Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	**MP-RX-FP-53-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	**11/30/2023**	**7/22/2026**
			Last Review Date: **7/22/2026**	**Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses the use of *Inclisiran (Leqvio®)* , a small interfering RNA (siRNA) approved by the Food and Drug Administration (FDA) as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in adults with hypercholesterolemia, adults and pediatric patients aged 12 years and older with heterozygous familial hypercholesterolemia (HeFH), and pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH).

Background Information:

This document addresses the use of Leqvio (inclisiran), a small interfering RNA (siRNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) mRNA. Leqvio is indicated as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in adults with hypercholesterolemia, adults and pediatric patients 12 years of age and older with heterozygous familial hypercholesterolemia (HeFH), and pediatric patients 12 years of age and older with homozygous familial hypercholesterolemia (HoFH). Leqvio is administered by a healthcare provider as a subcutaneous injection initially, again at 3 months, and every 6 months thereafter.

The effect of inclisiran on cardiovascular morbidity and mortality has not been determined. Ongoing cardiovascular outcomes trials include ORION-4, which is evaluating major adverse cardiovascular events, and other long-term outcome studies remain in progress.

In the clinical setting, statins are considered first-line drug therapy, in addition to healthy lifestyle interventions, in individuals requiring treatment for elevated LDL-C or hypercholesterolemia. Other lipid lowering therapies should be considered second-line options for individuals needing additional cholesterol lowering or when statins are not tolerated or are contraindicated.

The 2026 ACC/AHA multisociety guideline on the management of dyslipidemia uses LDL-C goals to guide intensification of therapy. For primary prevention, LDL-C goals are generally less than 100 mg/dL for borderline or intermediate-risk individuals and less than 70 mg/dL for high-risk individuals. For secondary prevention in very high-risk ASCVD, the recommended LDL-C goal is less than 55 mg/dL. When LDL-C remains above goal despite maximally tolerated statin therapy, the guideline supports addition of nonstatin therapy based on the individual's risk category and clinical circumstances.

Statins have labeled warnings for liver enzyme abnormalities and skeletal muscle effects including myopathy and rhabdomyolysis. Statin-induced adverse events leading to some degree of intolerance have been reported in as many as 5% to 30% of individuals, although incidence and prevalence vary. The National Lipid Association (NLA) has provided guidance defining statin intolerance as one or more adverse effects associated with statin therapy, which resolves or improves with dose reduction or discontinuation, and can be classified as complete inability to tolerate any dose of a statin or partial intolerance, with inability to tolerate the dose necessary to achieve the

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

individual-specific therapeutic objective. To classify an individual as having statin intolerance, a minimum of two statins should have been attempted, including at least one at the lowest approved daily dosage.

World Health Organization (WHO)/Dutch Lipid Clinic Network Criteria for Familial Hypercholesterolemia (FH) Diagnosis

Criteria	Points
Family History	
Known premature coronary and vascular disease (men <55 years, women <60 years) in first degree relative	1
Known LDL-C >95th percentile in first degree relative	1
Tendon xanthoma and/or corneal arcus in first degree relative	2
Children aged <18 years with LDL-C >95th percentile	2
Personal Clinical History	
Premature coronary artery disease (men <55 years, women <60 years)	2
Premature cerebral or peripheral vascular disease (men <55 years, women <60 years)	1
Clinical Exam	
Tendon xanthoma	6
Corneal arcus in individual aged <45 years	4
LDL-C Level	
> 329 mg/dL (>8.5 mmol/L)	8
250-329 mg/dL (6.5-8.4 mmol/L)	5
190-249 mg/dL (5.0-6.4 mmol/L)	3
155-189 mg/dL (4.0-4.9 mmol/L)	1
Genetic Testing	
Functional mutation in LDLR, ApoB or PCSK9 gene	8

Scoring: Definite FH:> 8 points; Probable FH: 6-8 points; Possible FH: 3-5 points; Unlikely FH: 0-2 points.

Approved Indications

A. As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:
- adults with hypercholesterolemia.
- adults and pediatric patients aged 12 years and older with heterozygous familial hypercholesterolemia (HeFH).
- pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH).

Other Uses

A. None.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Inclisiran (Leqvio®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Initial requests for Leqvio (inclisiran) may be approved when the following criteria are met:

i. Individual is at high risk for atherosclerotic cardiovascular disease (ASCVD) events as identified by one of the following:

A. Individual has Heterozygous Familial Hypercholesterolemia (HeFH) confirmed by (Singh 2015; Dutch Lipid Clinic Network criteria):

1. Presence of a mutation in LDLR, ApoB, PCSK9 or ARH adaptor protein (LDLRAP1) gene;

OR

2. Dutch Lipid Clinic Network criteria (DLCN) with score of greater than eight points;

OR

B. Individual has a history of clinical atherosclerotic cardiovascular disease (ASCVD) including one or more of the following (ACC/AHA 2026):

1. Acute coronary syndrome;
2. Coronary artery disease (CAD);
3. History of myocardial infarction (MI);
4. Stable or unstable angina;
5. Coronary or other arterial revascularization;
6. Stroke;
7. Transient ischemic attack (TIA);
8. Peripheral arterial disease (PAD);

OR

C. Individual has primary hypercholesterolemia / hyperlipidemia;

AND

ii. Individual meets one of the following:

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

A. Individual is on high intensity statin therapy or statin therapy at the maximum tolerated dose (high intensity statin is defined as atorvastatin 40 mg or higher or rosuvastatin 20 mg or higher) (ACC/AHA 2026);

OR

B. Individual is statin intolerant based on one of the following:

1. Inability to tolerate at least two statins, with at least one started at the lowest starting daily dose, demonstrated by adverse effects associated with statin therapy that resolve or improve with dose reduction or discontinuation (NLA 2022);

OR

2. Statin associated rhabdomyolysis or immune-mediated necrotizing myopathy (IMNM) after a trial of one statin;

OR

C. Individual has a contraindication for statin therapy including but not limited to active liver disease, unexplained persistent elevation of hepatic transaminases or pregnancy;

AND

iii. Individual has achieved suboptimal lipid lowering response despite at least 90 days of compliant lipid lowering therapy and lifestyle modifications, including maximally tolerated statin therapy and ezetimibe when clinically appropriate, as defined below: (ACC/AHA 2026, ACC 2022):

A. For individuals where initial LDL-C is known:

1. Less than 50% reduction in LDL-C;

OR

B. For individuals where initial LDL-C is unknown:

1. ASCVD and LDL-C remains greater than or equal to 55 mg/dL;

OR

2. No history of ASCVD and LDL-C remains greater than or equal to 100 mg/dL.

B. Criteria For Continuation of Therapy

Continuation requests for Leqvio (inclisiran) may be approved when the following criteria are met:

i. Individual continues to use maximally tolerated lipid-lowering therapy, including statin therapy and ezetimibe when clinically appropriate, unless contraindicated or the individual is statin intolerant;

AND

ii. Individual has achieved or maintained LDL-C reduction.

C. Authorization Duration

i. Initial Approval Duration: 1 year

ii. Reauthorization Approval Duration: 1 year

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Leqvio (inclisiran) may not be approved for the following:

i. In combination with Praluent Repatha, or other PCSK9 monoclonal antibody therapy;

OR

ii. When the above criteria are not met and for all other indications.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

Limits or Restrictions:

A. Therapeutic Alternatives

his medical policy may be subject to Step Therapy. Please refer to the document published on the MMM Website: https://www.mmm-pr.com/planes-medicos/formulario-medicamentos

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosage/Limit
Leqvio (inclisiran) 284 mg/1.5 mL prefilled syringe	• Recommended dosage: 284 mg SC administered as a single injection initially, again at 3 months, and then every 6 months thereafter. • Limit: 1 syringe per 6 months
Exceptions	
• Initiation of therapy: May approve one additional prefilled syringe within the first six months of initiating therapy. • If a planned dose is missed by less than 3 months, administer Leqvio and maintain the original schedule. If missed by more than 3 months, restart with a new dosing schedule: administer initially, again at 3 months, and then every 6 months.	

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E78.00	Pure hypercholesterolemia, unspecified
E78.011	Heterozygous familial hypercholesterolemia [HeFH]
E78.2	Mixed hyperlipidemia
E78.41	Elevated Lipoprotein(a)
E78.49	Other hyperlipidemia
E78.5	Hyperlipidemia, unspecified
G45.0-G45.9	Transient cerebral ischemic attacks and related syndromes
I20.0-I20.9	Angina pectoris
I21.01-I21.B	Acute myocardial infarction
I22.0-I22.9	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
I23.7	Postinfarction angina
I24.0-I24.9	Other acute ischemic heart diseases
I25.10-I25.9	Chronic ischemic heart disease
I63.00-I63.9	Cerebral infarction
I65.01-I65.9	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction
I66.01-I66.9	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
I67.2	Cerebral atherosclerosis
I67.82	Cerebral ischemia
I69.00-I69.998	Sequelae of cerebrovascular disease
I70.0-I70.92	Atherosclerosis
I73.9	Peripheral vascular disease, unspecified
Z83.42	Family history of familial hypercholesterolemia
Z86.73	Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits.
Z95.1	Presence of aorto coronary bypass graft
Z95.5	Presence of coronary angioplasty implant and graft
Z95.820-Z95.828	Presence of other vascular implants and grafts
Z98.61	Coronary angioplasty status
Z98.62	Peripheral vascular angioplasty status

HCPCS Codes:

Codes	Description

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	**MP-RX-FP-53-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	**11/30/2023**	**7/22/2026**
			Last Review Date: **7/22/2026**	**Frequently Revision:** **Annual**

J1306	Injection, inclisiran, 1 mg [Leqvio]

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	**MP-RX-FP-53-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	**11/30/2023**	**7/22/2026**
			Last Review Date: **7/22/2026**	**Frequently Revision:** **Annual**

Reference Information

1. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2022; Aug 24:[Epub ahead of print].
2. *2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia. Circulation.* 2026. Accessed May 19, 2026. Available at: https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423
3. Cheeley MK, Saseen JJ, Agarwala A, et. al. NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. J Clin Lipidol. 2022. https://doi.org/10.1016/j.jacl.2022.05.068. Accessed May 19, 2026.
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
5. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
6. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/ APhA/ASPC/NLA/ PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:e285–350.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2026; Updated periodically.
8. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. (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. Accessed May 19, 2026. Available at: https://www.jacc.org/doi/10.1016/j.jacc.2022.07.006.
9. National Center for Biotechnology Information. *Table 3. Dutch Lipid Clinic Network Diagnostic Criteria for FH.* In: *Familial Hypercholesterolemia.* Accessed May 19, 2026. Available at: https://www.ncbi.nlm.nih.gov/books/NBK593597/table/ch1.tab3/
10. Novartis Pharmaceuticals Corporation. (2026). *LEQVIO® (inclisiran) injection, for subcutaneous use: Prescribing information.* Revised February 2026. Accessed May 19, 2026. Available at: https://www.novartis.com/us-en/sites/novartis_us/files/leqvio.pdf
11. Singh S, Bittner V. Familial hypercholesterolemia--epidemiology, diagnosis, and screening. Curr Atheroscler Rep. 2015; 17(2):482.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Updated Background Information to align with the current Leqvio prescribing information, including the revised indication, the current dosing schedule, and clarification that the effect of inclisiran on cardiovascular morbidity and mortality has not been determined. Updated the guideline discussion to reflect the 2026 ACC/AHA multisociety dyslipidemia guideline and retained the current National Lipid Association statin intolerance framework. Revised the Initial Approval criteria to update guideline references, clarify hypercholesterolemia terminology, require ezetimibe when clinically appropriate, and update the HeFH diagnostic wording to the Dutch Lipid Clinic Network criteria. Revised Continuation of Therapy to require ongoing maximally tolerated lipid-lowering therapy, including statin therapy and ezetimibe when clinically appropriate, unless contraindicated or the individual is statin intolerant, and to require achievement or maintenance of LDL-C reduction. Updated Conditions Not Covered to clarify that Leqvio is not approved for use in combination with Praluent, Repatha, or other PCSK9 monoclonal antibody therapy. Updated the quantity limits table to add the initial two-dose phase within the first 6 months and maintenance dosing every 6 months thereafter. Coding Update: Removed ICD-10-CM E78.01 and added E78.011. Added ICD-10-CM E78.1, G45.0-G45.9, I63.00- I63.9, I65.01-I65.9, I66.01-I66.9, I67.2, I67.82, I69.00-I69.998, I70.0-I70.92, I73.9, Z98.61, Z98.62. Updated reference information and incorporated new policy template.	7/13/2026	7/22/2026
Annual Review	Revise primary hyperlipidemia criteria (Changed: "Individual has primary hyperlipidemia with an untreated LDL-C greater than or equal to 190 mg/dL (ACC 2022)" to "Individual has primary hyperlipidemia"). Coding Reviewed: No change. Wording and formatting changes.	8/25/2025	9/8/2025
Annual Review	Update Background Information. Update criteria with additional primary hyperlipidemia indication. Coding Reviewed: Add ICD-10-CM E78.00, E78.01, E78.2, E78.41, E78.49, E78.5, I21.01-I21.B, I22.0-I22.9, Z83.42, Z86.73, Z95.1, Z95.5, and Z95.820-Z95.828. Expanded codes I20.8, I20.9 to I20.0-I20.9. Changed I25.2-I25.9 to I25.10-I25.9 and changed the wording for the indication to Chronic ischemic heart disease. Changed I24.0-I24.8 to I24.0-I24.9 and changed the wording for the indication to Other acute ischemic heart diseases. Update criteria by removing step through ezetimibe; update LDL-C requirement for individuals with history of ASCVD; extend initial approval duration. Wording and formatting changes.	2/24/2025	3/6/2025
Policy Inception	8/18/2023 Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Inclisiran [Leqvio®]	MP-RX-FP-53-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/22/2026
			Last Review Date: 7/22/2026	Frequently Revision: Annual