



Original Effective Date: 05/01/2022
 Current Effective Date: 03/28/2025
 Last P&T Approval/Version: 01/29/2025
 Next Review Due By: 01/2026
 Policy Number: C23141-A

Leqvio (inclisiran)

PRODUCTS AFFECTED

Leqvio (inclisiran)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:

Primary hyperlipidemia

REQUIRED MEDICAL INFORMATION:

This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PRIMARY HYPERLIPIDEMIA:

1. Documented diagnosis of primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH])
AND
2. Documentation that other secondary causes of dyslipidemia have been excluded or maximally treated (e.g., high triglycerides, hypothyroidism, etc.)
AND
3. Documentation member is taking a maximally tolerated intensity/dose of statin OR has an FDA

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labeled contraindication to statins OR had serious side effects and is unable to tolerate an alternative dosing schedule (i.e., every other day dosing)

AND

4. Documentation of current (prior to requested therapy) LDL-C (within the last 3 months)
AND
5. Documentation member has an increased risk of heart disease (i.e., elevated LDL-C, hypertension, diabetes, etc.)
AND
6. Documentation in treatment plan member will be adherent to therapy AND continue adherence to maximally tolerated dose/intensity statin therapy (unless contraindicated as documented above) *Molina Reviewer Note: Verify member's medication fill history for compliance on statin therapy*
AND
7. Prescriber attests or clinical reviewer has found Leqvio (inclisiran) will not be used with PCSK9 inhibitors [Praluent (alirocumab), Repatha (evolocumab)]

CONTINUATION OF THERAPY:

A. PRIMARY HYPERLIPIDEMIA:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response to therapy as indicated by decrease in LDL- C OR achievement of individual LDL-C patient goal
AND
4. Documentation that the requested agent will continue to be used in combination with a maximally tolerated statin or member has an FDA labeled contraindication or serious side effects to statins

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

None

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

284 mg as a single injection initially, again at 3 months, and then every 6 months thereafter

PLACE OF ADMINISTRATION:

The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Subcutaneous

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DRUG CLASS:

Small interfering RNA (siRNA) PCSK9 Inhibitors

FDA-APPROVED USES:

Leqvio 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).

COMPENDIAL APPROVED OFF-LABELED USES:

None

APPENDIX

APPENDIX:

None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

High-intensity statin therapy: Atorvastatin (Lipitor) 40-80 mg per day, Rosuvastatin (Crestor) 20-40 mg per day, Simvastatin (Zocor) 80 mg per day

Moderate-intensity statin therapy: Atorvastatin (Lipitor) 10-20 mg per day, Rosuvastatin (Crestor) 5-10 mg per day, Simvastatin (Zocor) 20-40 mg per day, Pravastatin (Pravachol) 40-80 mg per day, Lovastatin (Mevacor) 40mg a day, Fluvastatin XL (Lescol XL) 80 mg per day, Fluvastatin (Lescol) 40 mg twice a day, Pitavastatin (Livalo) 2-4 mg per day

Low-intensity statin therapy: Simvastatin (Zocor) 10 mg per day, Pravastatin (Pravachol) 10-20 mg per day, Lovastatin (Mevacor) 20 mg per day, Fluvastatin (Lescol) 20-40 mg per day, Pitavastatin (Livalo) 1 mg per day

Inclisiran is a first in class small interfering RNA (siRNA) directed to PCSK9 (proprotein convertase subtilisin kexin type 9) mRNA indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C. Inclisiran is a double-stranded small interfering ribonucleic acid (siRNA), conjugated on the sense strand with triantennary N-Acetylgalactosamine (GalNAc) to facilitate uptake by hepatocytes. In hepatocytes, inclisiran utilizes the RNA interference mechanism and directs catalytic breakdown of mRNA for PCSK9. This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C levels in the circulation. Inclisiran was studied in three randomized, double-blind, placebo-controlled trials (ORION program) in adults with HeFH or clinical ASCVD on maximally tolerated statin therapy who required additional LDL-C lowering.

Patients taking PCSK9 inhibitors were excluded from the trials. The primary efficacy measure in these trials was percent change from baseline to day 510 in LDL-C. Inclisiran decreased LDL-C by 51%, 46%, and 40% in ORION-10, ORION-11, and ORION-9, respectively. The mean change compared to placebo was statistically significant in each study during the 510 days: -52% (95% CI: -56%, -49%; $p < 0.0001$), -51% ((95% CI: -54%, -47%; $p < 0.0001$), -48% (95% CI: 54%, -42%; $p < 0.0001$). Pharmacokinetic studies have shown the maintenance of LDL-C reduction through the duration of the dosing interval. Adverse reactions reported in at least 3% of inclisiran patients and more frequently than placebo were injection site reaction, arthralgia, urinary tract infection, diarrhea, bronchitis, pain in extremity, dyspnea.

Clinical trials are being conducted to determine the effect of inclisiran on cardiovascular morbidity and mortality.

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CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Leqvio (inclisiran) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Leqvio (inclisiran) include: Prior serious hypersensitivity to inclisiran or any of the excipients in Leqvio.

OTHER SPECIAL CONSIDERATIONS:

Leqvio should be administered by a health care professional. Inject Leqvio subcutaneously into the abdomen, upper arm, or thigh. Do not inject in areas of active skin disease or injury such as sunburns, skin rashes, inflammation, or skin infections. Inspect LEQVIO visually before use. It should appear clear and colorless to pale yellow. Do not use if particulate matter or discoloration is seen.

If a planned dose is missed by less than 3 months, administer Leqvio and maintain dosing according to the patient's original schedule. If a planned dose is missed by more than 3 months, restart with a new dosing schedule - administer Leqvio initially, again at 3 months, and then every 6 months.

CODING/BILLING INFORMATION

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
J1306	Injection, inclisiran, 1 mg

AVAILABLE DOSAGE FORMS:

Leqvio SOSY 284MG/1.5ML

REFERENCES

1. Leqvio® (inclisiran) injection, for subcutaneous use [prescribing information]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation: June 2024.
2. Raal F, et al. Inclisiran for the treatment of heterozygous familial hypercholesterolemia. *N Engl J Med.* 2020;382(16):1520–1530.
3. Ray KK, Wright RS, Kallend D, Koenig W, Leiter LA, Raal FJ, Bisch JA, Richardson T, Jaros M, Wijngaard PLJ, Kastelein JJP; ORION-10 and ORION-11 Investigators. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. *N Engl J Med.* 2020 Apr 16;382(16):1507-1519. doi: 10.1056/NEJMoa1912387. Epub 2020 Mar 18.
4. Warden BA, Duell PB. Inclisiran: A Novel Agent for Lowering Apolipoprotein B-containing Lipoproteins. *J Cardiovasc Pharmacol.* 2021 Aug 1;78(2):e157-e174. doi: 10.1097/FJC.0000000000001053.
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AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol [published online November 10, 2018]. *Circulation*. 2018.

7. Tomlinson, B., Chow, E., Chan, P. and Lam, C., 2022. An evaluation of the pharmacokinetics of inclisiran in the treatment of atherosclerotic cardiovascular disease. *Expert Opinion on Drug Metabolism & Toxicology*, pp.1-9.
8. Lloyd-Jones, D. M., Morris, P. B., Ballantyne, C. M., Birtcher, K. K., Covington, A. M., DePalma, S. M., Wilkins, J. T. (2022). 2022 ACC expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. *Journal of the American College of Cardiology*, 80(14), 1366-1418. doi:10.1016/j.jacc.2022.07.006

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION: Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation References	Q1 2025
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q1 2024
REVISION: Notable revisions: Diagnosis Required Medical Information Continuation of Therapy FDA-Approved Uses References	Q4 2023
REVISION: Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Contraindications/Exclusions/Discontinuation Other Special Considerations Coding/Billing Information References	Q1 2023
New Development	Q2 2022