Reference number(s)
5120-A

Standard Medicare Part B Management Leqvio

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Leqvio	inclisiran

Indications

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[1]

Leqvio is indicated as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:

- Adults with hypercholesterolemia
- Adult and pediatric patients aged 12 years of age and older with heterozygous familial hypercholesterolemia (HeFH)
- Pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH)

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

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Documentation

The following documentation must be available, upon request, for all submissions:

Initial requests:

- Genetic testing, chart notes or medical record documentation confirming the diagnosis of HoFH.
- With clinical atherosclerotic cardiovascular disease (ASCVD): Chart notes confirming clinical ASCVD or ASCVD event(s) (if applicable) (see Appendix A).
- Without ASCVD: Untreated (before any lipid lowering therapy) LDL-C level.
- If member has contraindication or intolerance to statins, chart notes or medical documentation confirming the contraindication or intolerance (see Appendix B).
- Current LDL-C level must be dated within six months preceding the authorization request.

Continuation requests:

Current LDL-C level must be dated within six months preceding the authorization request.

Coverage Criteria

Hypercholesterolemia [1-5,11,12]

Authorization of 12 months may be granted for treatment of hypercholesterolemia in adult members when one of the following criteria is met:

- Member meets all of the following criteria:
    - Member has a history of clinical ASCVD (see Appendix A).
    - Member meets either of the following criteria:
        - Member has a current LDL-C level greater than or equal to 70 mg/dL.
        - Member has a current LDL-C level greater than or equal to 55 mg/dL and has multiple ASCVD events (see Appendix A) or high-risk conditions (e.g., 65 years of age or older, familial hypercholesterolemia, diabetes, chronic kidney disease, history of congestive heart failure).
    - Member meets either of the following criteria:
        - Member has received at least three months of treatment with a high-intensity statin. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
        - Member has a contraindication or intolerance to statin therapy (see Appendix B).
- Member meets all of the following criteria:
    - Member had an untreated (before any lipid-lowering therapy) LDL-C level greater than or equal to 190 mg/dL in the absence of a secondary cause.

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- Member has a current LDL-C level greater than or equal to 100 mg/dL.
- Member meets either of the following criteria:
    - Member has received at least three months of treatment with a high-intensity statin. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
    - Member has a contraindication or intolerance to statin therapy (see Appendix B).

Heterozygous Familial Hypercholesterolemia (HeFH)[1-5,11,12]

Authorization of 12 months may be granted for treatment of hypercholesterolemia when either of the following criteria is met:

- Member meets all of the following :
    - Member is 18 years of age or older
    - Member has a history of clinical ASCVD (see Appendix A).
    - Member meets either of the following criteria:
        - Member has a current LDL-C level greater than or equal to 70 mg/dL.
        - Member has a current LDL-C level greater than or equal to 55 mg/dL and has multiple ASCVD events (see Appendix A) or high-risk conditions (e.g., 65 years of age or older, familial hypercholesterolemia, diabetes, chronic kidney disease, history of congestive heart failure).
    - Member meets either of the following criteria:
        - Member has received at least three months of treatment with a high-intensity statin. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
        - Member has a contraindication or intolerance to statin therapy (see Appendix B).
- Member meets all of the following criteria:
    - Member meets either of the following:
        - Member is 18 years of age or older and had an untreated (before any lipid-lowering therapy) LDL-C level greater than or equal to 190 milligrams per deciliter in the absence of a secondary cause.
        - Member is 12 years of age to less than 18 years of age and had an untreated (before any lipid-lowering therapy) LDL-C level greater than or equal to 160 milligrams per deciliter in the absence of a secondary cause.
    - Member has a current LDL-C level greater than or equal to 100 mg/dL.
    - Member meets either of the following criteria:
        - Member has received at least three months of treatment with a high-intensity statin. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
        - Member has a contraindication or intolerance to statin therapy (see Appendix B).

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Homozygous Familial Hypercholesterolemia (HoFH)[1,5,9,13]

Authorization of 12 months may be granted for treatment of homozygous familial hypercholesterolemia (HoFH) in members 12 years of age or older when all of the following criteria are met:

- Member has a documented diagnosis of homozygous familial hypercholesterolemia confirmed by any of the following criteria:
  - Variant in two low-density lipoprotein receptor (LDLR) alleles.
  - Presence of homozygous or compound heterozygous variants in apolipoprotein B (APOB) or proprotein convertase subtilisin-kexin type 9 (PCSK9) gene.
  - Member has compound heterozygosity or homozygosity for variants in the gene encoding low-density lipoprotein receptor adaptor protein 1 (LDLRAP1).
  - Member has an untreated LDL-C of greater than 400 mg/dL and has either of the following:
    - Presence of cutaneous or tendinous xanthomas before the age of 10 years.
    - An untreated LDL-C level of greater than or equal to 190 mg/dL in both parents.
- Member meets either of the following criteria:
  - Member has a current LDL-C level greater than or equal to 70 milligrams per deciliter.
  - Member has a current LDL-C level greater than or equal to 55 milligrams per deciliter and meets either of the following criteria:
    - Member has a history of a clinical ASCVD event (see Appendix A).
    - Member has major ASCVD risk factors (e.g., 65 years of age or older, familial hypercholesterolemia, diabetes, chronic kidney disease, history of congestive heart failure).
- Member meets either of the following criteria:
  - Member has received at least three months of treatment with a high-intensity statin dose in combination with ezetimibe. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used.
  - Member has a contraindication or intolerance to statin therapy (see Appendix B).

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with Leqvio.
- Leqvio is being used to treat an indication in the coverage criteria.
- The member is receiving benefit from therapy. Benefit is defined as achieved or maintained an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

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Appendix

Appendix A. Clinical ASCVD[4-6,9,10]

- 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 greater than or equal to 50% stenosis on cardiac computed tomography angiogram or catheterization)
- Coronary artery calcium (CAC) Score greater than or equal to 300

Appendix B. Contraindications to Statin Therapy[5,7,8]

- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI) and failed statin rechallenge
- Presence of statin-associated muscle symptoms with elevation in creatine kinase (CK) level greater than 3 times upper limit of normal (ULN)
- Statin-associated elevation in creatine kinase (CK) level greater than or equal to 10 times ULN
- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase [ALT] level greater than or equal to 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Leqvio.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia from the American Heart Association.

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- National Lipid Association recommendations for patient-centered management of dyslipidemia.
- 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.
- 2022 American College of Cardiology Expert Consensus Decision Pathway on the Role of Nonstatin therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk.
- 2024 Cardiovascular disease and risk management: standards of care in diabetes from American Diabetes Association.
- 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Leqvio and are included.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the goal LDL-C to achieve with lipid-lowering therapy can be found in the expert consensus decision pathway on the role of nonstatin therapies published by the American College of Cardiology (ACC), the standard of care in diabetes for cardiovascular disease (CVD) and risk management published by American Diabetes Association (ADA), and the guideline for the management of patients with acute coronary syndromes (ACS) published by American College of Cardiology/American Heart Association (AHA/ACC) joint committee on clinical practice guidelines. According to ACC's report, patients with ASCVD are categoried into 2 groups: not at very high risk and at very high risk. LDL-C goal of ≤ 70 mg/dL is recommended for patients not at very high risk where ≤ 55 mg/dL is recommended for patients at very high risk. Very high-risk is defined as patients with a history of multiple ASCVD events or 1 major ASCVD event and multiple high-risk conditions. High-risk conditions defined by the report include: age 65 years or older, HeFH, history of prior coronary artery bypass surgery or percutaneous coronoary intervention outside of the makor ASCVD event(s), diabetes, hypertension, chronic kidney disease, current smoking, persistently elevated LDL-C despite on maximally tolerated statin therapy and ezetimibe, and history of congestive heart failure. In the CVD risk and management standards of care in diabetes from ADA, the ADA recommends LDL-C goal of less than 55 mg/dL for patients with diabetes and ASCVD with a maximally tolerated statin, with the addition of ezetimibe or a PCSK9 inhibitor if this goal LDL-C is not achived. If patient is intolerant to statin therapy, PCSK9 inhibitor concomitant therapy with bempedoic acid or Leqvio as an alternative cholesterol-lowering therapy is recommended. Similarly, the ACS guideline recommends adding a nonstatin lipid-lowering agent, including inclisiran, in patients with ACS who are already on maximally tolerated statin therapy with LDL-C greater than or equal to 55 mg/dL or greater than or equal to 70 mg/dL, to reduce the risk of major adverse cardiovascular events (MACE). The guideline also recommends the use of nonstatin lipid-lowering therapy in those who are statin intolerant.

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Support for the diagnosis of homozygous familial hypercholesterolemia (HoFH) can be found in the European atherosclerosis society consensus statement on HoFH. According to the consensus statement, the diagnosis of HoFH can be determined by genetic confirmation of bi-allelic pathogenic/likely pathogenic variants on different chromosomes at the LDLR, APOB, PCSK9, or LDLRAP1 genes or more than or equal to 2 such variants at different loci or clinically if the member has an un-treated LDL-C of greater than 400 milligrams per deciliter (mg/dL) and has either cutaneous or tendon xanthomas before age of 10 years old or both the parents have untreated elevated LDL-C levels greater than or equal to 190 mg/dL.

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