PULSE Nursing IN PRACTICE

NOVARTIS

QUICK GUIDE

Primary care lipid optimisation in secondary prevention

This quick guide has been initiated and funded by Novartis Pharmaceuticals UK Ltd and discusses Novartis Pharmaceuticals UK Ltd products. It is intended for UK Healthcare Professionals only.

Prescribing Information and Adverse Events reporting can be found at the end of this article.

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The new 2023/24 Quality and Outcomes Framework (QOF) guidance makes a strong and clear statement that primary care should be focussing on lowering cholesterol in high-risk patients, with a view to reduce preventable cardiovascular events.[1] This is unsurprising given that 7.1% of all UK deaths are due to high cholesterol.[2] The QOF's ambition aligns with national drivers including the NHS Long Term Plan, Cardiac Transformation Programme, and the Academic Health Science Network (AHSN) Lipid Management Pathways.[3]

The new QOF cholesterol indicators reflect a strong evidence base that lowering low-density lipoprotein cholesterol LDL-C (or non-high-density lipoprotein cholesterol (HDL-C)) can significantly reduce cardiovascular events.[4,5]

Indicator	Thresholds
CHOL001. 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	70-95%
CHOL002. Percentage of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, or Stroke/TIA Register, who have a recording of non-HDL cholesterol in the preceding 12 months that is lower than 2.5mmol/L, or where non-HDL cholesterol is not recorded, a recording of LDL-cholesterol in the preceding 12 months that is lower than 1.8 mmol/L	20-35%

An LDL-C reduction of 1mmol/L, by statin therapy, is associated with a 21% reduction in risk of a first major cardiovascular event.*[5] Of deep concern, however, is that around 20% of people with established cardiovascular disease are not on a lipid lowering therapy (LLT) and fewer than 25% have an LDL-C <1.8mmol/L or non-HDL cholesterol <2.5mmol/L.[6] The latter reflects those high-risk patients on no LLT or those prescribed inadequate LLT. It should be noted that the European Society of Cardiology guidelines even advise an LDL-C <1.4mmol/L and a reduction in LDL-C of over 50% from baseline for secondary prevention patients.[7]

*The effect of inclisiran on cardiovascular morbidity and mortality has not yet been determined.

Inadequate LLT reflects people on lower than appropriate doses of high-intensity statins such as atorvastatin or rosuvastatin, those prescribed low-intensity statins such as simvastatin or pravastatin, or those who are not receiving non-statin-based therapies. The QOF guidance is clear that lipid lowering should not be limited to statins.[1] Lipid lowering therefore, just like hypertension, should use combination therapies to reach target.

A systematic, sustainable and holistic approach to optimising lipids is essential to improving outcomes for patients. We should recognise that lifestyle measures must not be ignored. Smoking cessation, exercise, weight management and dietary interventions, as well as medicines management, should all be considered.[8] For example, daily plant stanol esters can further reduce LDL-C by approximately 10%.[9]

The AHSN has developed a National Lipid Management Pathway to support the medical management of secondary prevention in primary care.[3] To help with more effective prescribing and efficient care delivery, it would be advisable to commence patients on a high-intensity statin as soon as possible after an acute event.[10] The rationale for a high-dose, high-intensity statin can be illustrated by the fact that simvastatin 80mg is approximately equivalent to atorvastatin 20mg.[10] Once optimised on the maximum tolerated dose of a statin, patients should be reviewed in three months.[10]

Doubling the dose of atorvastatin – for example, from 40mg to 80mg – only increases cholesterol lowering by 6%, whereas the addition of an alternative therapy, such as ezetimibe, showed a stronger ability of reducing LDL-C.[11,12] When combined with a statin, ezetimibe reduces LDL-C by a further 15% to 20%.[13] Clinicians may also consider LEQVIO®, in combination with a maximally tolerated statin, to help secondary prevention patients reach their LDL-C targets.[14,15]

LEQVIO® is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:[14]

- 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

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In the ORION-11 trial, LEQVIO® reduced LDL-C by 50% relative to placebo at month 17, as compared with baseline, in patients with atherosclerotic cardiovascular disease (ASCVD) (or risk equivalents) on a maximally tolerated statin (95% CI: −53.1 to −46.6; P<0.001).†[14,15] Time-adjusted LDL-C reductions were 49% (95% CI: −51.6 to −46.8; P<0.001) from baseline between months 3 and 18 relative to placebo.*[14,15] Additional advantages of LEQVIO® include:

- Only twice-yearly injection requirements, following an initial dose and a dose at 3 months[14]
- Generally well tolerated, with a safety profile similar to placebo apart from injection-site reactions [14,16]

Through QOF, primary care has now been contractually enabled to identify high-risk patients, systematically recall, and holistically optimise people to reduce their cardiovascular risk.[1] To support delivery, there is now an array of therapeutic oral and injectable options beyond statins which may be offered within primary care to reduce LDL-C levels across our population.

†Similar results were achieved in patients with ASCVD treated in ORION-10: at Month 17, inclisiran delivered placebo-corrected LDL-C reductions of 52%, as compared with baseline (95% CI: −55.7 to −48.8; P<0.001). Time-adjusted LDL-C reductions were 54% (95% CI: −56.2 to −51.3; P<0.001) from baseline between Months 3 and 18 relative to placebo. ORION-10 (N=1,561) and ORION-11 (N=1,617) were multicentre, double-blind, randomised, placebo-controlled 18-month clinical trials evaluating adult patients with ASCVD, and with ASCVD or risk equivalents, respectively. ASCVD was defined as coronary heart disease, cerebrovascular disease or peripheral arterial disease.[17] ASCVD risk equivalents included type 2 diabetes, HeFH, or a 10-year risk of a cardiovascular event of ≥20% as assessed by the Framingham Risk Score for Cardiovascular Disease or equivalent.

References

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Prescribing information

Great Britain Prescribing Information: LEQVIO® ▼ (inclisiran)
Important note: Before prescribing, consult the Summary of Product Characteristics (SmPC). Presentation: Pre-filled syringe containing inclisiran sodium equivalent to 284 mg inclisiran in 1.5 ml solution. I**ndication(s)**: 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. **Dosage and administration**: The recommended dose is 284 mg inclisiran administered as a single subcutaneous injection: initially, again at 3 months, followed by every 6 months. *Missed doses:* If a planned dose is missed by less than 3 months, inclisiran should be administered and dosing continued according to the patient's original schedule. If a planned dose is missed by more than 3 months, a new dosing schedule should be started – inclisiran should be administered initially, again at 3 months, followed by every 6 months. *Treatment transition from monoclonal antibody PCSK9 inhibitors:* Inclisiran can be administered immediately after the last dose of a monoclonal antibody PCSK9 inhibitor. To maintain LDL C lowering it is recommended that inclisiran is administered within 2 weeks after the last dose of a monoclonal antibody PCSK9 inhibitor. *Special populations:* No dose adjustment required for patients with mild or moderate hepatic impairment, mild, moderate or severe renal impairment or end-stage renal disease (use with caution in severe renal impairment) or elderly patients. *Administration:* Subcutaneous injection into abdomen (alternatively, the upper arm or thigh). Injections should not be given into areas of active skin disease or injury such as sunburns, skin rashes, inflammation or skin infections. Inclisiran is intended for administration by a healthcare professional. **Contraindications**: Hypersensitivity to active ingredient or any of the excipients. **Warnings/Precautions**: *Haemodialysis:* The effect of haemodialysis on inclisiran pharmacokinetics has not been studied. Considering that inclisiran is eliminated renally, haemodialysis should not be performed for at least 72 hours after inclisiran dosing. **Interactions**: Inclisiran is not a substrate for common drug transporters and, although *in vitro* studies were not conducted, it is not anticipated to be a substrate for cytochrome P450. Inclisiran is not an inhibitor or inducer of cytochrome P450 enzymes or common drug transporters. Therefore, inclisiran is not expected to have clinically significant interactions with other medicinal products. Based on the limited data available, clinically meaningful interactions with atorvastatin, rosuvastatin or other statins are not expected. **Fertility, pregnancy and lactation**: *Pregnancy:* No or limited data available from the use of inclisiran in pregnant women. Animal studies do not indicate any harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of inclisiran during pregnancy. *Breast feeding:* It is unknown whether inclisiran is excreted in human milk. Data in animals have shown excretion of inclisiran in milk. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from inclisiran therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. *Fertility:* No data on the effect of inclisiran on human fertility are available. Animal studies did not show any effects on fertility. **Undesirable effects:** Common (≥1/100 to <1/10): adverse reactions at injection site including site reaction, pain, erythema and rash. All reactions were mild or moderate in severity, transient and resolved without sequelae. *Other Adverse Effects:* Please consult the Summary of Product Characteristics for a detailed listing of all adverse events before prescribing. **Legal classification:** POM **Marketing Authorisation (MA) number, quantities and price:** PLGB 00101/1202 Leqvio 284mg pre-filled syringe £1987.36 (ex. VAT) per pack (1 pre-filled syringe). **Date of last revision of prescribing information**: October 2022 (ID 244658) **Full Prescribing Information available from**: Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Telephone: (01276) 692255.

Northern Ireland Prescribing Information: LEQVIO® ▼ (inclisiran)
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Adverse Event Reporting: Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis via uk.patientsafety@novartis.com or online through the pharmacovigilance intake (PVI) tool at novartis.com/report

If you have a question about the product, please contact Medical Information on 01276698370 or by email at medioinfo.uk@novartis.com