Leqvio (inclisiran)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Leqvio (inclisiran) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies. The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Leqvio is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C).

Limitations of Use:
The effect of Leqvio on cardiovascular morbidity and mortality has not been determined.

POLICY

Prescriber Requirement
The medication must be prescribed by or in consultation with a cardiologist, endocrinologist, lipid specialist, or cardiometabolic specialist.

Required Documentation
The following information is necessary to initiate the prior authorization review:

- Untreated baseline LDL level, LDL levels while receiving statin therapy (prior to starting Leqvio), and current LDL levels on Leqvio (if applicable).
- Chart notes demonstrating the patient is engaging in healthy lifestyle changes (e.g., heart-healthy diet and exercise regimen)
- Chart notes demonstrating statin intolerance or contraindication to statin therapy (if applicable)
- For heterozygous familial hypercholesterolemia: genetic testing or medical records (Appendix C) confirming the diagnosis of HeFH including untreated (before any lipid lowering therapy) LDL-C level.
- For clinical atherosclerotic cardiovascular disease (ASCVD), chart notes confirming clinical ASCVD (Appendix A).

Criteria for Initial Approval

A. Leqvio (inclisiran) may be considered **medically necessary** for the treatment of **clinical atherosclerotic cardiovascular disease ASCVD** (Appendix A) when all of the following criteria are met:

1. Patient is 18 years of age or older
2. Member has a history of clinical ASCVD (Appendix A)
3. Patient is engaging in healthy lifestyle changes
4. Patient has been unable to achieve an LDL-C < 70 mg/dL despite adherence† to the combination of lifestyle changes and at least three months of the following lipid lowering therapy:
   a). A trial of BOTH high-intensity statins (atorvastatin 40-80 mg and rosuvastatin 20-40 mg) at a maximum tolerated dose in combination with ezetimibe, **OR**
   b). A trial of TWO moderate intensity statins (e.g., pravastatin 40-80 mg, lovastatin 40 mg, fluvastatin 80 mg, pitavastatin 2-4 mg, simvastatin 20-40 mg) in combination with ezetimibe, only in the event the patient is unable to complete either of the high-intensity statin trials at the maximum approved dosing
5. Patient will continue to receive concomitant statin therapy
6. Leqvio will not be combined with other PCSK9-targeted therapy (e.g., Repatha, Praluent)
7. Dose does not exceed 284 mg initially and at 3 months, then every 6 months thereafter

OR

1. Patient is 18 years of age or older
2. Member has a history of clinical ASCVD (Appendix A)
3. Patient is engaging in healthy lifestyle changes
4. Leqvio will not be combined with other PCSK9-targeted therapy (e.g., Repatha, Praluent)
5. Dose does not exceed 284 mg initially and at 3 months, then every 6 months thereafter
6. Patient has a current LDL-C level ≥ 70 mg/dL
7. Patient has a documented contraindication (e.g., active liver disease, pregnancy, breastfeeding), or medically justifiable reason that precludes statin use (e.g., patient has experienced rhabdomyolysis, CK elevations ≥ 10x ULN, or statin intolerance).
   a). Statin intolerance shall be defined in accordance with the National Lipid Association definition:
      i. Inability to tolerate at least two statins (one at any dose, one at lowest daily dose) due to objectionable symptoms or abnormal biomarkers temporally related to statin use, reversible upon statin discontinuation and reproducible by re-challenge while excluding other known determinants. Other known determinants include low body mass index (BMI), acute infection, untreated or undertreated hypothyroidism, severe renal or hepatic dysfunction, organ transplant, recent severe trauma, HIV infection, Vitamin D deficiency, history of creatine kinase elevation, history of preexisting or unexplained

muscle or joint pain, high level of physical activity, illicit drug abuse, excess alcohol use. Each statin trial, both initial and re-challenge shall be at least two weeks duration.

- A trial of one statin at lowest starting daily dose
  - Rosuvastatin 5mg
  - Atorvastatin 10mg
  - Simvastatin 10mg
  - Lovastatin 20mg
  - Pravastatin 40mg
  - Fluvastatin 40mg
  - Pitavastatin 2mg
- One statin at any daily dose

B. Leqvio (inclisiran) may be considered **medically necessary** for the treatment of **heterozygous familial hypercholesterolemia** when the following criteria are met:

1. Patient is 18 years of age or older
2. Patient has a diagnosis of HeFH, which is documented and confirmed by ONE of the following:
   a). An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation; **OR**
   b). Definite or possible FH per Simon-Broome Diagnostic Criteria (Appendix B); **OR**
   c). Dutch Lipid Network Criteria greater than 5 (Appendix C)
3. Patient is engaging in healthy lifestyle changes
4. Patient has been unable to achieve an LDL-C reduction of < 100 mg/dL (or ≤ 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD] per Appendix A) despite adherence† to the combination of lifestyle changes and at least three months of the following lipid lowering therapy:
   a). A trial of BOTH high-intensity statins (atorvastatin 40-80 mg and rosuvastatin 20-40 mg) at a maximum tolerated dose in combination with ezetimibe, OR
   b). A trial of TWO moderate intensity statins (e.g., pravastatin 40-80 mg, lovastatin 40 mg, fluvastatin 80 mg, pitavastatin 2-4 mg, simvastatin 20-40 mg) in combination with ezetimibe, only in the event the patient is unable to complete either of the high-intensity statin trials at the maximum approved dosing
5. Patient will continue to receive concomitant statin therapy
6. Leqvio will not be combined with other PCSK9-targeted therapy (e.g., Repatha, Praluent)
7. Dose does not exceed 284 mg initially and at 3 months, then every 6 months thereafter

OR

1. Patient is 18 years of age or older
2. Patient has a diagnosis of HeFH, which is documented and confirmed by ONE of the following:
   a). An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation; **OR**
   b). Definite or possible FH per Simon-Broome Diagnostic Criteria (Appendix B); **OR**
   c). Dutch Lipid Network Criteria score greater than 5 (Appendix C)
3. Patient is engaging in healthy lifestyle changes
4. Dose does not exceed 284 mg initially and at 3 months, then every 6 months thereafter
5. Patient has a current LDL-C level ≥ 100 mg/dL (or level ≥ 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD])
6. Patient has a documented contraindication (e.g., active liver disease, pregnancy, breastfeeding), or medically justifiable reason that precludes statin use (e.g., patients has experienced rhabdomyolysis, CK elevations ≥ 10x ULN, or statin intolerance).

a). Statin intolerance shall be defined in accordance with the National Lipid Association definition:
   i. Inability to tolerate at least two statins (one at any dose, one at lowest daily dose) due to objectionable symptoms or abnormal biomarkers temporally related to statin use, reversible upon statin discontinuation and reproducible by re-challenge while excluding other known determinants. Other known determinants include low body mass index (BMI), acute infection, untreated or undertreated hypothyroidism, severe renal or hepatic dysfunction, organ transplant, recent severe trauma, HIV infection, Vitamin D deficiency, history of creatine kinase elevation, history of preexisting or unexplained muscle or joint pain, high level of physical activity, illicit drug abuse, excess alcohol use. Each statin trial, both initial and re-challenge shall be at least two weeks duration.
      - A trial of one statin at lowest starting daily dose
        - Rosuvastatin 5mg
        - Atorvastatin 10mg
        - Simvastatin 10mg
        - Lovastatin 20mg
        - Pravastatin 40mg
        - Fluvastatin 40mg
        - Pitavastatin 2mg
      - One statin at any daily dose

7. Leqvio will not be combined with other PCSK9-targeted therapy (e.g., Repatha, Praluent)

Initial approval will be for **6 months**

Continuation of Therapy

The continuation of therapy for Leqvio may be considered **medically necessary** for any patient who meets the following criteria:

- Must have a documented positive clinical response to therapy as defined by achieving or maintaining an LDL-C reduction (i.e., LDL-C is now at goal or 50% reduction of LDL-C from baseline); **AND**
- Patient will continue to receive concomitant statin therapy if no contraindication or intolerance.
- Patient continues to engage in healthy lifestyle changes
- Leqvio will not be combined with other PCSK9-targeted therapy (e.g., Repatha, Praluent)
- Dose does not exceed 284 mg every 6 months

Renewals will be approved for **12 months**

†Please note: Documentation of LDL-C levels are required (untreated baseline and current [within 90 days of prior authorization request])

Leqvio is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

APPENDIX

APPENDIX A: Clinical Atherosclerotic Cardiovascular Disease (ASCVD)

- Acute coronary syndromes

- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease (PAD) of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)
- Coronary Artery Calcium (CAC) Score ≥ 1000

APPENDIX B: Simon Broome Register diagnostic criteria for Heterozygous Familial Hypercholesterolemia

Definite familial hypercholesterolemia:

- Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL in patients less than 16 years of age

AND

- Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt); OR presence LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.

Possible familial hypercholesterolemia:

- Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dL or LDL-C > 155 mg/dL in patients less than 16 years of age

AND

- Family history of at least one of the following:
  - Family history of myocardial infarction at age 60 years or younger in first degree relative or age 50 years or younger in second-degree relative

  OR

  - Family history of elevated total cholesterol of greater than 290 mg/dL in adult first- or second-degree relative or total cholesterol greater than 260 mg/dL in child, brother or sister aged younger than 16 years

APPENDIX C: Dutch Lipid Clinic Network diagnostic criteria for Familial Hypercholesterolemia

Diagnostic Scoring for Heterozygous Familial Hypercholesterolemia			
Family History			
First degree relative with known premature (men < 55 yrs, women < 60 yrs) coronary vascular disease			1
First degree relative with known LDL-cholesterol >95th percentile for age and sex			
and/or			
First degree relative with tendon xanthomata and/or arcus cornealis			2
Children below 18 yrs with LDL-cholesterol >95th percentile for age and sex			
Clinical History			
Patient has premature (men < 55 yrs, women < 60 yrs) coronary artery disease			2
Patient has premature (men < 55 yrs, women < 60 yrs) cerebral or peripheral vascular disease			1
Physical Examination			
Tendon xanthomata			6
Arcus cornealis below the age of 45 yrs			4
Laboratory Analysis			
	mmol/L	mg/dL	
LDL-cholesterol	> 8.5	> 330	8
LDL-cholesterol	6.5 – 8.4	250 – 329	5

LDL-cholesterol	5.0 – 6.4	190 – 249	3
LDL-cholesterol	4.0 – 4.9	155 – 189	1
(HDL-cholesterol and triglycerides are normal)			
DNA Analysis			
Functional mutation low-density lipoprotein receptor gene present			6
Diagnosis of HeFH is:			
Certain When		> 8 points	
Probable When		6-8 points	
Possible When		3-5 points	

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD-CM diagnostic codes.

- J1306 - Injection, inclisiran, 1 mg

REFERENCES

- Leqvio [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2021.
- Ray KK, Wright RS, Kallend D, et al. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. N Engl J Med. 2020;382:1507-1519. DOI: 10.1056/NEJMoa1912387.
- Raal FJ, Kallend D, Kausik KR, et al. Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia. N Engl J Med. 2020; 382:1520-1530. DOI: 10.1056/NEJMoa1913805.
- McGowan MP, Hosseini Dehkordi SH, Moriarty PM, et al. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. J Am Heart Assoc. 2019; 8:e013225. DOI: 10.1161/JAHA119.013225.
- Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. J Clin Lipidol. 2015;9:129–169.
- Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC guideline on the management of blood cholesterol: report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018.
- Min JK, Labounty TM, Gomez MJ, et al. Incremental prognostic value of coronary computed tomographic angiography over coronary artery calcium score for risk prediction of major adverse cardiac events in asymptomatic diabetic individuals. Atherosclerosis. 2014;232(2):298-304.
- Banach M, Rizzo M, Toth PP, et al. Statin intolerance – an attempt at a unified definition. Position paper from an International Lipid Expert Panel. Arch Med Sci. 2015;11:1-23.
- Mesi O, Lin C, Ahmed H, et al. Statin Intolerance and New Lipid-lowering Treatments. Cleve Clin J Med. 2021; 88(7)381-387. DOI: 10.3949/ccjm.88a.20165.
- Rosenson, RS. Miller, K, Bayliss M, et al. The Statin-Associated Muscle Symptom Clinical Index (SAMS-CI): Revision for Clinical Use, Content Validation and Inter-rater Reliability. Cardiovasc Drugs Ther. 2017;31:179-186. DOI: 10.1007/s10557-017-6723-4.

*Some content reprinted from CVSHealth

POLICY HISTORY

Policy #: 05.04.60
Policy Creation: April 2022
Reviewed: October 2022
Revised: October 2022
Current Effective Date: November 27, 2022