DRIVING DATA INTO ACTION

WHY ADHERENCE MATTERS:

*MANAGING LDL-C WITH LEQVIO® AFTER A CORONARY EVENT**

> **LDL-C MANAGEMENT IS CRUCIAL AFTER A RECENT CORONARY EVENT.** We must stress the importance of lowering LDL-C in post-event patients by taking swift action to manage their levels and creating long-term plans to reach and maintain LDL-C targets.

ABOUT DR WRIGHT

- More than 46 years as a cardiologist and currently manages over 1000 patients a year with ASCVD and elevated LDL-C
- Past-President of the American College of Cardiology, California chapter
- Recipient of the Specialist of the Year award from the American College of Cardiology, California
- Recognized as one of the top cardiologists, according to peer surveys
- Coauthored the US guideline on management of patients with heart failure

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The perspectives provided within this newsletter by Dr Wright are his own and not reflective of his affiliation. The medical expert in this newsletter has been compensated by Novartis Pharmaceuticals Corporation to provide their perspectives.

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; NSTEMI, non–ST-elevation myocardial infarction; STEMI, ST-elevation myocardial Infarction; US, United States.

*An event is defined as acute coronary syndrome (unstable angina, STEMI, or NSTEMI) and/or coronary revascularization.[1]

INDICATION

LEQVIO® (inclisiran) injection is indicated as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C).

IMPORTANT SAFETY INFORMATION

LEQVIO is contraindicated in patients with a prior serious hypersensitivity reaction to inclisiran or any of the excipients in LEQVIO. Serious hypersensitivity reactions have included angioedema. Adverse reactions in clinical trials (≥3% of patients treated with LEQVIO and more frequently than placebo) were injection site reaction, arthralgia, and bronchitis.

Please click here for LEQVIO full Prescribing Information.

LEQVIO®
(inclisiran) injection 284 mg/1.5 mL

AFTER A RECENT CORONARY EVENT, GETTING TO AND STAYING BELOW LDL-C TARGET IS CRITICAL

more total cardiovascular events were observed in patients who failed to reach LDL-C target[2*]

The effect of LEQVIO® (inclisiran) on cardiovascular morbidity and mortality has not been determined.

Statins alone may not be enough to get patients to guideline-recommended LDL-C targets. **I believe in the strong patient—physician bond to ensure patients take their therapy as prescribed**, which is key to helping patients reach their LDL-C targets.

Up to 80%
of patients do not reach the LDL-C guideline-recommended target of <70 mg/dL[3-6]

Patients who do get to LDL-C target only stayed there for

<6 months on average[2*]

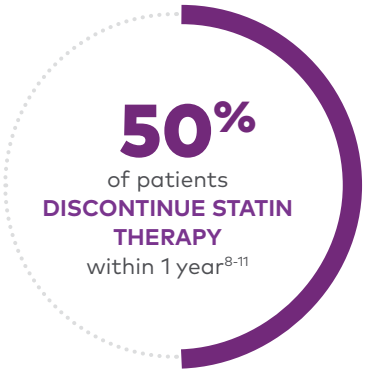
Additional therapies are needed to complement treatment with maximally tolerated statin therapy in LDL-C management[3,7]

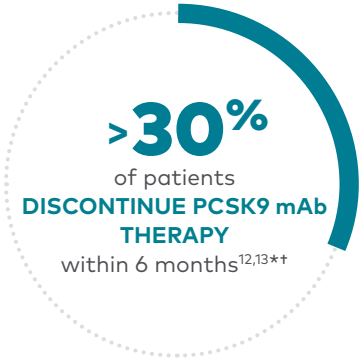
LDL-C, low-density lipoprotein cholesterol; US, United States.

*Based on study data (N=38,110,734) that evaluated the annual cardiovascular event rates in a subset of guideline-defined high-risk patients of the Family Heart Database, which comprised diagnostic, procedure, lab, and prescription data from claims in the US from 2012 to 2021.[2]

NONADHERENCE MAY PREVENT PATIENTS FROM GETTING TO AND STAYING BELOW LDL-C TARGET

> **A pill that stays in a bottle won't lower LDL-C**; patients need to take charge of their LDL-C management by taking the medication as prescribed.





> Polypharmacy and comorbidities are important clinical considerations because patients do not want to be on more medications. **You have to leverage the patient—physician bond to convince patients that lipid-lowering therapy is in their best interest.**

PATIENTS WITH ASCVD MAY STRUGGLE WITH ADHERENCE TO THEIR LDL-C–LOWERING THERAPY DUE TO VARIOUS REASONS[14,15]

- Treatment side effects
- Frequent dosing burden
- Cost
- Fear/avoidance of self-injections
- Inconvenience
- Lack of motivation/belief in efficacy
- Polypharmacy challenges
- Statin intolerance

Adherence matters when considering a LDL-C–lowering therapy in patients who have had a recent coronary event[14,15]

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; mAb, monoclonal antibody; PCSK9, proprotein convertase subtilisin/kexin type 9.

*From an analysis of a large IQVIA open claims dataset of patients (N=72,001) between September 2020 and January 2023.[12]

†In a retrospective cohort study of pharmacy and health plan claims of patients who initiated PCSK9 mAb (N=13,151) between January 1, 2016 and June 30, 2016, who were followed for a minimum of 6 months following their first prescription fill. Discontinuation was defined as a gap of 60 days or more between the last day of supply of 1 prescription and the start of the next prescription. Specific reasons for discontinuation were unknown; however, it could have been due to poor tolerability, noncompliance, unwillingness to perform injections, and insurance or cost issues. Gaps in therapy were derived from actual prescription fill data.[13]

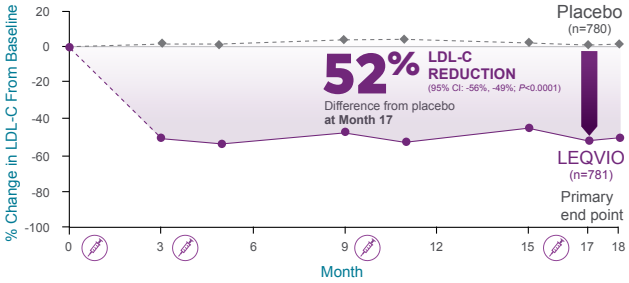
LEQVIO® DEMONSTRATED POWERFUL AND CONSISTENT LDL-C REDUCTION WITH JUST 2 DOSES A YEAR*

> **The magnitude of benefit through LDL-C reduction** is a key attribute for LEQVIO. This benefit is seen across different patient populations.

ORION-10 (n=1561) and ORION-11 (n=1617) were multicenter, double-blind, randomized, placebo-controlled, 18-month, Phase 3 trials in patients with established ASCVD (ORION-10 and ORION-11) or increased risk of CVD† (ORION-11)[16,17]

Patients were taking a maximally tolerated statin with or without other lipid-lowering therapy and required additional LDL-C reduction[16‡]

In ORION-10, on top of maximally tolerated statin:



84%

of ASCVD patients achieved guideline-recommended LDL-C targets§ with LEQVIO compared with 18% of patients treated with placebo at Month 17[17]

Results were similar in ORION-11 in patients with ASCVD or increased risk of CVD.[17]

LEQVIO IS WELL TOLERATED WITH A PROVEN SAFETY PROFILE

Phase 3 studies of LEQVIO (ORION-9, ORION-10, and ORION 11)[16]

Most Common Adverse Reactions Occurring in ≥3% of Patients Treated With LEQVIO (n=1833) and More Frequently Than Placebo (n=1822)

Injection site reaction¶	**8%**	**2%**
Arthralgia	**5%**	**4%**
Bronchitis	**4%**	**3%**

✔ No warnings and precautions[16]

2.5% of patients discontinued LEQVIO vs 1.9% of patients with placebo[16]

Injection site reactions were the most common causes for treatment discontinuation (0.2% of patients taking LEQVIO vs 0% taking placebo)[16]

✔ No clinically significant drug-drug interactions expected[16]

> **Tolerability** is an important piece if you want people to stay on a therapy.

ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; CVD, cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus.

*After 2 initial doses and taken with statin therapy.[16]

†Factors that increase risk of ASCVD include HeFH, T2DM, or 10-year risk of ≥20%.[17]

‡Maximally tolerated is defined as the maximum dose of statin that can be taken on a regular basis without intolerable adverse events.[17]

§LDL-C <70 mg/dL for ASCVD and LDL-C <100 mg/dL for patients at increased risk of ASCVD.[3]

¶Includes related terms such as injection site pain, erythema, and rash.[16]

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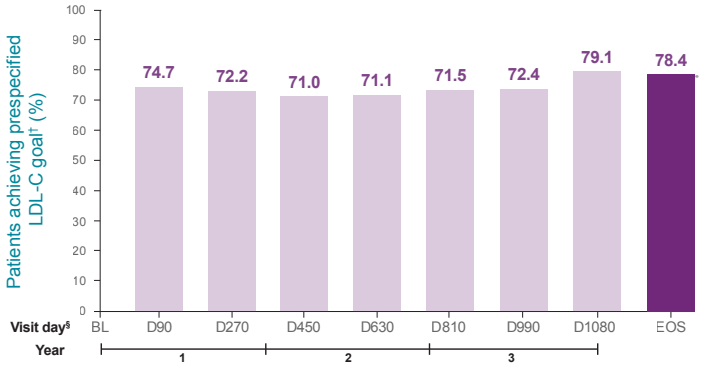
CONSISTENT EFFICACY AND SAFETY WITH LEQVIO® WAS OBSERVED BEYOND 6 YEARS*

Long-term data for a lipid-lowering therapy is important in demonstrating consistent LDL-C reduction with a well-tolerated safety profile over time. **ASCVD is a lifelong disease, and I aim to help my patients keep their LDL-C below the guideline-recommended target.**

In ORION-8 (n=3274), long-term safety data beyond 6 years* were consistent with Phase 3 trials[18]

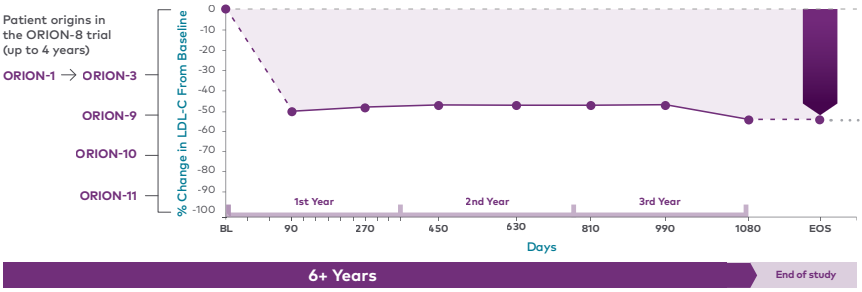
ORION 8 was an open-label extension trial that included 3274 patients from ORION-9, ORION-10, ORION-11, and ORION-3 studies[18]

ORION-8 was designed to assess the long-term safety, efficacy, and tolerability of LEQVIO in patients with ASCVD or increased risk for CVD† and elevated LDL-C, despite ongoing treatment with lipid-lowering therapy[18]



78%

of patients achieved their prespecified LDL-C target‡ with LEQVIO at end of study§ (78%; 95% CI: 77, 80)[18]



~50% LDL-C REDUCTION

with LEQVIO at end of study§ (-49% mean change in LDL-C; 95% CI: -50%, -48%)[18]

Limitations: Study was not blinded nor controlled and includes inherent self-selection bias for continuing onto the extension trial. The open-label design and absence of a control group may present difficulties in the interpretation of results, allowing comparisons only to baseline values.

ASCVD, atherosclerotic cardiovascular disease; BL, baseline; CI, confidence interval; CVD, cardiovascular disease; D, Day; EOS, end-of-study; LDL-C, low density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus.

*209 (6.4%) patients had exposure to LEQVIO for 6+ years, 213 (6.1%) patients had exposure to LEQVIO for 5+ years, 1553 (47%) patients had exposure for 4+ years, and 2095 (63.6%) patients had exposure for 3+ years.[18]

†Factors that increase risk of ASCVD include HeFH, T2DM, or 10-year risk of ≥20%.[17]

‡LDL-C target was <70 mg/dL for patients with ASCVD and <100 mg/dL for patients with increased risk for ASCVD.[3]

§"Baseline" was defined as baseline at the 4 feeder studies, and "end of study" was defined as Day 1080 or ≥90 days after the last LEQVIO dose.[18]

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WHEN CONSIDERING ADHERENCE TO LIPID-LOWERING TREATMENTS IN PRACTICE

If you do not take a drug as prescribed, it's not going to be useful. Adherence is an important clinical consideration to ensure patients receive the full benefit of their medication. **We blindly assume patients are going to stay on their therapy, but data do not support that.**

12-MONTH REAL-WORLD ADHERENCE FOR LEQVIO® VS PCSK9 mAbs

A retrospective, observational, real-world study evaluating 12-month adherence and persistence for newly initiated patients on LEQVIO (n=852), evolocumab (n=27,171), and alirocumab (n=8878) using administrative claims databases[19]*

Adherence

Adherence was defined as the proportion of days covered (PDC)†; fully adherent patients were defined as having a PDC of ≥0.8[19]

79% **of patients receiving LEQVIO were fully adherent at 12 months**

vs 56% of patients for either evolocumab or alirocumab[19‡§]

Persistence

Persistence was defined as patients who remained on therapy for 12 months after index date with ≤90 days' gap for LEQVIO and ≤60 days' gap for evolocumab and alirocumab between last day of days' supply and start of the next prescription[19]

80% **of patients were persistent on LEQVIO for 12 months after initiation**

vs 56% of patients for evolocumab and 57% of patients for alirocumab[19‡§]

LEQVIO is HCP-administered.

Therefore, claims ensure patients received the injection

Evolocumab and alirocumab claims do not confirm self-administration, so PDC for PCSK9 mAbs may be overestimated

The comparison pertains only to differences in adherence or persistence as defined by this analysis and should not be considered a comparison of efficacy or safety.

Limitations: The study was conducted using administrative claims data (collected for non-research purposes), with limited details on clinical variables and susceptibility to missing data and coding-related errors. Clinical characteristics and medications were captured during the 12 months prior to the initiation period; anything beyond the 12-month period was not observable. LEQVIO is HCP-administered; therefore, claims ensure patients received the injection, whereas evolocumab and alirocumab claims do not confirm self-administration, thus PDC for PCSK9 mAbs may be overestimated.

HCP, health care professional; mAb, monoclonal antibody; PCSK9, proprotein convertase subtilisin/kexin type 9; US, United States.

*Komodo Health, a nationally representative longitudinal database that captures 330 million patients in the US from open and closed administrative databases, was utilized from January 2021 to October 2023.[19]

†PDC calculates the proportion of days a patient has access to their prescribed medication over a defined period of interest, which was 12 months for this study.[19]

‡The allowable window of administration for all treatments was specified in the Prescribing Information: For LEQVIO, it was +90 days, and for evolocumab and alirocumab, it was +7 days.[19]

§Data were adjusted to account for differences in baseline characteristics among cohorts.[19]

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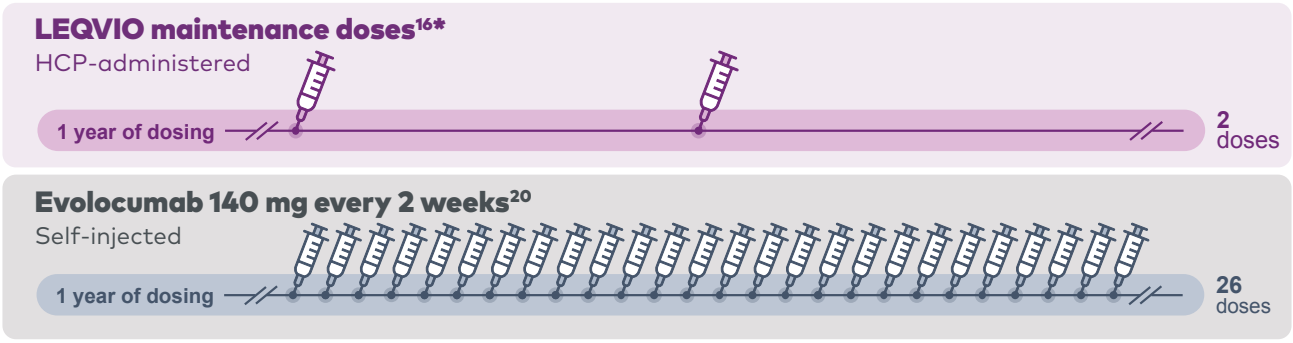
AFTER HCP ADMINISTRATION OF LEQVIO®, THERE'S NO CHANCE OF A MISSED DOSE FOR 6 MONTHS*

> **The dosing and administration of LEQVIO align well with my clinical practice,** fitting seamlessly with my patients' clinical visits, which are usually every 6 months.



This is not a complete list of all the available treatments for patients with primary hyperlipidemia. The comparison pertains only to differences in dosing and administration and should not be considered a comparison of efficacy or safety.

Alirocumab is dosed every 2 weeks (75 mg-150 mg), equating to 26 injections per year.[21] The monthly dose of PCSK9 mAbs is administered by giving 2 or 3 injections consecutively, which equates to 24 to 36 injections per year.[20,21]

FLEXIBLE PATHWAYS FOR LEQVIO ACQUISITION AND ADMINISTRATION

Acquire LEQVIO for in-office administration

Set up your own **buy-and-bill** process to control acquisition,* reimbursement, and administration logistics

*Specialty pharmacies can be used to acquire LEQVIO for in-office administration.

Download the Buy-and-Bill 5 Step Guide PDF at **leqvio.link/bnb**

Refer out administration

Collaborate with a local **alternate site of care** that manages acquisition, reimbursement, and administration logistics

Find an alternate site at **leqvio-locator.com**

ADDITIONAL SUPPORT FOR YOUR OFFICE

Access & Reimbursement Manager
Dedicated support team member available for in-office visits or by phone to offer information on acquisition and coding and billing

LEQVIO® Service Center
Use the Service Center to verify benefits and insurance coverage. Dedicated Novartis team available to conduct benefits investigations and provide information and resources to support you through the claim submission process.

EXPLORE HERE

mAb, monoclonal antibody; HCP, health care professional; PCSK9, proprotein convertase subtilisin/kexin type 9; US, United States.

*After 2 initial doses and taken with statin therapy.[16]

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We need to do a better job of LDL-C management in patients after a recent coronary event. We must shift our practice paradigms and collaborate with patients to choose a lipid-lowering treatment plan they will adhere to and benefit from.

LEARN MORE

LDL-C, low-density lipoprotein cholesterol.

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