BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.40.032

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Cardiovascular Agents	**Original Policy Date:**	January 21, 2022
Subject:	Leqvio	**Page:**	1 of 6

Last Review Date: March 7, 2025

Leqvio

Description

Leqvio (inclisiran)

Background
Leqvio (inclisiran) is a small interfering RNA (siRNA) directed to PCSK9 (proprotein convertase subtilisin kexin type 9) messenger RNA (mRNA). Leqvio targets the mRNA preventing the synthesis of the PCSK9 protein. PCSK9 binds to the low-density lipoprotein cholesterol (LDL-C) receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. By preventing synthesis of PCSK9, more receptors are available to clear LDL cholesterol from the blood, thereby lowering LDL cholesterol levels (1).

Regulatory Status
FDA-approved indication: 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) (1).

Based on the mechanism of action of Leqvio, may cause fetal harm. By reducing the cholesterol levels in circulation, it may also reduce other biologically active substances derived from cholesterol. Leqvio should be discontinued when pregnancy is recognized (1).

The safety and effectiveness of Leqvio in pediatric patients less than 18 years of age have not been established (1).

Related policies
Evkeeza, Juxtapid, Nexletol/Nexlizet, Praluent, Repatha

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Leqvio may be considered **medically necessary** if the conditions indicated below are met.

Leqvio may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** the following:

1. Heterozygous familial hypercholesterolemia (HeFH)
    a. LDL-C level ≥ 100 mg/dL in the past 6 months

    AND ONE of the following for HeFH:
    a. Confirmed diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis
    b. Dutch Lipid Clinic Network Criteria score > 5
    c. Simon-Broome Diagnostic Criteria for definite familial hypercholesterolemia

2. Atherosclerotic cardiovascular disease (ASCVD)
    a. LDL-C level ≥ 70 mg/dL in the past 6 months

AND ONE of the following for ASCVD:
    a. Patient has had at least **ONE** of the following atherosclerotic cardiovascular disease (ASCVD) or cardiovascular events:
        i. Acute coronary syndrome (ACS)
        ii. Myocardial infarction (MI)
        iii. Stable or unstable angina

iv. Coronary or other arterial revascularization procedure (such as PTCA, CABG)
v. Transient ischemic attack (TIA)
vi. Peripheral arterial disease (PAD) presumed to be of atherosclerotic origin
vii. Findings from CT angiogram or catheterization consistent with clinical ASCVD

b. At high risk for atherosclerotic cardiovascular disease (ASCVD) or cardiovascular event based on 10- year risk score used by **ONE** of the following tools:
   i. ASCVD Pooled Cohort Risk Assessment: score ≥ 7.5%
   ii. Predicting risk of cardiovascular disease EVENTs (PREVENT): score ≥ 7.5%

AND ALL of the following for **ALL** indications:
1. Patient will be assessed for response (i.e., LDL-C reduction) and adherence to the prescribed lipid lowering regimen after 3 months
2. Inadequate treatment response to 3 months of at least **ONE** high intensity statin **OR** patient has an intolerance or contraindication to statin therapy
3. Inadequate treatment response, intolerance, or contraindication to a subtilisin/kexin type 9 (PCSK9) inhibitor
4. **NO** dual therapy with another Prior Authorization (PA) lipid lowering agent (see Appendix 1)

Prior–Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Heterozygous familial hypercholesterolemia (HeFH)
2. Atherosclerotic cardiovascular disease (ASCVD)

AND ALL of the following:
a. Patient has had **ONE** of the following:

i. Percentage reduction of LDL-C level is ≥ 40%, compared to the level immediately prior to starting a PCSK9 inhibitor
ii. Absolute LDL-C < 100mg/dL

b. Patient will be assessed for adherence to the prescribed lipid lowering regimen
c. **NO** dual therapy with another Prior Authorization (PA) lipid lowering agent (see Appendix 1)

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity 3 single-dose prefilled syringes

Duration 12 months

Prior–Approval *Renewal* Limits

Quantity 2 singe-dose prefilled syringes

Duration 12 months

Rationale

Summary

Leqvio (inclisiran) is a small interfering RNA (siRNA) therapy targeted to the messenger RNA (mRNA) that codes for proprotein convertase subtilisin kexin type 9 (PCSK9). Leqvio prevents the production of PCSK9 and increases the number of LDL receptors available on the surface of hepatocytes available to bind and degrade LDL-C, thereby reducing LDL cholesterol levels. The safety and effectiveness of Leqvio have not been established in patients younger than 18 years of age (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Leqvio while maintaining optimal therapeutic outcomes.

References

1. Leqvio [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation.; June 2024.

Policy History

Date	Action
January 2022	Addition to PA
Mach 2022	Annual review
June 2022	Annual review
September 2022	Removed required documentation for HeFH LDL-R DNA sequencing test or APOB mutational analysis. Revised initiation LDL-C levels to drawn level in the past 6 months. Removed required documentation of ASCVD event or high-risk score. Revised requirements for statin inadequate response and intolerances (myalgia, myositis, and hepatotoxicity). Removed required documentation for renewal LDL level.
October 2022	Per FEP, added requirement to try and fail a PCSK9 inhibitor. Changed policy number to 5.40.032
December 2022	Annual review
March 2023	Annual editorial review. Revised wording of no dual therapy requirement for consistency and added Appendix 1
March 2024	Annual review and reference update
March 2025	Annual editorial review and reference update. Per SME, added PREVENT score as an optional ASCVD scoring tool, removed Framingham risk score as an option

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.

Appendix 1 - List of PA Lipid Lowering Agents

Generic Name	Brand Name
alirocumab	Praluent
bempedoic acid	Nexletol
bempedoic acid/ezetimibe	Nexlizet
evolocumab	Repatha
inclisiran	Leqvio
lomitapide	Juxtapid

*Dual therapy with Evkeeza (evinacumab-dgnb) is allowed