Inclisiran as an option for lipid management - Information for Primary Care

NICE approved indication

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 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.

The NICE technological appraisal for inclisiran can be found here.

Mechanism of action

Inclisiran is a small interfering RNA (siRNA) that works by inhibiting the production of PCSK9 in the liver. This increases the number of LDL-C receptors able to clear LDL-C from the bloodstream and reduces the level of LDL-C in the blood.

Place in the lipid management pathway

Inclisiran can be used when statins and other lipid lowering therapies do not control LDL-C well enough, or when people are intolerant to statins. The appropriate position of inclisiran in the treatment pathway is after maximum tolerated statins with ezetimibe.

A summary of national guidance for lipid management for primary and secondary prevention of CVD can be found here. An updated version is under review to include inclisiran and will be accessible under the same link.

Inclisiran has shown an average LDL reduction of 52% in studies so far. CV outcome data is not yet available. This compares to approximately 40-50% for high intensity statins, 24% for ezetimibe, 28% for bempedoic acid and 60% for PCSK9i-mabs.

Optimisation of statins

It is important to note that NHSEI/AAC are clear that for our population the optimisation of statins should be prioritised in any work on lipid management.

Safety

- The trial results indicated that inclisiran was generally well tolerated. Adverse reactions were mild with none being severe or persistent. The most frequently reported adverse reactions were at the injection site.
- Please report any suspected adverse reactions via the Yellow Card Scheme.
- **Contraindications:** Hypersensitivity to any of the components.

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- **Interactions:** No clinically meaningful interactions are predicted.

Where should it be prescribed?

Guidelines recommend that inclisiran initiation is intended to be carried out within the primary care setting where most patients with ASCVD are currently managed. The cost of inclisiran in primary care will predominantly be centrally funded by NHS England and Improvement.

Administration

- The recommended dose of inclisiran is 284mg administered as a single subcutaneous injection using a single-use, pre-filled syringe into the abdomen. Alternative injection sites include the upper arm or thigh.
- After an initial dose, inclisiran is administered again at 3 months, followed by every 6 months thereafter.
- No dose adjustments are required for patients with mild or moderate hepatic impairment, mild, moderate or severe renal impairment or end-stage renal disease, or elderly patients.
- Novartis "How do I administer inclisiran?" information available here

Monitoring

- No additional monitoring is required for inclisiran. Following initiation, cholesterol monitoring and adherence to medication should be in line with lipid guidelines.
- There are no additional monitoring requirements in reduced renal or hepatic function.

How does the supply and funding work?

- Inclisiran will be available in primary care as a personally administered item via an FP34D form or on an FP10 prescription.
- Inclisiran will be available from the wholesaler (AAH) at a cost of £45 which is payable 30 days from the end of that month.
- Inclisiran is listed in the Drug Tariff as a 'zero discount' item (no claw-back applicable) and will be listed at a reimbursed price of £55 per injection via FD34D submission.
- If the injection purchased by the practice/PCN and claimed for via FP34D the the £10 difference is retained by primary care and can be used to fund the cost of administration.
- As with other FP34D drugs, you will need to record the prescriber's name and the number of injections to ensure that you will be reimbursed.
- The cost to the primary care prescribing budget will be £55. As this is set at a nominal price, a separate payment will be made to the manufacturer for the difference from a central NHS budget. Supply via secondary care is not part of this arrangement.

How to order inclisiran

- AAH pharmaceuticals is the sole distributer of inclisiran.
- It is available to order for same or next day delivery from your local branch
- AAH customer care are available 9am-5pm Monday to Friday on 0344 5618899.
- This number can be used to set up an account if you don't have one. Once you have an account, inclisiran (Leqvio) can be ordered using using the following codes:
    - EAN code: 7613421044237
    - PIP code: 4174751

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