Inclisiran prescribing, ordering and cost information

RAG List Status: Inclisiran is RAG rated GREEN – suitable for primary care prescribing.

NICE Technology appraisal guidance (TA733) states:

Inclisiran is recommended 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:

1. ***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

2. ***Low density lipoprotein cholesterol (LDL-C) concentrations are persistently 2.6 mmol/l* or more, despite maximally 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

Considerations before prescribing

- Further information on inclisiran is available in the *Medicines Optimisation Pack for Inclisiran*
- Consider secondary causes of hypercholesterolaemia such as excess alcohol, uncontrolled diabetes, hypothyroidism, liver disease and nephrotic syndrome (NICE CG181)
- Consider referral to lipid clinic for:
  - Possible familial hyperlipidaemias.
  - If triglyceride (TG) >20 mmol/L once (urgent if not a result of excess alcohol or poor glycaemic control) or > 10 mmol/L more than once
  - If LDL-C is persistently above 3.5mmol/l and the patient is at very high risk of cardiovascular disease or LDL-C is persistently above 4.0mmol/l and the patient is at high risk of cardiovascular disease, consider for treatment with PCSK9 inhibitors. There is some patient orientated outcomes evidence for these drugs.

    Further information regarding treatment criteria for PCSK9 inhibitors including definitions of "very high risk" and "high risk" is available in NICE TAs 393 and 394. Like inclisiran, these are injectable therapies and while they are given more frequently (usually fortnightly), they are presented in formulations suitable for patient self-administration.
- Ensure patients have made appropriate dietary modifications and are actually taking their maximum tolerated dose of statin (refer to AAC statin intolerance pathway if necessary), ezetimibe and any other medication prescribed to lower cholesterol if not contra-indicated and clinically suitable
- If patient eligible for inclisiran ensure fully informed patient consent and document the following:
  - Inclisiran has demonstrated considerable effectiveness in lowering LDL-C
  - However, no patient-orientated outcome evidence such as a reduction in heart attacks or strokes is available. This will not become available until 2026 or 2027.
  - No safety signals have been seen during clinical trials for inclisiran which have been published so far. However, the longest duration of any clinical trial to date is 18 months. Slightly more than 200 patients have now been followed up over 4 years where inclisiran displayed sustained reductions in LDL cholesterol and was well tolerated with injection site reactions the only

undesirable effect
    - There is limited other medical experience with treatments using the same mechanism of action - small interfering RNA molecules
- Tools are available from the local Academic Health Sciences Network – Health Innovation Manchester – which will identify patients who may be considered for treatment with inclisiran.
- If primary care clinicians require further support prior to initiation of inclisiran, an advice and guidance referral to the lipid clinic should be made via e-RS.
- While the NHS England approach intends for inclisiran to be prescribed in primary care, some patients may be prescribed this from secondary care and GPs will be asked to take over prescribing. Similarly, some secondary care clinics may make recommendations to GPs to prescribe. Such requests should be considered sympathetically and actioned after ensuring all the above has been taken into consideration before prescribing.

Selected prescribing information: Full prescribing information may be found in the Summary of Product Characteristics

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

Administration: 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.

Inclisiran (pre-filled syringe) must be administered by a healthcare professional.

The current licence for inclisiran does not cover self-administration, nor is it available in a patient-friendly device.

Intended duration of use: Long-term.

Co-prescribing of lipid lowering agents: Patients should continue to take any other lipid lowering agents which they were taking prior to initiation of inclisiran e.g., statins and ezetimibe, as well as maintaining a healthy diet.

Safety considerations: Inclisiran is a “Black Triangle” ▼drug and all suspected side effects should be reported via the Yellow Card system.

Drug interactions: Inclisiran is not expected to have clinically significant interactions with other medicinal products. This is because inclisiran is not a substrate for common drug transporters and it is not anticipated to be a substrate for cytochrome P450. Inclisiran is not an inhibitor or inducer of cytochrome P450 enzymes or common drug transporters. However as this is a new drug, prescribers should be aware of anything they suspect to be an interaction with another drug.

Hepatic and renal function: The manufacturer recommends that no dose adjustment is necessary in patients with mild, moderate, or severe renal impairment. 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 dosing.

No dose adjustment is necessary in patients with mild to moderate hepatic impairment. Inclisiran has not been studied in patients with severe hepatic impairment.

Pregnancy: Inclisiran is best avoided during pregnancy.

Breastfeeding: It is unknown whether inclisiran is excreted in human milk. Pharmacodynamic / toxicological data in animals have shown excretion of inclisiran in milk. A risk to newborns / infants cannot be excluded. A risk benefit decision needs to be made with the mother as to whether to discontinue/abstain from inclisiran therapy or to discontinue breastfeeding.

Monitoring: Following initiation, cholesterol monitoring and adherence to medication should be in line with local lipid management guidelines, however there is no mandated laboratory monitoring by NICE or the product licence.

Stopping: Checking of LDL-C may be performed between second and third injections (between 3 and 9 months). A reduction of at least 30% from baseline is recommended as a criterion for continuation. In clinical trials, inclisiran reduced LDL-C by around 50% even in people already taking high-intensity statins.

Patients who are having difficulties with their medications should receive a Structured Medication Review from an appropriate Healthcare Professional.

Ordering

Inclisiran (Leqvio) from Novartis, funded by NHS England is available to all pharmacies and GPs for prescribed patients. Available to order for same day or next day delivery from your local branch, you can order inclisiran using AAH Point or your PMR system using:

Product Name	EAN Code	PIP Code
Inclisiran (Leqvio)	7613421044237	4174751

If you need any further support regarding ordering, please contact AAH Customer Care. You can Live Chat via AAH Point from 9am-5pm Monday to Friday or call them on 0344 561 8899. Inclisiran is available to order directly from AAH Customer Care team on: 08457419442.or e-mail: commercial.team@novartis.com

Cost & Reimbursement

The preference is for primary care to purchase stock from the wholesaler (AAH) and then to make a claim on the monthly submitted FP34D form. The patient will not incur a prescription charge and the practice will receive the £5 reimbursement, detailed below.

Inclisiran can also be supplied by an FP10 prescription, with the patient bringing the injection to the surgery for administration. If issued via FP10 the patient would pay the prescription charge, if they normally do so, and the practice **will not** receive the £5 reimbursement.

Inclisiran will be available from the wholesaler (AAH) at £45, which is payable 30 days from the end of that month.
It is listed in the Drug Tariff as a “zero discount” item (no claw-back applicable) and will be listed in the Drug Tariff at a reimbursed price of £50 per injection at the end of the month. The practice will only receive the £5 reimbursement if submitted via the FP34D form.

The cost to the primary care prescribing budget will be the Drug Tariff price.
For further advice and guidance, consult a specialist, usually via e-RS

Based on original documents from Salford and Tameside & Glossop CCGs with thanks.
Updated June 2023 to reflect revised Drug Tariff reimbursement prices and include information about longer term use.
Reference: *Long-term efficacy and safety of inclisiran in patients with high cardiovascular risk and elevated LDL cholesterol (ORION-3): results from the 4-year open-label extension of the ORION-1 trial (Lancet Diabetes Endocrinol 2023 published online https://doi.org/10.1016/S2213-8587(22)00353-9)*