Eastern AHSN

East of England Medical Directors and ICS leaders

Briefing on Leqvio® (inclisiran)

June 2023

Part of The AHSN Network

Office for Life Sciences

NHS

Purpose of this document

The overall purpose of this document is to support medical directors, integrated care boards and healthcare professionals with the rapid decision making required to enable the prescribing of inclisiran, a NICE-approved novel therapy. The aim is to support equitable access to and mainstreaming of inclisiran, with the wider objective of supporting cholesterol optimisation and reducing cardiovascular deaths and disease across the East of England.

Your support is particularly relevant because of the varying formulary positions for inclisiran across the East of England, which gives rise to significant inequality of access and the lowest prescribing rates for inclisiran for any region in England (see slide 15).

Skip to the following sections:

Background
Data on inclisiran prescribing
Practical tips
FAQs

INCLISIRAN BACKGROUND

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Further background

The introduction of inclisiran into the lipid management pathway is seen as an opportunity to address **a current gap in the range of treatment options available for people with ASCVD** in whom lipid targets cannot be met on maximum tolerated statins alone or with ezetimibe.

Inclisiran uses the small interfering RNA (siRNA) mechanism of action to lower LDL-C5, 6 by blocking the production of the PCSK9 enzyme. The normal role of the PCSK9 enzyme is to block LDL- C receptors and prevent them from binding to LDL-C in the blood stream, leading to higher LDL-C levels. By "silencing" or switching off the gene responsible for the production of the PCSK9 enzyme or protein, LDL-C receptors are no longer blocked, and can clear LDL-C from the bloodstream. The numbers of LDL-C receptors on the surface of liver cells can also increase again. This results in lower LDL-C levels in the blood.

A collaboration was established between **NHS England, the Accelerated Access Collaborative (AAC) and Novartis Pharmaceuticals UK Ltd** to take a **Population Health Management approach** to offer this clinical intervention to a large at-risk ASCVD patient population. The AHSN Network is the delivery partner working with local healthcare systems to adapt lipid management pathways.

There is a **summary of the national guidance** for lipid management for primary and secondary prevention of CVD and the **NICE guidance** on the recommendations to utilise inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia.

Stoekenbroek RM et al. inclisiran for the treatment of cardiovascular disease: the ORION clinical development program. Future Cardiol 2018;14(6):433-442. https://doi.org/10.2217/fca-2018-0067
Klinovski M et al. inclisiran: A Small Interfering RNA Molecule for Treating Hypercholesterolemia. In: CADTH Issues in Emerging Health Technologies. 2019 Dec Issue 180. https://www.ncbi.nlm.nih.gov/books/NBK555477/pdf/Bookshelf_NBK555477.pdf
Collaborative working agreement: https://www.novartis.com/uk-en/about/partnerships/collaborative-working

Background

The NHS Long Term Plan (LTP) identifies cardiovascular disease (CVD) as a clinical priority and the **single biggest area where lives can be saved over the next 10 years**. It sets out a major ambition to prevent **150,000 strokes, heart attacks and dementia cases**. Low density lipoprotein cholesterol (LDL-C) is a proven risk factor for patients with CVD, and the NICE FAD for inclisiran highlights that hypercholesterolemia is undertreated.

Inclisiran is a novel potent therapy that reduces LDL-C and, after an initial dose and another at 3 months, is maintained by two doses a year by subcutaneous injection. inclisiran has been identified by NHS England as a medicine that it wishes to **adopt systematically and at scale to help address sub-optimal lipid management in high-risk patient populations**.

Prior to the license for inclisiran, there were **four classes of lipid-lowering medicines** available in the lipid management pathway, for patients with atherosclerotic cardiovascular disease (ASCVD):

- High intensity statins[4]
- Ezetimibe for use as an adjunct when statin monotherapy is ineffective, or as monotherapy for those patients that are intolerant to statins[4]
- PCSK9 inhibitors (alirocumab, evolocumab) for use either alone or in combination with statins or ezetimibe (NICE TA3935 3946)
- Bempedoic acid with ezetimibe for treating primary hypercholesterolaemia or mixed dyslipidaemia as an adjunct to diet in adults (NICE TA6947)

NHS England. The NHS Long Term Plan. January 2019. https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-planversion-1.2.pdf
NICE Final Appraisal Document. inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia. Published September 2021.https://www.nice.org.uk/guidance/gid-ta10703/documents/html-content-2
GOV.uk. Press Release: New heart disease drug to be made available for NHS patients. Published January 2020. https://www.gov.uk/government/news/new-heart-disease-drug-to-be-made-available-for-nhs-patients
NHS England. Lipid Management - Rapid Uptake Product. Accessed July 2021. https://www.england.nhs.uk/aac/what-we-do/what-innovationsdo-we-support/rapid-uptake-products/lipid-management/

Narrative

The need to reduce CVD events

Cardiovascular disease (CVD) is associated with brain, heart and vascular health risks and makes up the **leading cause of death in England** [2]

- 137,000 deaths per year of which 37,000 (26%) are premature[2]
- 6.8 million living with CVD[2]
- £7.4bn in costs to the NHS, and £15.8bn with the wider economy[2]

Preventing and managing CVD and its risk factors has the potential to improve population health and ease pressures on overstretched health and care systems by reducing demand for services.

Increase lipid management to improve CVD outcomes

Lipid management in England **must improve** to drive better CVD outcomes

- Every 1 mmol/L reduction in LDL-C is tied to a 22% reduction in major vascular events after 1 year[3]
- A EU-wide study revealed that 61% of high-risk ASCVD patients are unable to reach an LDL-C goal of <1.8mmol (ESC target) signposting the need for a different approach[4]

Lipid control is a vital part of this: 43% of all adults live with LDL-C levels above national guidelines[2]

Tackling CVD through 2023/24 QOF

LDL-C management for secondary prevention is a clinical priority for patients and the NHS, as recognised by incentives in the 2023/2024 QOF amounting to 30 points and ~£36 million in funds [1].

The 2023/2024 updates of QOF include a non-HDL target that is lower than 2.5 mmol/L or where non-HDL cholesterol is not recorded an LDL-C target of lower than 1.8 mmol/L for secondary prevention patients. [1]

The 1.8 mmol/L LDL-C target in the QOF may not be reachable for some patients with statins alone.[4]

Many high-risk CVD patients could still benefit from further treatment optimisation and access to further combination therapies within the lipid management pathway

The need for inclisiran

Despite other successful lipid management initiatives by the **AAC and AHSNs** in England, many high-risk CVD patients could still benefit from further **treatment optimisation** and access to further **combination therapies.**

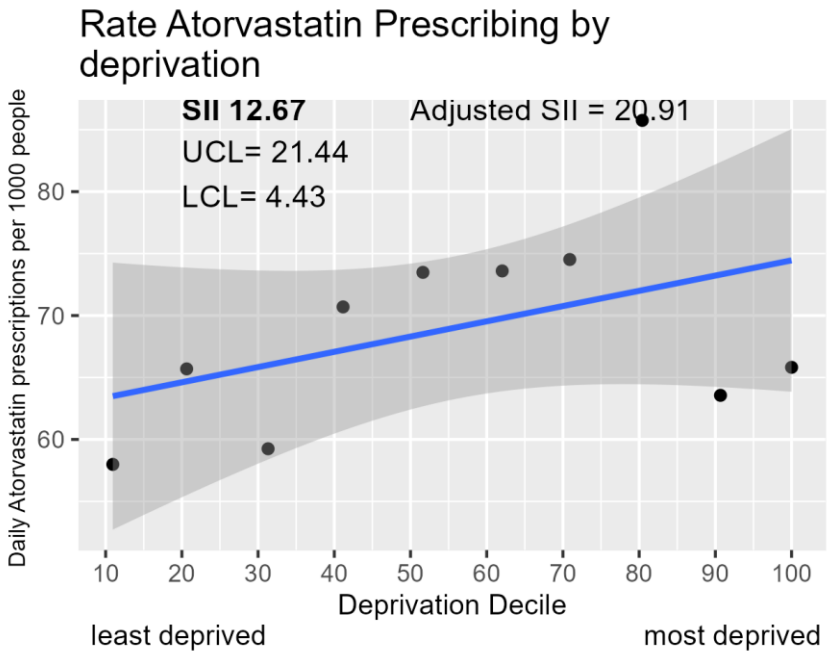
Inclisiran should be delivered as part of a lipid management pathway in support of improving CVD prevention in England which has been recognised as a priority reflected by the introduction of two new lipid management incentives into QOF. [1]

Inclisiran is an effective LDL-C lowering therapy that can help primary care practices achieve QOF cholesterol targets recommend by NICE as a treatment option for high-risk patients with sub-optimal lipid management.[5]

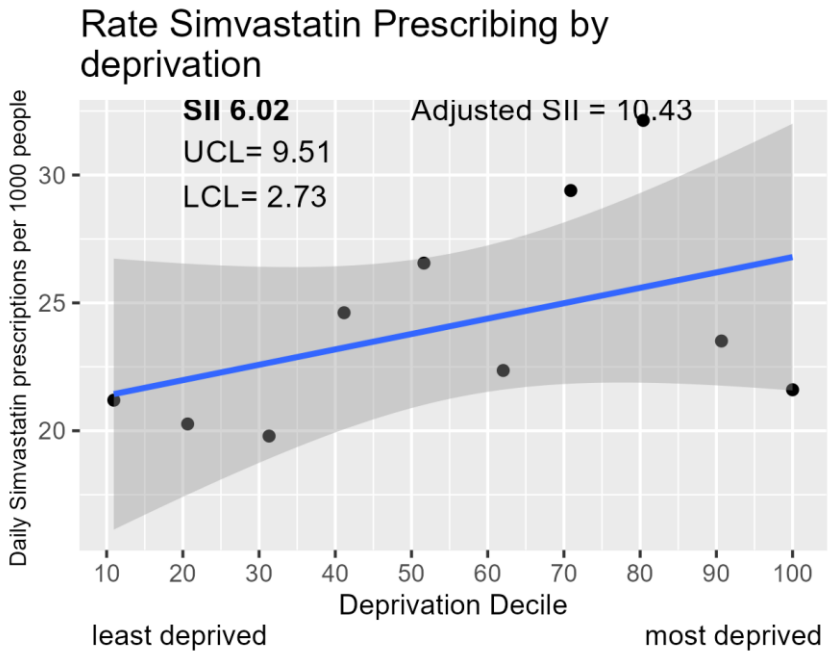
NHSE has a PHM access agreement for inclisiran to **enable access to the product at scale**; providing a further option for combination therapies within the 2023/24 LDL-C Management QOF. [1]

2. https://www.bhf.org.uk/what-we-do/our-research/heart-statistics/heart-statistics-publications (Accessed 4 April 2023)
3. Lancet 2012;380:581-590. Available at https://pubmed.ncbi.nlm.nih.gov/22607822/. (Accessed 4 April 2023)
4. Ray KK et al. Eur J Prev Cardiol 2021;28(11):1279-1289. Available at https://academic.oup.com/eurjpc/article/28/11/1279/5898664 (accessed 4 April 2023)
5. inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia. Technology appraisal guidance [TA733]Published: 06 October 2021. Available at https://www.nice.org.uk/guidance/TA733/chapter/1-Recommendations (Accessed 4 April 2023)

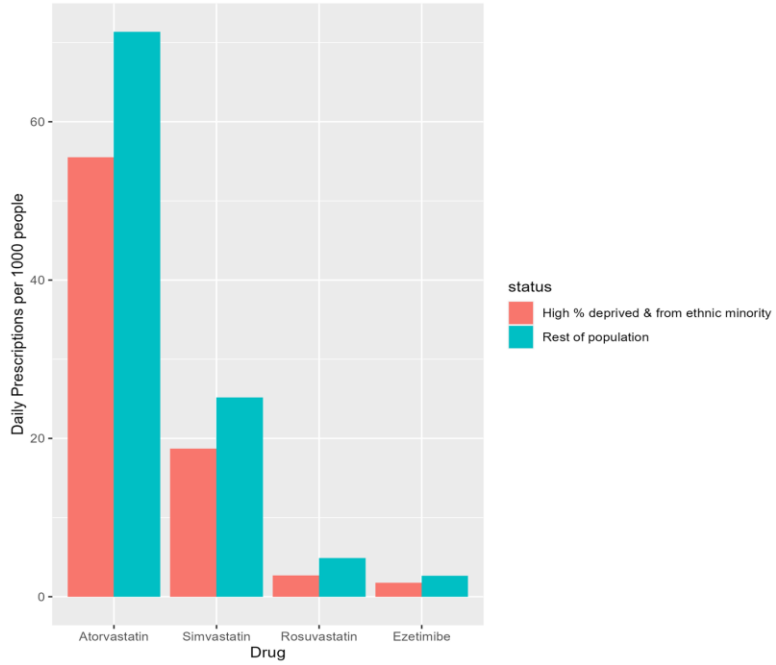
Health equity
Lipid management



There are ~21 more daily prescriptions of Atorvastatin per 1000 people in the most compared with the least deprived deciles



There are ~10 more daily prescriptions of Simvastatin per 1000 people in the most compared with the least deprived deciles



There are decreased number of prescriptions of all cholesterol lowering medications with increasing proportions from ethnic minorities and more deprived areas

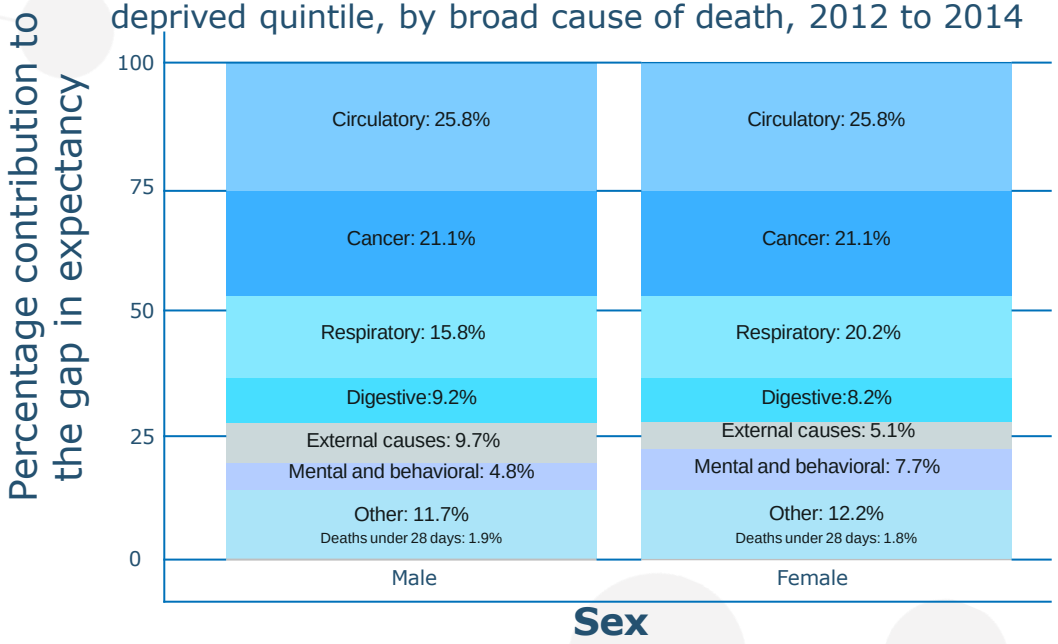
Source: http://www.easternahsn.org/wp-content/uploads/2022/08/CVD-Evidence-Briefing-Aug-2022.pdf

UNIVERSITY OF CAMBRIDGE

Eastern AHSN

The greatest impact on population health through improved lipid management will be achieved by reaching patients in areas of high deprivation

Scarf chart showing the breakdown of the life expectancy gap between England most deprived quintile and England least deprived quintile, by broad cause of death, 2012 to 2014



The Segment Tool has been developed by Public Health England's Epidemiology and Surveillance team and provides information on the causes of death that are driving inequalities in life expectancy at local area level.

Circulatory diseases includes coronary heart disease and stroke. Respiratory diseases includes flu, pneumonia and chronic obstructive airways disease. Digestive diseases includes alcohol-related conditions such as chronic liver disease and cirrhosis. External causes include deaths from injury, poisoning and suicide. Mental and behavioural includes dementia and Alzheimer's disease.[8]

People living in England's most deprived areas are almost four times more likely to die prematurely of CVD than those in the least deprived areas

7. Gov.uk. https://www.gov.uk/government/news/new-heart-disease-drug-to-be-made-available-for-nhs-patients.
8. NHS England: Cardiovascular Disease and Respiratory Programme Board presentation – Sarah Marsh (Feb 20). Available at: https://www.healthcheck.nhs.uk/search-results/?search=sarah+marsh&submit=Go. Accessed June 2021.

INCLISIRAN DATA

CVDPrevent
National orders
East of England orders
Eligibility data
Formularies

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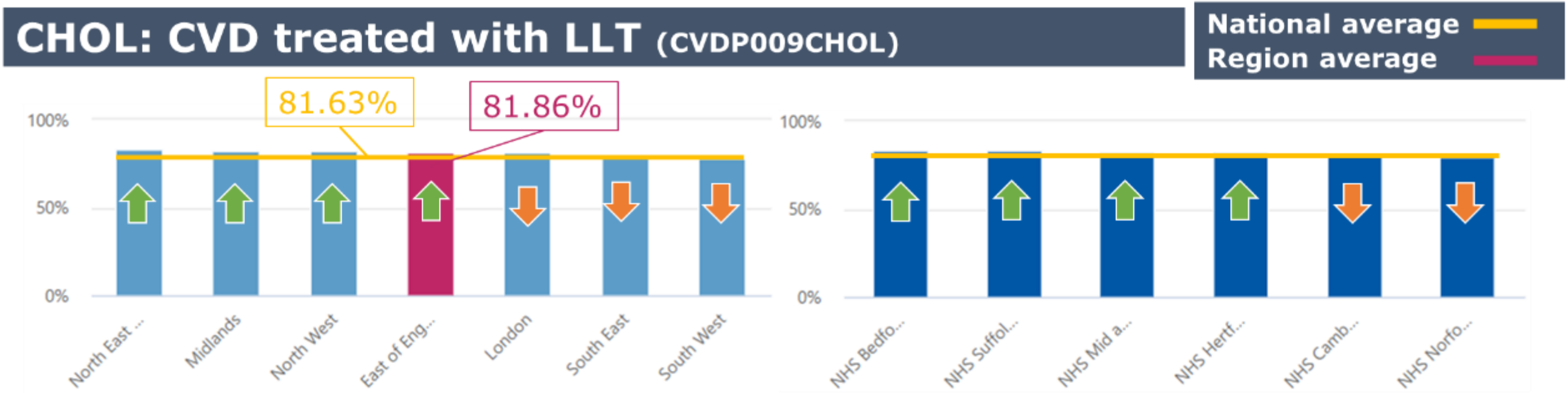
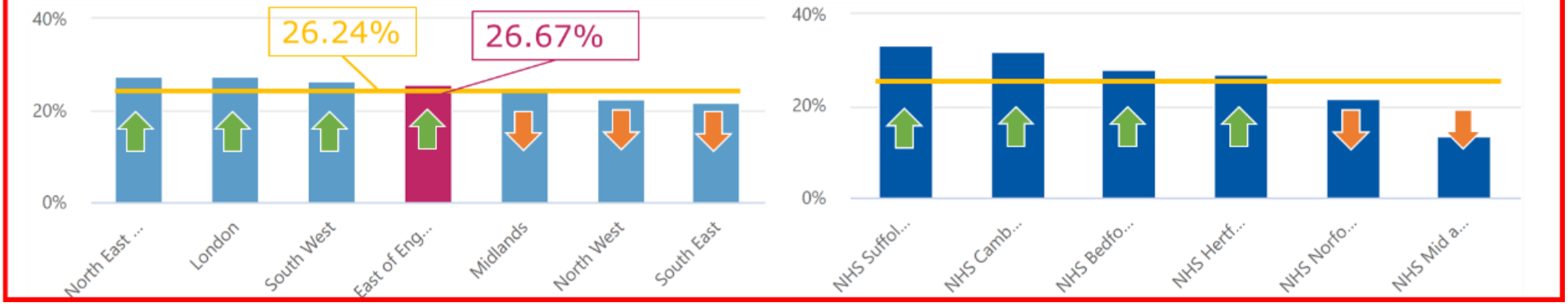
Secondary prevention data (those with established CVD)

CHOL: CVD treated with LLT (CVDP009CHOL)

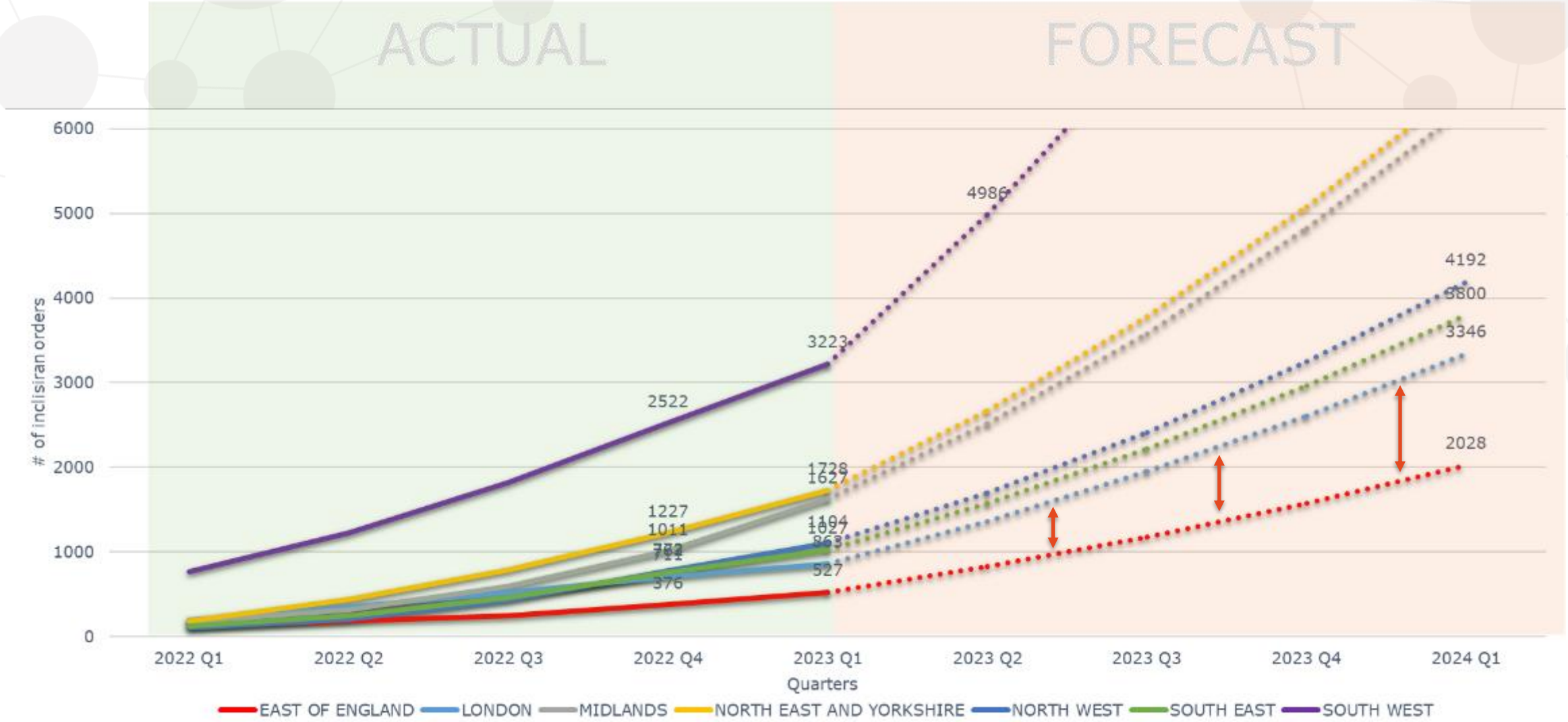


CHOL: CVD treated to threshold (CVDP007CHOL)



Source: Cardiovascular Disease Prevention Audit (CVDPREVENT). Produced by Office for Health Improvement and Disparities and the NHS Benchmarking Network, December 2022.

National breakdown of inclisiran orders



*Data as of **12.6.23** representing 1st Oct 21 to 12th Jun 23, Novartis data & analytics team*
**For some regions, the data shows a slight reduction in orders during 2023 Q2, this is due to data being received halfway through June and therefore not representing a full quarter yet*

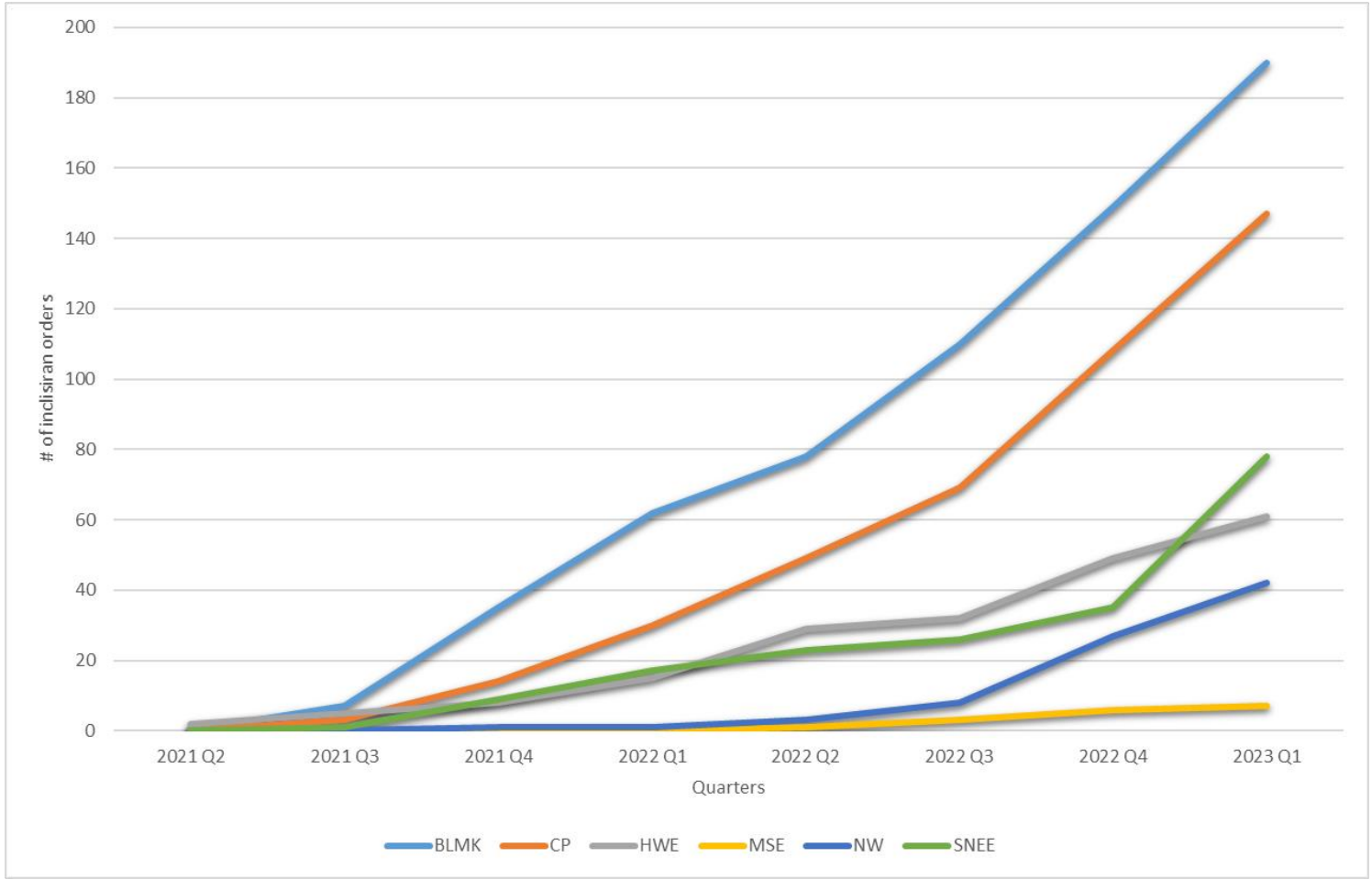
East of England breakdown of inclisiran orders

Total

ICB	# of inclisiran orders
Bedfordshire, Luton and Milton Keynes	190
Cambridgeshire and Peterborough	147
Suffolk and North East Essex	78
Hertfordshire and West Essex	61
Norfolk and Waveney Health & Care Partnership	42
Mid and South Essex	7

To note: only C&P and BLMK can initiate in Primary Care as per recommended pathway. All others restricted to either specialist or secondary care referral / prescribing.

Trend



Data as of 12.6.23, Novartis data & analytics team

National breakdown of inclisiran orders

ACTUAL / FORECAST	QUARTER	EAST OF ENGLAND	LONDON	MIDLANDS	NORTH EAST AND YORKSHIRE	NORTH WEST	SOUTH EAST	SOUTH WEST	TOTAL
ACTUAL	2021 Q2	2	3	0	0	0	1	2	8
	2021 Q3	16	34	11	12	4	14	28	119
	2021 Q4	67	103	77	69	23	64	307	710
	2022 Q1	127	197	175	184	106	125	769	1683
	2022 Q2	185	348	316	439	207	251	1223	2969
	2022 Q3	250	520	592	790	429	459	1817	4857
	2022 Q4	376	711	1011	1227	773	762	2522	7382
	2023 Q1	527	863	1627	1728	1104	1027	3223	10099
FORECAST	2023 Q2	825	1365	2511	2665	1698	1571	4986	15621
	2023 Q3	1175	1949	3576	3782	2412	2216	7039	22149
	2023 Q4	1575	2611	4822	5075	3245	2960	9347	29635
	2024 Q1	2028	3346	6253	6536	4192	3800	11900	38054

*Data as of **12.6.23** representing 1st Oct 21 to 12th June 23, Novartis data & analytics team*
**For some regions, the data shows a slight reduction in orders during 2023 Q2, this is due to data being received half way through June and therefore not representing a full quarter yet*

Eligible population for inclisiran

	Number of people						
	EoE	BLMK	C&P	H&WE	M&SE	N&W	SNEE
Patients registered at GP Practices (all ages)	7,181,942	1,104,486	1,033,643	1,630,852	1,265,521	1,088,308	1,059,132
Adult population	5,648,685	868,692	812,973	1,282,685	995,348	855,968	833,020
Diagnosed prevalence primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia	440,597	67,758	63,412	100,049	77,637	66,765	64,976
People receiving or who have previously received lipid lowering therapy	402,706	61,931	57,958	91,445	70,960	61,024	59,388
Of these, people whose low-density lipoprotein cholesterol concentrations are persistently above 2.6mmol/L	144,974	22,295	20,865	32,920	25,546	21,969	21,380
Of these, people who are prescribed statins and have had at least one recorded instance of a cardiovascular event, angina or peripheral arterial disease (secondary prevention)	56,151	8,635	8,081	12,751	9,894	8,509	8,281
Estimated eligible population for inclisiran	**56,151**	**8,635**	**8,081**	**12,751**	**9,894**	**8,509**	**8,281**

Data sources:
NHS Digital Patients Registered at a GP Practice, Rob Danks, 11 May 2023 Publication
Resource impact template: inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia (TA733)

Formularies status in the East of England

(NB NICE recommendation can be prescribed in primary care)

ICS	Formulary Status	What this means	Other projects / funding
SNEE	**UNLISTED**	SNEE has approved inclisiran in line with NICE Technology Appraisal (TA) 733 but are **working with local specialists to develop a safe pathway to introduce this drug** into the health economy. The ICS has developed an **inclisiran task & finish group** with the objective of identifying a suitable solution and delivery model with the aim of moving to a green formulary position as soon as possible. However, the preferred chosen delivery model is dependent on **Collaborative Lipids Funding** (£126,000) from NHSE, due to be announced at the end of June. This funding is at risk because of the time already taken to get to this stage.	• STF project funding • National Lipids Programme Workforce Support (1 PCN) • Halcyon project funding (1 PCN) • CLF project *(at risk – reapplied funding)*
M&SE	**RED➡AMBER**	As of this quarter the formulary position moved from red to amber allowing prescribing with **Specialist initiation.**	
H&WE	**AMBER**	**Initiated by specialists in secondary and tertiary care** with prescribing and monitoring continued by GPs. Secondary care is struggling with capacity to deliver the injection within their clinics.	• National Lipids Programme Workforce Support (1 PCN)
N&W	**GREEN/AMBER**	**Specialist advice required from clinician with relevant expertise prior to primary care initiation**. When specialists encounter patients who are likely to benefit from receiving therapy in accordance with the criteria in the NICE TA, this will be communicated to the patient's GP for **initiation in Primary Care.**	
C&P	**GREEN**	**Initiation in Primary Care** aligned to NICE recommendation as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults for eligible patients.	• Halcyon (1 PCN) • InHIP
BLMK	**GREEN**	**Initiation in Primary Care** aligned to NICE recommendation as an option for treating primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia as an adjunct to diet in adults for eligible patients.	• STF • Halcyon (ICB)

INCLISIRAN PRACTICAL TIPS

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Call to action for inclisiran

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Step 1

Formulary positions

- IMOC and MO leads to enable a green formulary position as per

2

Step 2

Use available mechanisms

- Adoption of LM pathways
- QOF
- Search tools
- Funding & supply
- Advice & Guidance from secondary care
- LES (in some ICBs)

3

Step 3

Advocacy, roles & responsibilities

- Primary care
- Secondary care
- ICSs

Step 1: Formulary position

We recommend that all non-green ICSs take urgent steps to approve the prescribing of inclisiran to eligible patients in primary and secondary care to enable maximum patient benefit and reduce the current inequity of access

ICS	SNEE	M&SE	H&WE	N&W	C&P	BLMK
Formulary Status	UNLISTED	AMBER	AMBER	GREEN/AMBER	GREEN	GREEN

Step 2: Pathways from AAC, NICE and AHSN

Lipid management in England must improve to drive better CVD outcomes and, to address the clinical priority of improved lipid management, two pathways – one for acute cardiovascular disease in secondary care and one for primary care clinicians – have been developed to provide clear and simple guidance for clinicians on how optimal lipid management may be achieved and provide an additional resource to support patient management. Click the links below which take you to these two pathways.

- Pathway for secondary care – following an Acute Cardiovascular Event
- Pathway for primary care – for Secondary Prevention in Primary Care

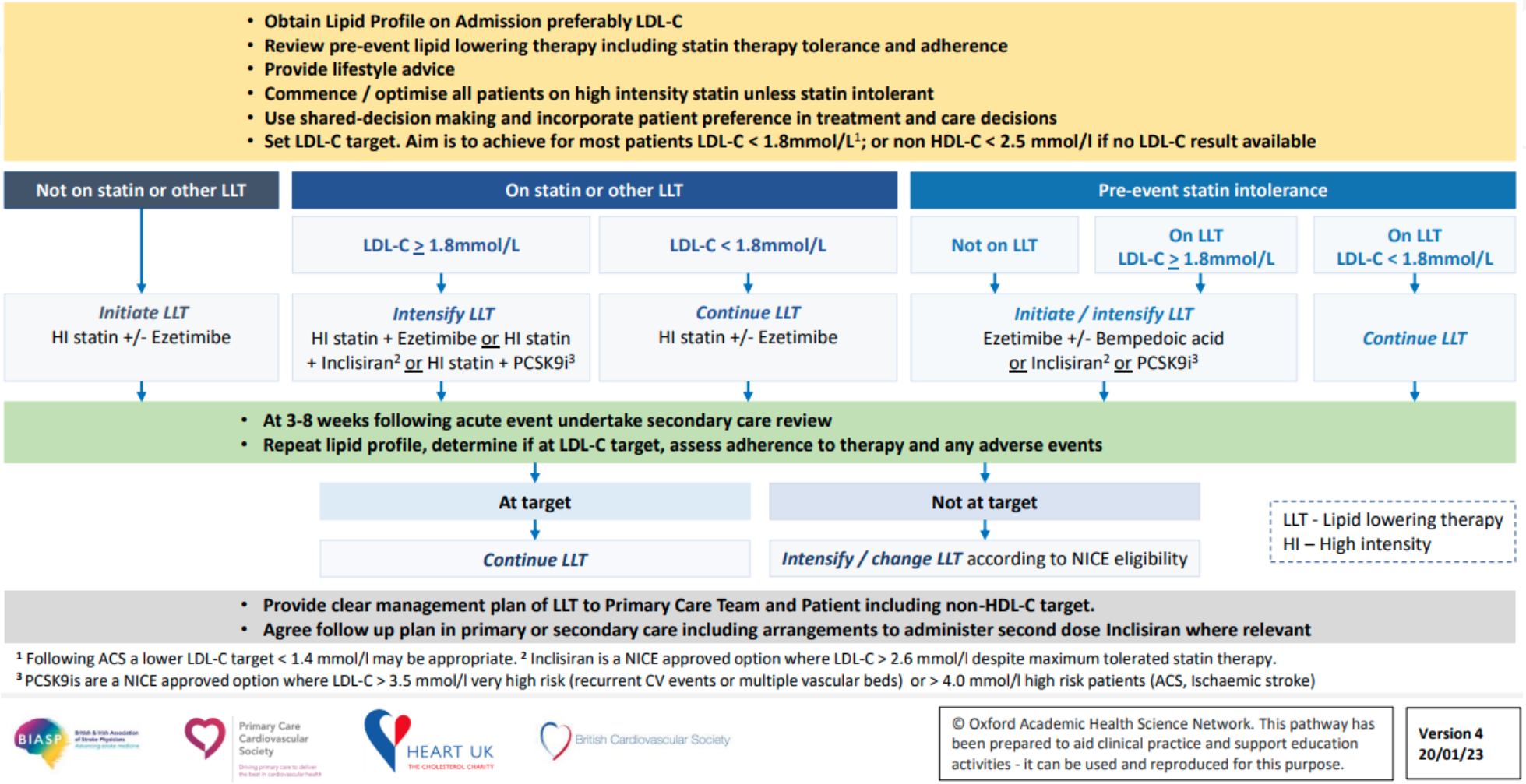
The pathways provide an additional resource which can be used to support patient management. They have been developed to support healthcare professionals in implementing NICE and other relevant evidence in lipid management in secondary prevention. These are not comprehensive clinical guidelines setting out all clinical scenarios, nor do they seek to set out the clinical evidence base for interventions which is covered in the relevant NICE Technology Appraisals.

Every 1 mmol/L reduction in LDL-C is tied to a 22% reduction in major vascular events after 1 year. The 1.8 mmol/L LDL-C target in the QOF may not be reachable for some patients with statins alone and many high-risk CVD patients could still benefit from further treatment optimisation and access to further combination therapies within these pathways.

https://www.ahsnnetwork.com/programmes/cardiovascular-disease/lipid-management-and-familial-hypercholesterolemia/lipid-management-pathways/

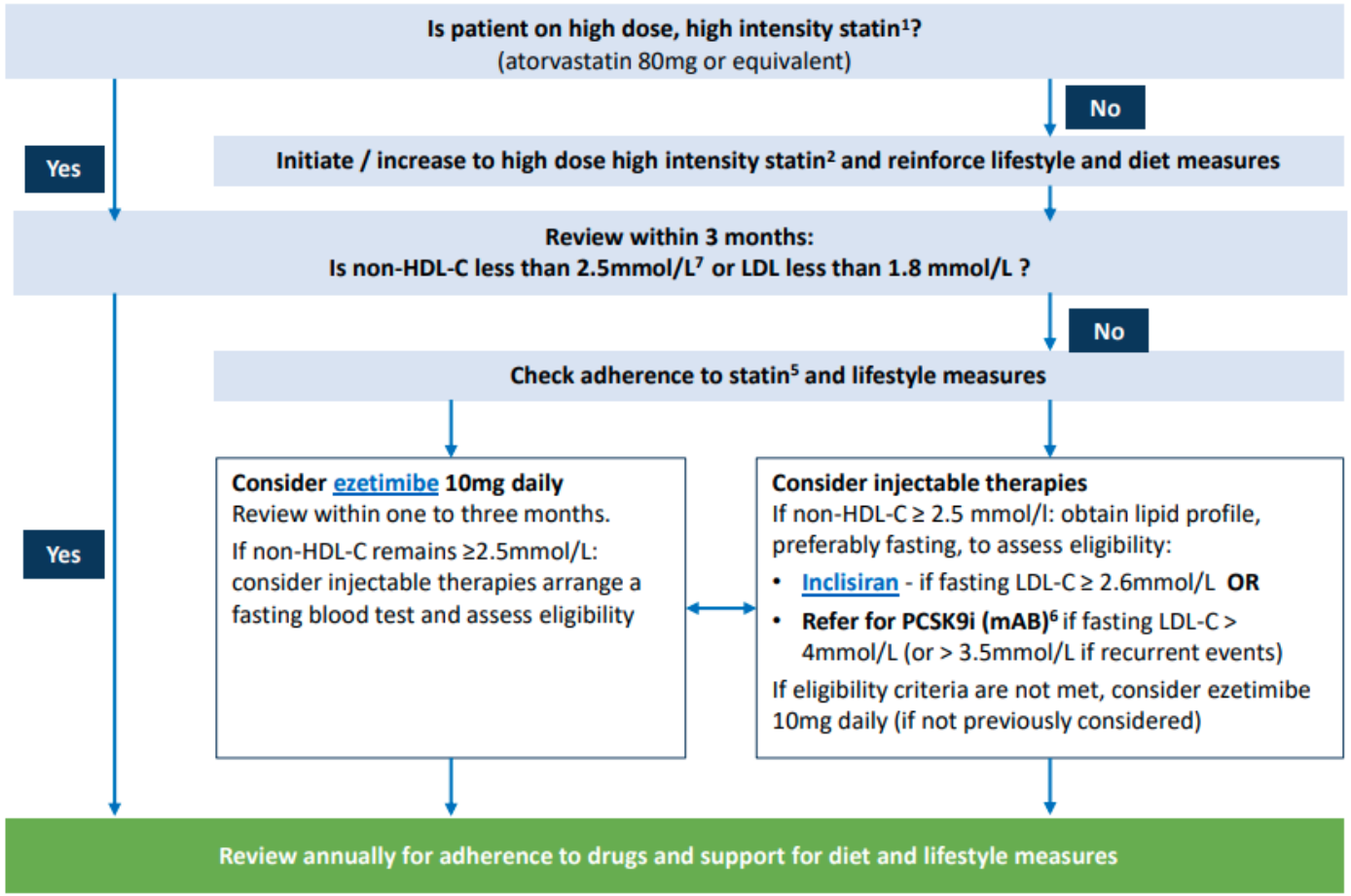
Step 2: Pathway for secondary care

Pathway for secondary care – following an Acute Cardiovascular Event



Step 2: Pathway for primary care

Pathway for primary care – for Secondary Prevention in Primary Care



Optimal High Intensity Statin for secondary prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	80mg
Rosuvastatin	20mg

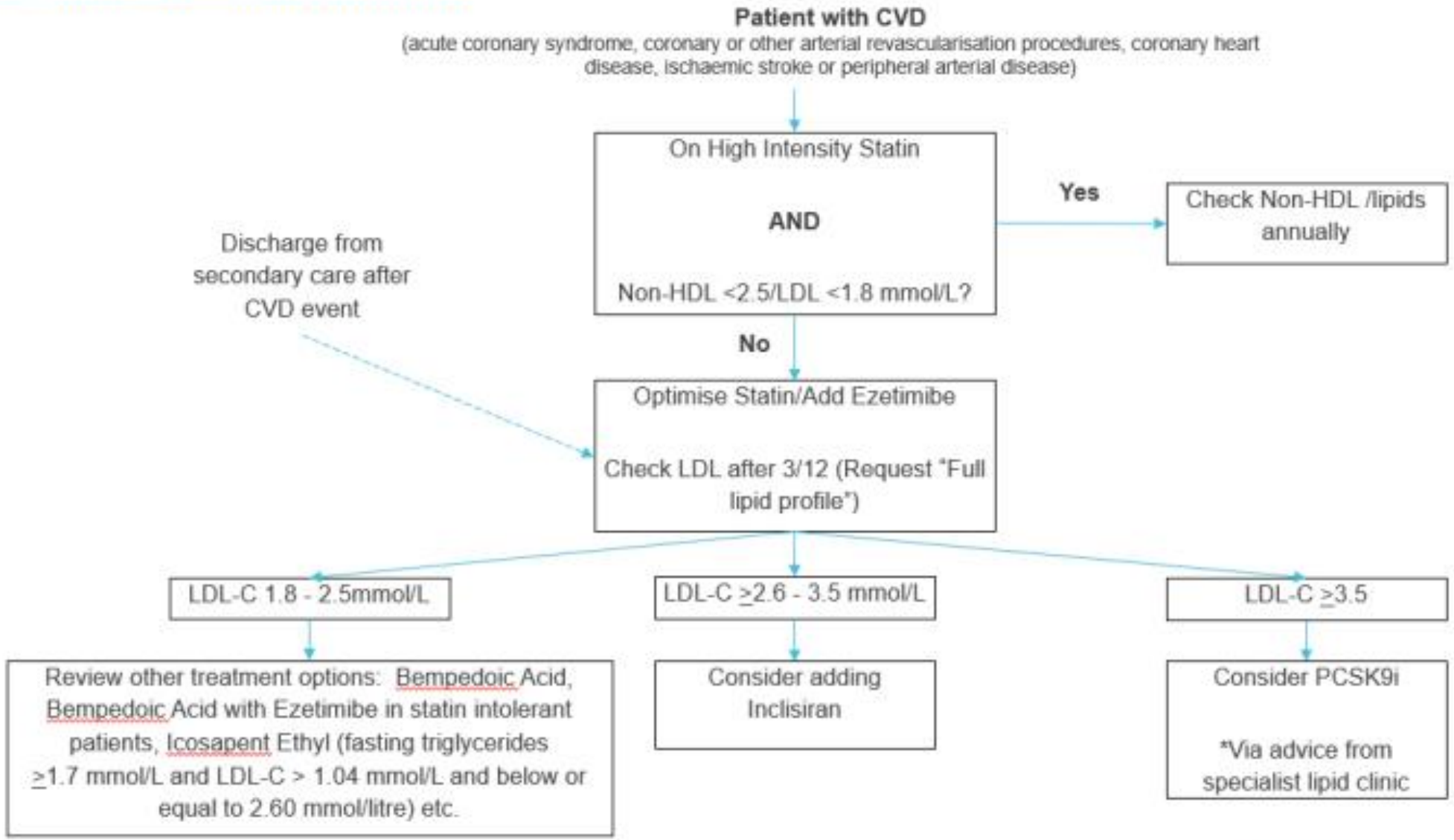
1. Dose may be limited, for example if:
   - eGFR<30ml/min
   - Drug interactions
   - Intolerance
   - Older age / frailty
2. See statin intensity table. Use shared-decision making and incorporate patient preference in treatment and care decisions.
3. NICE CG181 CVD Risk Assessment and Reduction
4. NICE approved Summary of National Guidance for Lipid Management
5. If statin not tolerated, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily. If non HDL-C remains ≥ 2.5mmol/L despite other lipid lowering therapies consider injectable therapies.
6. NICE Guidance: Evolocumab, Alirocumab
7. Non-HDL LDL targets are identified in order to aid optimal lipid management, current NICE Guidance (under review) recommends a greater than 40% reduction in non HDL cholesterol

Based on a pathway developed by: UCLPartners

Version 6
03/02/23

Step 2: Pathways (national example)

Example Inclisiran Pathway:



https://improvement.kssahsn.net/wp-content/uploads/2022/12/CVD-Central-Resource-Pack-inclisiran-implementation-V3.Dec2022.Final_.pdf

Step 2: 2023/24 QOF cholesterol indicators

There is a heightened focus on the role of cholesterol within secondary prevention with two new cholesterol indicators (worth 30 points~£36m) which were added to the **2023/2024 Quality Outcome Framework (QOF).**

QOF has been streamlined in 2023/24 and includes:

- A non-HDL target that is lower than 2.5 mmol/L or,
- where non-HDL cholesterol is not recorded, an LDL-C target of lower than 1.8 mmol/L for secondary prevention patients.

This recognises that LDL-C management for secondary prevention is a clinical priority for patients and the NHS which will contribute to reducing the number of cardiovascular disease events in England.

Step 2: Patient search tools

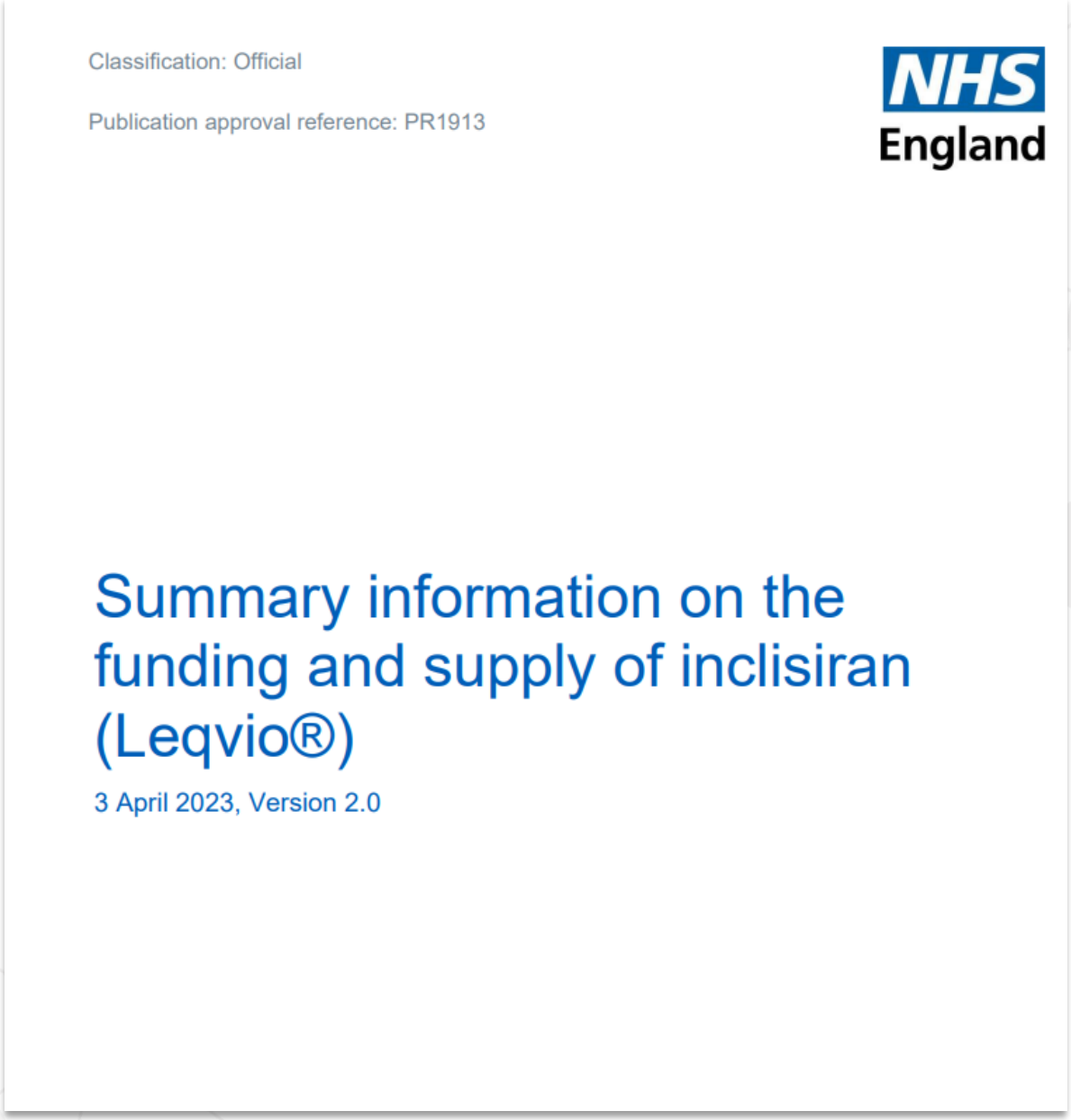
The aim of the patient search tool resource review is to provide clinicians with an overview of some of the key existing search tools available to support them in identifying at risk patients, treatment options and review points

https://www.ahsnnetwork.com/wp-content/uploads/2023/02/Patient-Search-Tool-publication-pack-update.pdf

Step 2: Funding and supply

Funding and supply of inclisiran

This document describes the funding and supply arrangements for inclisiran (Leqvio®) as an option in the lipid management pathway. These arrangements follow from the recommendations set out in TA733 by NICE on 06 October 2021. An overview is provided for both primary care and secondary care.



https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2023/04/B1913-summary-information-on-the-funding-and-supply-of-inclisiran-v-april-2023.pdf

Step 3: Advocacy, roles & responsibilities

The role of Integrated Care System Leaders

- ICSs are critical to the delivery of prevention programmes as the NHS continues to move from reactive care towards a model embodying active population health management
- Much of the prevention agenda will be delivered in primary care. For this to happen, the ICS will have to focus on PCN support and development.
- ICS leaders will seek to understand any variation across the system. Insight from system partners can be used to understand what might be driving variation and how this may be addressed
- ICSs have a duty to engage with local communities, especially those who are reluctant or hesitant to engage with services.
- There may be opportunities to apply learning from experience with other local initiatives. ICSs can encourage the sharing of good practice and ideas to spread innovation and reduce variation
- Within each CCG/ICS Medicines Optimisation team is a dedicated group of pharmacists and pharmacy technicians working towards the common goal of improving the use of medicines across the local health system

Oxford AHSN. CVD prevention during the COVID-19 pandemic: guidance for integrated care systems Available at: https://www.oxfordahsn.org/wpcontent/uploads/2020/12/CVD-prevention-during-the-COVID-19-pandemic-guidance-for-system-level-change-December-2020.pdf Accessed July 2021.

Step 3: Advocacy, roles & responsibilities

The role of ICSs

- Prevention of cardiovascular disease is a strategic imperative for ICSs
- A critical role in aligning action between partners to achieve their shared purpose: to improve outcomes and tackle inequalities, to enhance productivity and make best use of resources and to strengthen local communities.
- The ICS Integrated Care Board should focus on achieving the four purposes of the wider ICS: improving outcomes in population health and healthcare; tackling inequalities in outcomes, experience and access; enhancing productivity and value for money; and contributing to broader social and economic development
- As part of its function in arranging for the provision of health services, the ICS has responsibility for convening and supporting providers (working both at scale and at place) to lead major service transformation programmes
- Leaders of all organisations involved in collaboration across the ICS have to adopt a 'one workforce' approach and develop shared principles and ambitions for people and culture with local authorities, the VCSE sector and other partners.
- Guidance from NHSEI states that "tackling inequalities of outcome is central to the investments we will make this year to improve outcomes on cancer, cardiovascular disease, mental health and maternity services as well as to expand smoking cessation and weight management services

Step 3: Advocacy, roles & responsibilities

The role of Local Medicine Committees (LMCs)

It is important to be aware of LMCs and their role in local decision-making. In some ICS the LMC could play a role in representing the views of GP colleagues and in the transformation of primary care

The LMC has a statutory duty to represent GPs at a local level and may sit on the ICS integrated care board

At a national level, LMCs interact and work with, and through, the GPC (general practitioners committee) as well as other practice committees and local specialist medical committees

LMCs may have concerns about:

- The initiation of new, advanced medicines in primary care prior to familiarisation in specialist care. Although recent adoption of the COVID-19 vaccine may have alleviated some concerns
- Increased workload for GPs and the wider general practice
- Appropriate funding for GP practices to cover any investment in new services

Wessex LMC. Available at: https://www.wessexlmcs.com/gprepresentationtheroleofthelmc. Accessed July 2021. 2] The British Medical Association. Available at: https://www.bma.org.uk/what-we-do/local-medical-committees. Accessed July 2021.

Step 3: Advocacy, roles & responsibilities

The role of Primary Care (GP Practices & PCNs)

- Primary care is expected to think about the wider health of their population, taking a proactive approach to managing population health and assessing the needs of their local population
- The introduction of the new 2023/24 QOF CHOL indicators aim to support primary care to manage and optimise CVD patients. Usually a statin is recommended as first line therapy for the secondary prevention of CVD. Options recommended by NICE when a statin is declined or clinically unsuitable due to contraindications or intolerance include Ezetimibe, PCSk9, inhibitors and/or inclisiran.
- Primary care can also ensure that all patients with established cardiovascular disease, defined as Coronary Heart Disease, Peripheral Arterial Disease, or Stroke/TIA are considered for intensification of therapy where there is an insufficient reduction in cholesterol with first line therapy, usually a statin.

Primary care can:

- Use searches and risk-stratification tools to identify patients for preventative support and CVD prevention
- Maximise any face-to-face encounters
- Use the wider primary care team to support CVD prevention
- Ensure patients are on optimal medication to reduce their cholesterol in line with NICE thresholds
- Embed inclisiran prescribing within the local lipid management pathway
- Encourage patients to access NHS Health Checks
- Recruit staff under the ARRS scheme to support the CVD DES
- Consider other ways to optimise the lipid management programme through collaborative working

https://www.england.nhs.uk/wp-content/uploads/2023/03/PRN00289-quality-and-outcomes-framework-guidance-for-2023-24.pdf

Step 3: Advocacy, roles & responsibilities

The role of AHSNs

- AHSNs are the only partnership bodies that bring together all partners across a regional health economy to improve the health of local communities enabling AHSNs to foster collaborative solutions.
- All AHSNs are currently delivering a multi-year national programme with the aim of improving patient care and outcomes by effectively treating patients with hypercholesterolaemia.
- The AHSN Network is the delivery partner for the implementation of inclisiran
- All AHSNs will continue to collaborate as with existing work on lipid management, sharing learning and experience form deployment.

INCLISIRAN FAQs

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General information

What are the licencing details for inclisiran?

Inclisiran (Leqvio®) is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin, or statin with other lipid lowering therapies, in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin, or
- alone or in combination with other lipid lowering therapies in patients who are statin intolerant, or for whom a statin is contraindicated.

Which healthcare professionals can prescribe inclisiran?

Inclisiran is a prescription only medicine and can be prescribed by all independent prescribers in accordance with The Human Medicines Regulations 2012

Are there any specific storage requirements for inclisiran?

Inclisiran does not require any special storage conditions. It should not be frozen. Further details here

How to report a concern or incident relating to inclisiran?

Side effects and incidents related to inclisiran should be reported to MHRA via the Yellow Card scheme here: Yellow Card

Patients

Which patients may be suitable for inclisiran?

All patients with pre-existing ASCVD with last LDL-C of 2.6 mmol/L or higher. Further info **HERE**.

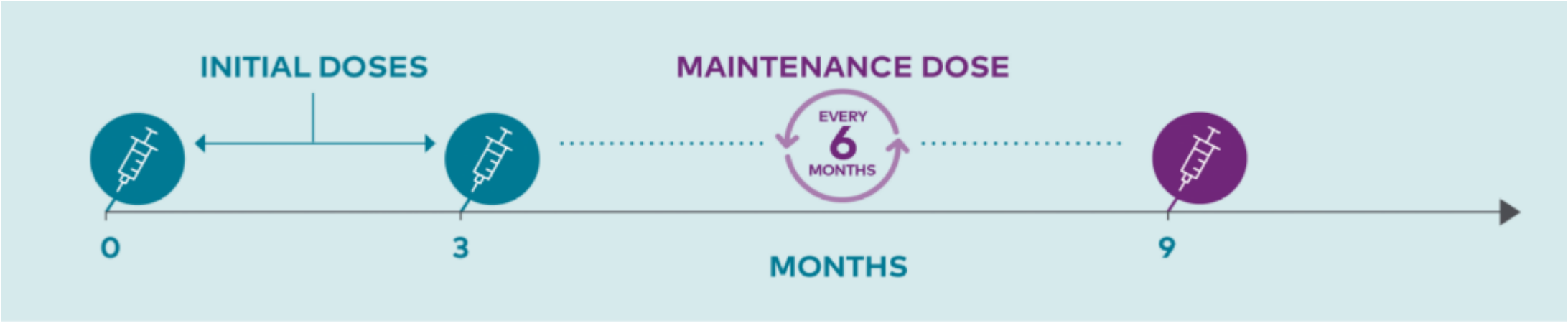
How do I identify eligible patients?

They may be identified from an annual QOF review or by running searches such as Ardens or other search tools used in the practice.

How does it work?

Inclisiran uses the small interfering RNA (siRNA) mechanism of action to lower LDL-C by blocking the production of the PCSK9 enzyme. The normal role of the PCSK9 enzyme is to block LDL- C receptors and prevent them from binding to LDL-C in the blood stream, leading to higher LDL-C levels. By "silencing" or switching off the gene responsible for the production of the PCSK9 enzyme or protein, LDL-C receptors are no longer blocked, and can clear LDL-C from the bloodstream. The numbers of LDL-C receptors on the surface of liver cells can also increase again. This results in lower LDL-C levels in the blood.

The recommended dose of inclisiran is 284 mg, administered subcutaneously via a single pre-filled syringe: as an **initial dose**, again at 3 months, followed by **a dose every 6 months**.



Ordering

How do I order inclisiran?

inclisiran initiation and management is intended to be carried out predominantly within the primary care setting where most patients with ASCVD are currently managed. However, it is possible to order in primary and secondary care, as described in the funding and supply document **HERE**

Safety / efficacy

The most recent long-term study for the 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.

Whether long-term treatment with the twice-yearly, siRNA therapeutic inclisiran, which reduces hepatic production of proprotein convertase subtilisin/kexin type 9 (PCSK9), results in sustained reductions in LDL cholesterol with an acceptable safety profile is not known. The aim of this study was to assess the effect of long-term dosing of inclisiran in patients with high cardiovascular risk and elevated LDL cholesterol.

Twice-yearly inclisiran provided sustained reductions in LDL cholesterol and PCSK9 concentrations and was well tolerated over 4 years in the extension study. This is the first prospective long-term study to assess repeat hepatic exposure to inclisiran.

https://www.thelancet.com/journals/landia/article/PIIS2213-8587(22)00353-9/fulltext#seccestitle10

Further information

Where can I find more information about inclisiran?

General information about inclisiran▼ (Leqvio®) can be found for UK healthcare professionals, NHS relevant decision makers and patients using the following links:

For patients

For health care professionals

NICE TA733: inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia

Evidence-based recommendations on inclisiran (Leqvio) for treating primary hypercholesterolaemia or mixed dyslipidaemia in adults: **NICE inclisiran Guidance**

National Guidance for Lipid Management

A summary of national guidance for lipid management for primary and secondary prevention of cardiovascular disease (CVD): **The national lipid management pathway, which includes inclisiran**

Resources and training

HEART UK has partnered with the NHS Accelerated Access Collaborative (AAC) and the Academic Health Science (AHSN) Network to provide a comprehensive and varied education programme for healthcare professionals.

Tackling Cholesterol Together is a comprehensive and varied education programme for healthcare professionals delivered in partnership between The AHSN Network, HEART UK and the NHS Accelerated Access Collaborative (AAC).

All available resources, webinars can be found on the **Tackling Cholesterol Together homepage**

Tackling Cholesterol Together

The AHSN Network

ACCELERATED ACCESS COLLABORATIVE

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THE CHOLESTEROL CHARITY

NHS

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To learn more about our work in this area and find available resources, visit our **lipid management page**

Part of The AHSN Network

Office for Life Sciences

NHS