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

Last Review Date: June 16, 2022

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 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).

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** for patients 18 years and older for the treatment of heterozygous familial hypercholesterolemia (HeFH), or for patients that have atherosclerotic cardiovascular disease; 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. Provided documentation (medical records, laboratory reports) of baseline and/or current LDL-C level ≥ 100 mg/dL in the past 90 days

AND ONE of the following for HeFH:
    a. Provided documentation (medical records, patient's chart) of 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. Laboratory report or medical records of LDL-C 70 mg/dL or greater in the past 90 days

AND ONE of the following for ASCVD:

a. Documented history of **ONE** of the following atherosclerotic cardiovascular disease (ASCVD) or cardiovascular events:
    i. Acute coronary syndrome
    ii. Myocardial infarction
    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 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 greater than or equal to 7.5%
    ii. Framingham Risk Score: score greater than or equal to 20%

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

1. Patient will be assessed for response (ie., LDL-C reduction) and adherence to the prescribed lipid lowering regimen
2. **NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Evkeeza, Juxtapid, Nexletol, Nexlizet, Praluent or Repatha

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

1. Inadequate response to 3 months of prior therapy with at least **ONE** trial of a high intensity statin in combination with Zetia (ezetimibe)
2. Intolerance to a statin
    a. Provide medical records of documentation of the following intolerable adverse reactions with **ONE** of the following:

i. Intolerable and persistent (i.e., more than 2 weeks) muscle symptoms (e.g., muscle pain, weakness, cramps) with **ONE** of the following:
   1) Myalgia (muscle symptoms without CK elevations): Patient has undergone prior therapy with at least **TWO** trials of different statins with or without Zetia (ezetimibe) with a documented reappearance of the muscle symptoms
   2) Myositis (muscle symptoms with CK elevations): Documentation provided indicated creatinine kinase (CK) levels greater than 3 times upper normal limit and/or rhabdomyolysis with CK levels greater than 2,500 IU/L)

b. Intolerable and persistent hepatotoxicity after **TWO** trials of different statins with or without Zetia (ezetimibe) with **ALL** of the following:
   i. Documentation indicating persistent elevations (>3 times the upper limit of normal occurring on 2 more occasions) of serum transaminases or the presence of jaundice
   ii. Secondary causes of elevations in hepatic transaminase levels have been ruled out (e.g., infection, medications, herbal supplements)

3. Contraindication to a statin must have **ONE** of the following:
   a. Currently pregnant or may become pregnant
   b. Nursing mother
   c. Severe allergic reaction to a statin (e.g., anaphylaxis, angioedema, severe rash)

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

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. Documentation has been provided indicating the reduction in LDL-C (i.e., chart notes, medical record, and/or laboratory reports) of **ONE** of the following:
   i. Percentage reduction of LDL-C level is greater than or equal to (≥) 40%, compared to the level immediately prior to starting a PCSK9 inhibitor
   ii. Absolute LDL-C is less than (<) 100mg/dL
b. Patient will be assessed for adherence to the prescribed lipid lowering regimen
c. **NO** dual therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, Evkeeza, Juxtapid, Nexletol, Nexlizet, Praluent or Repatha

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity 3 single-dose prefilled syringe
Duration 12 months

Prior–Approval *Renewal* Limits

Quantity 2 singe-dose prefilled syringe
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.; December 2021.

Policy History

Date	Action
January 2022	Addition to PA
Mach 2022	Annual review
June 2022	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.