This material was created and fully funded by Novartis Pharmaceuticals UK, and is intended for UK healthcare professionals only.

LEQVIO® inclisiran

WHAT VALUE COULD LEQVIO®▼ (INCLISIRAN) BRING TO PATIENTS AND HEALTHCARE SERVICES?

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.[1]

Optimising cholesterol management can benefit your eligible patients with CVD:[2]

~6.4 m people are living with **CVD conditions**[2]

30% of the **125,445 deaths from CVD in 2021 were premature**[2]

CVD costs **~£600 m** in lost workdays and has a total economic cost of **~£1.3 bn**[2]

An initial CV event costs the NHS £4,594 during the first 6 months, with hospitalisations accounting for **95%** of acute incremental costs*[,3]

High cholesterol can increase the risk of CVD[2]

Each 1 mmol/L reduction in LDL-C is associated with a 21% relative risk reduction of major vascular events (RR=0.79; 95% CI: 0.77–0.81)†[,5]

Every £1 spent on CVD prevention[4]

Provides an estimated £2.30 return on investment†[,4]

~1 in 5 **patients with CVD do not have a current prescription for lipid-lowering therapy** and therefore remain at high risk for CV events and death§[,6]

The effect of LEQVIO on CV morbidity and mortality has not yet been determined.[1]

LEQVIO offers a way to help patients reach their LDL-C targets:

LEQVIO offers a way to help patients reach their LDL-C targets:
NICE recommends LEQVIO, within its licensed indication, as an option for the treatment of adult patients who:[7]

1. **Have already had certain CV events** (acute coronary syndrome such as MI or unstable angina needing hospitalisation, coronary or other arterial revascularisation procedures, coronary heart disease, ischaemic stroke or PAD)
2. **Have persistently elevated LDL-C levels (≥2.6 mmol/L)** despite maximum tolerated statins with or without other lipid-lowering therapies, or other lipid-lowering therapies when statins are not tolerated or are contraindicated

- NICE states that LEQVIO is cost-effective in this patient population[7]
- LEQVIO is suitable for use in **primary** and **secondary care**[1,7]

The administration profile of LEQVIO and its cost-effectiveness within the NICE-recommended population make it suitable in both of these settings[1,7]

LEQVIO is funded through the central NHS budget in primary and secondary care[1,7,8]

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With **straightforward, twice-yearly maintenance dosing,** LEQVIO can be integrated into your patients' routine appointments¶,[1]

After an initial dose, LEQVIO is administered again at 3 months, followed by every 6 months.[1]

- HCP-administered
- Subcutaneous injection
- No refrigeration required
- 284 mg Fixed dose

How the medication schedule of LEQVIO compares with that of other add-on therapies:

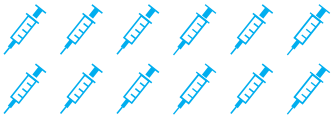
LEQVIO
following initial 2 doses

2 maintenance doses**
per year

HCP-administered

PCSK9 mAbs
every month

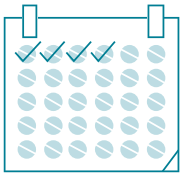
12 doses a year††,[9]



Self-injections

Ezetimibe 10 mg
1 tablet daily

365 doses a year[10]



Self-administered

****After an initial dose, LEQVIO is administered again at 3 months, followed by every 6 months.[1]**

††PCSK9 mAbs may have shorter treatment intervals based on clinical decision.[9,11] Evolocumab dosing options are clinically equivalent for primary hypercholesterolaemia or mixed dyslipidemia;[9] alirocumab usual starting dose is every 2 weeks, however can be individualised based on patient characteristics.[11]

Please see SmPCs of the individual therapies for full dosing information.

Other lipid-lowering therapies are available.

LEQVIO offers a dosing schedule your patients may prefer

LEQVIO may fit into your patients' routine appointments in primary care[1]

Approximate number of LEQVIO injections per primary care practice per week:

<2

Based on two maintenance doses per year

There are **multiple opportunities** in inpatient and outpatient settings **within secondary care to initiate LEQVIO and make every contact count for patients with ASCVD**.

These include patients who:

- Have been admitted to hospital multiple times
- Have been given an appointment for elective PCI
- Have attended an outpatient follow-up appointment post discharge

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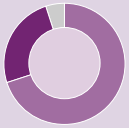
The 2024/2025 QOF guidance recognises the importance of **proactive cholesterol management for patients who have already had a CV event**[12]

The effect of LEQVIO on CV morbidity and mortality has not yet been determined.

Addressing both **CHOL003** and **CHOL004** will give you **30 points**, which has a potential **value of ~£6,618**[‡‡,12,13]

Indicator	Points	Thresholds
CHOL003. Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, Stroke/TIA or Chronic Kidney Disease Register **who are currently prescribed a statin**, or where a statin is declined or clinically unsuitable, **another lipid-lowering therapy**[12]	14	70–95% 
CHOL004. Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease or Stroke/TIA Register, who have a recording of **LDL cholesterol in the preceding 12 months that is 2.0 mmol/L or lower**, or where LDL cholesterol is not recorded, a recording of non-HDL-C in the preceding 12 months that is 2.6 mmol/L or lower[12]	16	20–35% 

Using LEQVIO when statins alone are not enough **may help bring the 2.0 mmol/L LDL-C QOF target within reach** for eligible patients[§§,12,14]

With two maintenance doses a year, almost 80% of patients with ASCVD on LEQVIO achieved the LDL-C target of <1.8 mmol/L, in combination with a maximally tolerated statin (baseline LDL-C of 2.9 mmol/L ±1.2)[‖‖,15]

After an initial dose, LEQVIO is administered again at 3 months, followed by every 6 months.[1] Mean cumulative exposure to LEQVIO in ORION-8 was 3.7 years with a maximum of 6.8 years.[15]

LEQVIO had a similar safety profile to placebo in clinical trials,[14] apart from injection-site reactions:[1]

- Adverse reactions at the injection site occurred in 8.2% of patients in the LEQVIO group and 1.8% in the placebo group
- The proportion of patients in each group who discontinued treatment due to adverse reactions at the injection site was 0.2% and 0.0%, respectively
- All of these adverse reactions were mild or moderate in severity, transient and resolved without sequelae

Please refer to the LEQVIO Summary of Product Characteristics for full details on the safety profile of LEQVIO and before prescribing.

*Direct medical costs to the NHS during the first 6 months of CV events among individuals on lipid-lowering therapies who had their first event between January 2006 and March 2012 (first event: N=24,093; second event: n=5,274).[3] †The estimated societal return on investment over 10 years, including the value placed on improved health.[4] ‡Based on a meta-analysis of data from randomised statin trials over an average of 5.1 years (N=174,149 patients). The estimated absolute reduction in major vascular events in participants with a 5-year risk <10% was around 11 per 1,000 over 5 years for each 1.0 mmol/L LDL-C reduction. Major vascular events were major coronary events (ie, non-fatal myocardial infarction or coronary death), strokes, or coronary revascularisations.[5] §National data received from 96.6% of GP practices, including ~18 million patients.[6] ¶In combination with a maximally tolerated statin. **After an initial dose, LEQVIO is administered again at 3 months, followed by every 6 months.[1] ††PCSK9 mAbs may have shorter treatment intervals based on clinical decision.[9,11] Evolocumab dosing options are clinically equivalent for primary hypercholesterolaemia or mixed dyslipidemia;[9] alirocumab usual starting dose is every 2 weeks, however can be individualised based on patient characteristics.[11] Please see SmPCs of the individual therapies for full dosing information. ‡‡Calculation of potential gain based on the value of £220.62 per QOF point. Note that the value of a QOF point varies depending on the size of the practice and on the prevalence of the condition or risk factor.[12] §§Data from the multicentre, double-blind, randomised, placebo-controlled, 18-month ORION-10 (N=1,561) and ORION-11 (N=1,617) clinical trials evaluating adult patients on a maximally tolerated statin with ASCVD, and with ASCVD or risk equivalents, respectively. The baseline mean (±) LDL-C levels were 2.70 ±1.02 mmol/L with LEQVIO and 2.71 ±0.96 mmol/L with placebo in ORION-10, and 2.77 ±1.08 mmol/L with LEQVIO and 2.68 ±0.94 mmol/L with placebo in ORION-11. The proportion of patients achieving an LDL-C goal of 1.8 mmol/L at Month 17 with LEQVIO vs placebo was 74% vs 15% in ORION-10 (19.2; 14.7–25.2), and 81% vs 18% in ORION-11 (17.1; 13.2–22.0).[1,14] ‖‖ORION-8 (N=3,274) assessed the long-term efficacy and safety of LEQVIO in patients who entered an open-label extension after completing either ORION-3, ORION-9, ORION-10 or ORION-11 trials. Patients had a baseline LDL-C of 2.92 mmol/L (±1.2), and the primary endpoints were the proportion of patients achieving pre-specified LDL-C goals at end of the study, and safety.[15,16,17]

ASCVD=atherosclerotic cardiovascular disease; CI=confidence interval; CV=cardiovascular; CVD=cardiovascular disease; GP=general practitioner; HCP=healthcare professional; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; NICE=National Institute for Health and Care Excellence; PCI=percutaneous coronary intervention; QOF=Quality and Outcomes Framework; RR=rate ratio; TIA=transient ischaemic attack.

References

1. LEQVIO Summary of Product Characteristics; **2.** HEART UK. Prevention pays. Available from: https://www.heartuk.org.uk/downloads/health-professionals/prevention-pays-analysis-infographic.pdf [Last accessed: December 2024]; **3.** Danese MD, et al. *BMJ Open* 2016(8);6:e011805; **4.** Public Health England. Health matters: preventing cardiovascular disease (February 2019). Available from: https://www.gov.uk/government/publications/health-matters-preventing-cardiovascular-disease/health-matters-preventing-cardiovascular-disease [Last accessed: December 2024]; **5.** CTT Collaborators. *Lancet* 2012;380(9841):581–590; **6.** HQIP, Third annual audit report. Available from: https://www.hqip.org.uk/wp-content/uploads/2023/03/Ref-376-CVDPREVENT-Third-Annual-Audit-Report.pdf [Last accessed: December 2024]; **7.** NICE. Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia (TA733). Available from: https://www.nice.org.uk/guidance/ta733 [Last accessed: December 2024]; **8.** NHS England. Summary information on the funding and supply of inclisiran (LEQVIO). 29 June 23. Available from: https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2023/04/B1913_Summary-information-on-the-funding-and-supply-of-inclisiran_v3_June-2023.pdf [Last accessed: December 2024]; **9.** Repatha (evolocumab) Summary of Product Characteristics; **10.** Ezetrol (ezetimibe) Summary of Product Characteristics; **11.** Praluent (alirocumab) Summary of Product Characteristics; **12.** NHS England. Quality and Outcomes Framework guidance for 2024/25. 1 April 2024. Available from: https://www.england.nhs.uk/wp-content/uploads/2024/03/PRN01104-Quality-and-outcomes-framework-guidance-for-2024-25.pdf [Last accessed: December 2024]; **13.** Gov.UK. General Medical Services Statement of Financial Entitlements Directions 2024. Available from: https://www.gov.uk/government/publications/general-medical-services-statement-of-financial-entitlements-directions [Last accessed: December 2024]; **14.** Ray KK et al. *N Engl J Med* 2020;382(16):1507–1519 and supplementary information; **15.**Wright RS, et al. *Cardiovasc Res* 2024;120(12):1400-1410; **16.** Ray KK, et al. *Lancet Diabetes Endocrinol* 2023;11(2):109-119; **17.** Raal FJ, et al. *N Engl J Med* 2020;382(16):1520-1530

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