North East London
Barts Health NHS Trust
Homerton Healthcare NHS Foundation Trust
Barking, Havering and Redbridge University Hospitals NHS Trust

Primary care guidance for prescribing and supplying inclisiran

Document control	
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Produced by	Sadeer Fhadil
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This document provides:

- Primary care inclisiran treatment pathway
- Prescribing & Supply information summary
- Resources
- Inclisiran checklist

1. Introduction

WHAT IS INCLISIRAN?

Inclisiran (Leqvio®) is a Low Density Lipoprotein cholesterol (LDL-C) lowering therapy that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9) production. It is a small interfering RNA (siRNA) drug, which directs the catalyst breakdown of mRNA responsible for producing PCSK9 protein. PCSK9 directs the degradation of LDL-C receptor. Therefore, by reducing PCSK9 production, inclisiran increases LDL-C receptor expression on hepatocyte cell surface, which increases LDL-C uptake that lowers LDL-C levels in circulation. ORION-10 and ORION-11 studies have demonstrated a reduction LDL-C by an average of 50%, compared to placebo.

Trials are currently underway to confirm cardiovascular clinical outcome. NICE approval was based on observations that lipid lowering effects of inclisiran will result in significant CVD clinical benefits.

Inclisiran is an option for secondary prevention as an adjunct to diet with maximally tolerated lipid-lowering therapy or alone if statin intolerant or contraindicated and not achieving treatment target. For full details refer to the current summary of national guidance for lipid management and/ or North East London (NEL) lipid pathway and guidance.

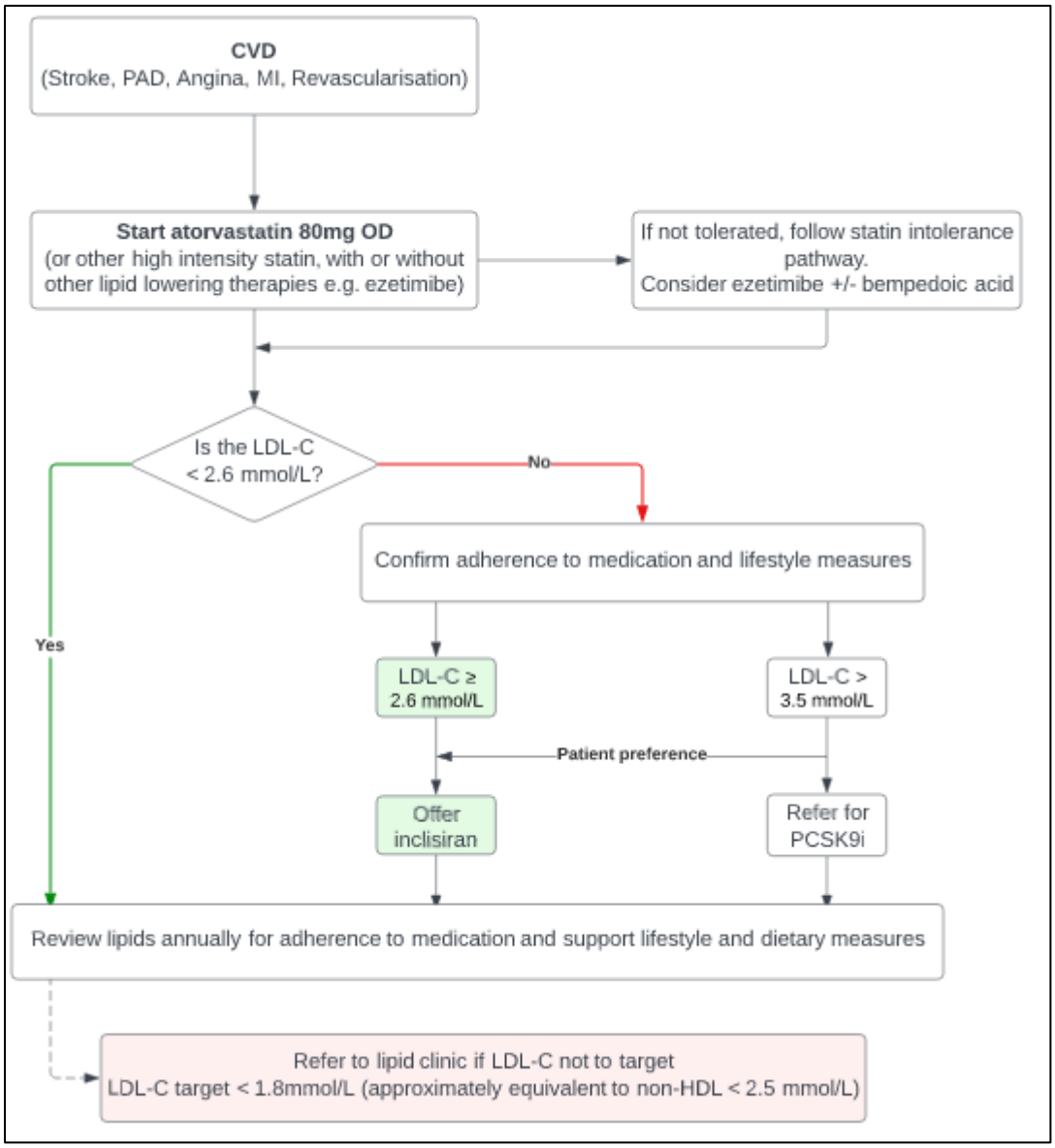
NATIONAL GUIDANCE

NICE TA733 recommend inclisiran for adults ≥ 18 years with:

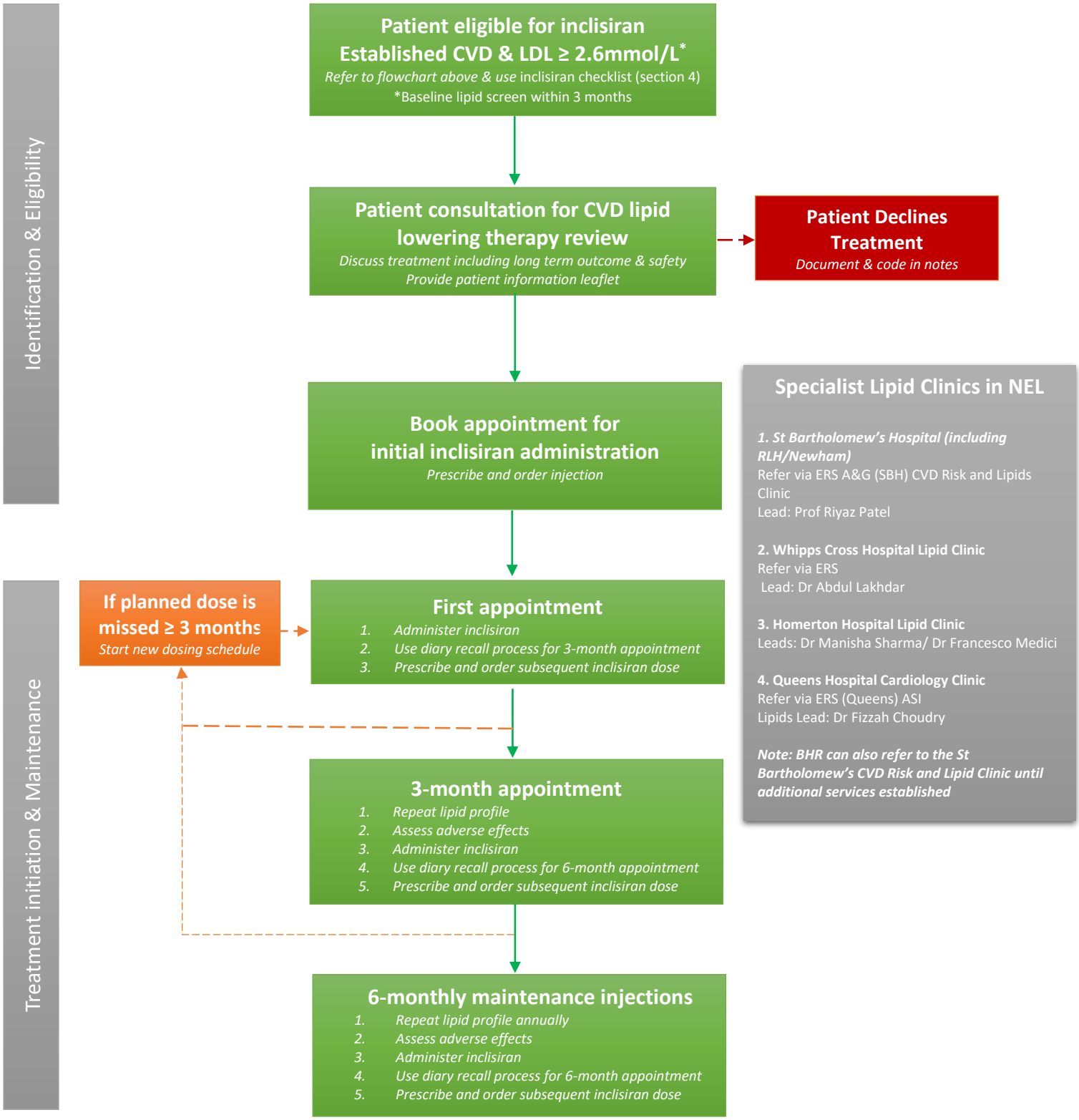
- History of cardiovascular disease (ischaemic heart disease (IHD), ischaemic stroke and/ or peripheral arterial disease (PAD) with
- Persistent LDL-C levels ≥2.6mmol/L despite having the maximum tolerated lipid-lowering therapy
- Alone or in combination with lipid lowering therapy if statin intolerant or contraindicated

Across NEL, primary care prescribers can initiate inclisiran in line NICE TA733 outlined above. Should individuals need clarification or further support, this can be sought through advice from a specialist lipid clinic through advice and guidance (see page 3 for details). Where treatment has been initiated in secondary care, ongoing maintenance is continued in primary care.

INCLISIRAN - PLACE IN THERAPY



2. Primary care Inclisiran identification and treatment initiation and maintenance algorithm



Support is available via advice and guidance from Specialist Lipid Clinics in NEL (see grey box above).

3. Prescribing & Supply Information Summary

Dosing & Administration
Inclisiran is administered as a subcutaneous injection by an accredited healthcare professional into the abdomen, upper arm or thigh (inclisiran-dosing-admin-how-to-guide.pdf (novartis.co.uk)).

The recommended dose is 284mg loading dose at 0 month and 3 months, then long-term maintenance every 6 months.

There is no dose adjustment requirement for renal or hepatic impairment; however, should be used in with caution in severe hepatic impairment and end-stage renal disease due to limited data.

Missed doses
If a planned dose is **missed by ≤ 3 months**: administer inclisiran and **continue dosing according to the original schedule**.

If a planned dose is **missed by > 3 months**: start a **new dosing schedule** (i.e. administer initial dose, second dose at 3 months, followed by a dose every 6 months)

Caution
- Severe renal impairment (CrCl <30 ml/min) or requiring haemodialysis due to limited clinical experience. Haemodialysis should not be performed for at least 72 hours after inclisiran dosing.
- Severe liver impairment (Child-Pugh class C) due to limited clinical experience.
- Each inclisiran injection contains <1 mmol (23mg) sodium.

Contraindication
- Hypersensitivity to active ingredient or any of the excipients
- Pregnancy / breastfeeding due to no or limited clinical experience

Adverse effects
Mild to moderate injection site reaction are transient and resolve: pain, erythema, rash

Monitoring

Baseline	Month 3 and then annually thereafter
• Full lipid profile (including LDL-C) • Liver function • Renal function • Thyroid • HbA1c	• Full lipid profile (including LDL-C)

Following initiation check for side effects/intolerances at each visit. As this is a new medication, report all suspected adverse drug reactions (ADRs) to yellow card scheme or search for MHRA yellow card in the Google Play or Apple App Store.

Refer to lipid clinic if LDL-C remains > 1.8 mmol/L on treatment or on any aspect of patient care, which is of concern and may affect treatment.

Drug Interactions

Inclisiran is not an inhibitor or inducer of cytochrome P450 enzymes or common drug transporters. Therefore, **it is not expected to have clinically significant interactions with other medicinal products**.

Inclisiran and PCSK9 inhibitor monoclonal antibodies (i.e. alirocumab or evolocumab) should not be prescribed concomitantly.

Supply and Ordering

Inclisiran should be prescribed in primary care as a **personally administered item**. Practices can purchase stock directly from the wholesaler AAH using AAH Point, PMR system or calling the customer care team on 0344 561 8899. Alternatively, it can be prescribed on FP10 prescription https://www.england.nhs.uk/aac/publication/summary-information-on-the-funding-and-supply-of-inclisiran-leqvio/.

Practices purchasing inclisiran from AAH should submit claims using the monthly FP34D form to NHS BSA. In this case practice's will be reimbursed their drug costs and a personally administered drug fee via their FP34D claim. Practice's using FP10 prescriptions to obtain inclisiran can still use the FP34D form to claim for the personally administered drug fee only.

Storage

No special storage conditions. Do not freeze.
Shelf life is 3 years.

Resources

- Patient Leaflets hard copies are available directly from Novartis or use the following link https://www.health.novartis.co.uk/sites/health.novartis.co.uk/files/inclisiran-patient-leaflet.pdf
- Heart UK Getting Treatment Inclisiran information
- Inclisiran dosing and administration How to guide
- Optimising lipid management (mimslearning.co.uk)
- Videos on inclisiran & programme
- Videos 'How inclisiran works'

4. Inclisiran Checklist

1. **Does the patient have a history of cardiovascular disease (CVD)?** (Tick all that apply)

☐ Acute Coronary Syndrome (ACS) e.g. Non-ST elevation myocardial infarction (NSTEMI) / ST-elevation myocardial infarction (STEMI) or Coronary Heart Disease (CHD) e.g. angina
☐ Previous coronary/arterial revascularisation e.g. percutaneous coronary intervention (PCI) / coronary artery bypass graft (CABG)
☐ Ischaemic stroke/transient ischaemic attack (TIA)
☐ Peripheral arterial disease (PAD)
☐ None of the above – **inclisiran not indicated**

2. **Check Low density lipoprotein cholesterol (LDL-C)**: Enter result here: ☐
(Most recent results should be within the recent 3 months)

If LDL-C ≥2.6mmol/L – continue to question 3
If LDL-C < 2.6mmol/L – **inclisiran not indicated**

3. Has the patient taken or tried the **maximum tolerated dose of a high intensity statin such as atorvastatin 80mg or rosuvastatin 40mg (20mg for patients of Asian origin) for at least 3 months** prior to review?

☐ Yes – go to question 5
☐ No – optimise and / or go to question 4

4. If **statin intolerance**- have you followed the statin intolerance pathway?

☐ Yes – go to question 5
☐ No – follow pathway and reassess

5. Does your patient have any **contra-indications** to inclisiran? (Tick any that apply)

☐ Pregnancy/breastfeeding
☐ Age <18 years
☐ Hypersensitivity to active ingredient or any of the excipients

If any of the above ticked, not for inclisiran

6. Please ensure you have undertaken shared decision making and discussed the following with your patient:

☐ Need to attend regular appointments for injections at least every 6 months (noting second dose is repeated at 3 months and then 6 monthly thereafter).

☐ Informed consent, including the absence of long-term cardiovascular benefit and unknown long term safety profile of this new and novel medication (see supporting sheet overleaf).

☐ As with any black triangle drug, the need to report all side-effects, however minor, via the MHRA "yellow card" scheme.

Support is available via advice and guidance from Specialist Lipid Clinics in NEL (see section 2)

5. References:

1. Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia. NICE TA733 5/12/22 (Accessed 5/12/22) Overview | Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia | Guidance | NICE
2. Ray KK *et al.* Two Phase 3 Trials of Inclisiran in Patients with elevated LDL cholesterol. *N Eng J Med. 2020; 382: 1507-1519*
3. Summary of product characteristics Leqvio© 284mg solution for injection in prefilled syringe. Last updated Dec 2020. (Accessed 5/12/22) https://www.medicines.org.uk/emc/product/12039
4. NHS Accelerated Access Collaborative. Updated April 2022. Summary of national guidance for lipid management. Available at Lipid-Management-Pathway-NEW.pdf (england.nhs.uk)
5. NHS Accelerated Access Collaborative. Updated April 2022. Statin intolerance pathway. Available at https://www.england.nhs.uk/aac/publication/statin-intolerance-pathway/