solus distribution arrangement.

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 £50 if prescribed via the FP34D route.**

Dose, frequency and titration[5]

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 can be found here:

- **National Guidance: Lipid Management for Primary & Secondary Prevention of CVD**
- **Statin Intolerance Pathway**

Adverse effects[5] (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 BNF should be consulted for full information. As a new medicine, inclisiran has ▼ status and is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme: www.mhra.gov.uk/yellowcard

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Minor updates Dec 21 to include AAC/NICE pathway: Feb 22 to correct pricing and black triangle info Sept 22: BMA/RCGP info added. Apr 23: Pricing section update. Dec 23: BSW ICB position statement added. Contacts updated.

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Cautions and contra-indications[5] (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 <1 mmol sodium (23 mg) per dose, essentially "sodium-free".

Interactions[5]:

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.

Other information:

Dec 2023: BSW position statement. BSW ICB acknowledges the current challenging situation regarding the provision of inclisiran. The expressed NHSE intention for the ongoing administration of this medication to take place in primary care (and the associated resourcing) continues to be debated. BSW ICB maintains in close contact with these discussions and will continue to seek advice regionally and nationally on how we can come to an optimal resolution. In the meantime, the ICB continues to follow the guidance published by NHSE on 2 April 2023 which states at 2.1 that 'NHS England are funding inclisiran centrally from a national NHS budget in order that local finances are not a barrier to access. Inclisiran should be prescribed in primary care as per the instructions in the green box at the top of P2 of this guidance. As the national discussions continue about the use of inclisiran for management of hypercholesterolaemia or mixed dyslipidaemia, we will be sure to keep all our provider colleagues updated.

BSW Specialist contact information:

Lipid specialists	E-mail/address	Telephone
Dr Mayur Patel (GWH)	mayur.patel3@nhs.net	
Dr Paul Downie/ Dr Niki Meston (SFT)	shc-tr.bioenquiries@nhs.net	01722 336262 ext 5427

The Specialist teams listed above can deal with queries about this new lipid treatment as well as the NHS BSW ICB Medicines Optimisation team on bswicb.formulary@nhs.net or bswicb.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 (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;2018 .e185554. doi:10.1001/jamanetworkopen.2018.5554 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2717559 (Accessed 8/11/21)
4. AHSN lipid webinar 14th October 2021, Dr Graham Bayley, consultant chemical pathologist; (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 prefilled 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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