Therapeutics Advisory Group

Improving lives together
Norfolk and Waveney Integrated Care System

Primary Care Prescribing Advice for Lipid Management in Secondary Prevention AND Information for Prescribing and Management of Inclisiran

Inclisiran NICE TA733 - Norfolk and Waveney ICB Primary care prescribing guidance for the treatment of primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia	
Formulary Status	**Advice - Prescribing can be initiated or continued in Primary care on advice from specialist in hospital, community or by a GP with Specialist Interest, providing all the criteria in TA733 are met.**
Background	**What is 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. 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 **NICE TA733, October 2021,** recommends Inclisiran as an **option** for adults ≥ 18 years **for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia** as an adjunct to diet in adults, 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.
Primary care prescribing?	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**. Inclisiran is classified as **ADVICE - Specialist advice required from clinician with relevant expertise prior to initiation.** This means that any cardiologist, lipidologist, endocrinologist or GP with specialist interest and experience can **recommend Inclisiran for initiation within primary care.** It is restricted for use only in those patients who meet the criteria listed in the NICE TA guidance. It is the clinician's responsibility to ensure that they initiate Inclisiran in line with the TA guidance.
When is it appropriate to seek advice or refer for injectable therapies?	**Primary Care Prescribers can seek advice from a specialist for injectable therapies** • if maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months **and** • all other suitable Secondary Prevention options as addition to statins or used as monotherapy in the National Guidance for Lipid Management including Ezetimibe and Bempedoic acid have been considered and optimised, does not control non-HDL-C/LDL-C well enough after a further 3 months **and** • **the non-HDL-C remains> 2.5mmol/l.**

Initiation	Before or on initiation, the specialist should: - Ensure that the patient meets the criteria outlined by the NICE TA733. In particular, • maximum tolerated dose of statin has not controlled non-HDL-C/LDL-C well enough. • Other options have been considered; non-HDL-C remains >2.5mmol/L despite maximum tolerated lipid lowering therapy AND • Fasting blood test LDL-C is ≥2.6mmol/L - Patients should be informed that the effect of Inclisiran on cardiovascular morbidity and mortality has not yet been determined - The shared decision-making discussion **should include stopping criteria.** - Ensure that the patient is able to access the "A patient's guide to Inclisiran (Leqvio ®" information: https://www.health.novartis.co.uk/sites/health.novartis.co.uk/files/inclisiran-patient-leaflet.pdf
Primary care responsibilities	Key roles to be undertaken in primary care following a recommendation from specialist: • Monitor as per the pathway – see below • Organise the administration of Inclisiran in line with the dosing schedule • Seek advice from the specialist where necessary
Dose	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.
Administration	Inclisiran is for administration by a Healthcare Professional, **not** the patient – see reimbursement guidance below for FP34D submission.
Contraindications	Hypersensitivity to the active substance or to any of the excipients.
Cautions	**Use with caution** - in severe renal impairment due to limited experience in this patient group - in severe hepatic impairment due to lack of data
Monitoring	As per advice from specialist
Purchase and reimbursement	**Secondary Care** In NHS England has reviewed and updated the position of Inclisiran provided by secondary care clinicians. From 1st April 2022, Inclisiran will be added to the excluded drug list enabling provision by secondary care and re-charge to secondary care by NHSE. **Primary Care** AAH UK will supply Inclisiran to primary care in England under a Solus distribution arrangement. as agreed within the commercial agreement between Novartis and NHSE&I. Inclisiran is listed the new part VIIIC category in the drug tariff see: https://psnc.org.uk/our-news/inclisiran-leqvio-added-to-a-new-section-in-the-drug-tariff-part-viiic/ and should be prescribed in primary care - as a **personally administered** item. Practices to purchase stock from wholesaler (AAH) and reimbursement claim via the monthly submitted FP34D. No patient prescription charge via this method. - Alternatively, it may be **prescribed on FP10**. Patient prescription charges apply.
Stopping Criteria	Only to be continued if target lipid level is reached and maintained

SECONDARY PREVENTION: Norfolk and Waveney ICB medicine optimisation for lipid management based on National Guidance

1) **Check baseline bloods** (non-fasting FULL lipid profile (TC,TG,HDL,LDL-C), LFTs, HbA1c, thyroid and renal function), Measure BMI.
2) **Consider** secondary causes of hyperlipidaemia and manage as needed
3) **Support the self-management** of modifiable risk factors eg. smoking, diet, obesity, alcohol intake, physical activity, blood pressure and glycaemic control (HbA1c)
3) **Offer high dose high intensity statin** therapy **with atorvastatin 80mg *or 20mg if CKD (people with eGFR< 60 mL/min/1.73m2)* (alternative is rosuvastatin 20-40mg)* to adults with CVD**: this includes acute coronary syndromes (ACS), angina, previous myocardial infarction (MI), revascularisation, stroke, or transient ischaemic attack (TIA),

START PATIENTS on High Intensity Statin (do not delay whilst managing modifiable risk factors)
Atorvastatin 80mg or *20mg if CKD* (alternative is rosuvastatin 20mg-40mg)*-consider further *dose adjustments: eGFR<30ml/min, drug interactions, intolerance*

At 3 months check **non-fasting** lipid profile (TC,TG,HDL,LDL-C); LFTs

Has non-HDL-C reduced by 40% or more from baseline? If no baseline value *: consider a target of non-HDL-C < 2.5mmol/L or LDL-C < 1.8 mmol/L? as recommended by Joint British Societies (JBS3). **this scenario is not covered by NICE CG181* IF NO –

YES

Discuss statin choice: check adherence to medication, timing of dose and lifestyle.

- Reinforce lifestyle and dietary measures.
- Check statin tolerance and offer lower dose or alternative statin if side effects.
- If higher risk and started on lower dose, consider increasing to 80mg atorvastatin

After 3 months check non-fasting lipid profile (TC,TG,HDL,LDL-C); LFTs

Has non-HDL-C reduced by 40% or more from baseline? If no baseline value: consider a target of non-HDL-C < 2.5mmol/L or LDL-C < 1.8mmol/L? IF NO

YES

- Check adherence to medication and lifestyle. Reinforce lifestyle and dietary measures. Check statin tolerance
- No intolerance - Consider **adding Ezetimibe 10mg daily to current intensified statin (NICE TA385) or consider injectable therapies**
- If statin intolerance, follow intolerance algorithm. If confirmed – consider **Ezetimibe Monotherapy (NICE TA385)**

Shared decision making. Consider Injectable therapies when patients' LDL-C levels are not lowered enough with maximally tolerated dose of statins. Where non-HDL-C is >2.5mmol/L measure fasting LDL-C to assess eligibility

After 3 months check non-fasting lipid profile (TC,TG,HDL,LDL-C); LFTs

Has non-HDL-C reduced by 40% or more from baseline? If no baseline value: consider a target of non-HDL-C <2.5mmol/L or LDL-C < 1.8mmol/L? IF NO

YES

- Check adherence to medication and lifestyle. Reinforce lifestyle and dietary measures. Check statin tolerance
- No intolerance - Consider **adding injectable therapies to current intensified statin and Ezetimibe**
- Statin intolerance and not achieving target -Consider adding **Bempedoic acid 180mg to Ezetimibe monotherapy (TA694)**

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If non-HDL-C remains > 2.5mmol/L despite other lipid lowering therapies, arrange a fasting blood test to measure LDL-C to assess eligibility criteria for Inclisiran (TA733) **or** PCSK9i (TA393 Alirocumab) (TA394 Evolocumab) **PCSK9i initiation is via specialist services ONLY**

YES

Inclisiran –despite maximum tolerated lipid lowering therapy (TA733)		**PCSK9i NICE TA 393 Alirocumab and NICE TA 394 Evolocumab – Patients with CVD**		
			High Risk	**Very High Risk**
LDL-C ≥ 2.6mmol/L		**Primary Non-FH or Mixed Dyslipidaemia**	LDL C > 4.0 mmol/L	LDL C > 3.5mmol/L
		Primary Heterozygous-FH	LDL C > 3.5 mmol/L	

Therap

Review annually for adherence to medications, support for diet and lifestyle measures, and check required bloods eg lipid profile, LFTs if indicated

SECONDARY PREVENTION: MONITORING SUMMARY - National Guidance for Lipid management Summary

Baseline Measurements

In addition to full lipid profile, measure renal, thyroid and liver profiles (including albumin) and HbA1c to exclude secondary causes and co-morbidities. **Measure baseline liver transaminase** (ALT or AST) before starting a statin. Measure Creatinine Kinase(CK) if unexplained muscle pain before starting a statin. CK should not be measured routinely especially if a patient is asymptomatic.

	Secondary Prevention	
	Lipid Profile	**ALT or AST**
Baseline	**√**	**√**
3 months	**√**	**√**
6-9 months	If <40% non-HDL-C reduction, up titration required. Repeat full lipid profile and ALT or AST within 3 months of each up-titration of statin dose or addition of ezetimibe as required.	
12 months	**√**	**√**
Annually	**√ ***	

* Consider an annual **non-fasting full lipid profile** to inform the discussion around effectiveness of lipid lowering therapy and any medicines non-adherence

Medication Reviews

Provide annual medication reviews for people taking statins to discuss effectiveness of therapy, medicines adherence, lifestyle modification and address CVD risk factors.

Monitoring

Repeat full lipid profile is non-fasting. Measure liver transaminase within 3 months of starting treatment and then within 3 months of every additional up titration and then again at 12 months, but not again unless clinically indicated.

If ALT or AST are greater than 3 times the upper limit of normal then do not initiate a statin or discontinue statin therapy already prescribed and repeat the LFTs in a month.

If ALT or AST are elevated but are less than 3 times the upper limit of normal then:

- Continue the statin and repeat in a month.
- If they remain elevated but are less than 3 times the upper limit of normal then continue statin and repeat again in 6 months

Title	Primary Care Prescribing Advice for Lipid Management in Secondary Prevention AND Information for Prescribing and Management of Inclisiran
Description of policy	To inform healthcare professionals
Scope	
Prepared by	Medicines Optimisation Team
Evidence base / Legislation	Level of Evidence: *A. based on national research-based evidence and is considered best evidence* ***B. mix of national and local consensus*** *C. based on local good practice and consensus in the absence of national research based information.*
Dissemination	Is there any reason why any part of this document should not be available on the public website? Yes / No
Approved by	
Authorised by	*TAG / D+TC / Planned Care and Medicines Management Working Group*
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Version	Date	Author	Status	Comment
1.1	June 2022	Marion Sully, Head of Interface and Formulary, NWICB	Final	New document to support prescribing following publication of NICE TA733 - Inclisiran
2.0	Feb 2024	Marion Sully, Head of Interface and Formulary, NWICB	Draft	'Primary care prescribing', 'initiation' and 'purchase and reimbursement' sections updated. Pathway checked and clarified as per NICE

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