

5.40.032

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<b>Subsection:</b>	Cardiovascular Agents	<b>Original Policy Date:</b>	January 21, 2022
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**Last Review Date:** March 10, 2023

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## Leqvio

### Description

#### Leqvio (inclisiran)

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#### 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 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) (1).

#### Limitations of Use:

The effect of Leqvio on cardiovascular morbidity and mortality has not been determined (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).

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

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**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** for patients 18 years and older for the treatment of heterozygous familial hypercholesterolemia (HeFH), or for patients that have atherosclerotic cardiovascular disease (ASCVD); and if the conditions indicated below are met.

Leqvio may be considered **investigational** in patients less than 18 years of age and 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  $\geq$  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  $\geq$  70 mg/dL in the past 6 months

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**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  $\geq 7.5\%$
  - ii. Framingham Risk Score: score  $\geq 20\%$

**AND ALL** of the following for **ALL** diagnoses:

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**

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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  $\geq 40\%$ , compared to the level immediately prior to starting a PCSK9 inhibitor
  - ii. Absolute LDL-C  $< 100\text{mg/dL}$
- 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

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#### Prior-Approval *Renewal* Limits

**Quantity** 2 single-dose prefilled syringes

**Duration** 12 months

### Rationale

#### Summary

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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.; December 2021.

#### 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

#### Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 10, 2023 and is effective on April 1, 2023.**

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**Appendix 1 - List of PA Lipid Lowering Agents**

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