Medical Drug Clinical Criteria

Subject: Leqvio (inclisiran)

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Overview

This document addresses the use of Leqvio (inclisiran), a small interfering RNA (siRNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) mRNA approved by the Food and Drug Administration 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). Leqvio is administered by a healthcare provider as a subcutaneous injection on day 1, day 90 and every 6 months thereafter. The effect of Leqvio on cardiovascular morbidity and mortality has not been determined.

In the clinical setting, statins are considered first-line drug therapy, in addition to healthy lifestyle interventions, in individuals requiring treatment for abnormal cholesterol. Other lipid lowering therapies should be considered second-line options for individuals needing additional cholesterol lowering or who cannot tolerate moderate to high doses of statins.

In 2018, the American Heart Association (AHA)/American College of Cardiology (ACC) released guidelines on the management of blood cholesterol. In very high-risk ASCVD, the guidance recommends considering adding non-statins to statin therapy when LDL-C remains greater than or equal to 70 mg/dL. Ezetimibe is the first agent to consider adding on to maximally tolerated statin therapy. PCSK9 inhibitors can be considered for addition if LDL-C remains greater than or equal to 70 mg/dL on statin therapy combined with ezetimibe.

The 2018 AHA/ACC guidelines recommend using an LDL-C threshold of greater than or equal to 100 mg/dL to consider adding non-statins to statin therapy in individuals with severe primary hypercholesterolemia. Ezetimibe is the first non-statin to consider adding to therapy. PCSK9 inhibitors can be considered for addition if LDL-C remains greater than or equal to 100 mg/dL on statin therapy combined with ezetimibe.

Statins have labeled warnings for liver enzyme abnormalities and skeletal muscle effects including myopathy and rhabdomyolysis. Statin-induced adverse events leading to some degree of intolerance is reported in as many as 5% to 30% of individuals although incidence and prevalence vary. The National Lipid Association (NLA) has provided guidance defining statin intolerance as one or more adverse effects associated with statin therapy, which resolves or improves with dose reduction or discontinuation, and can be classified as complete inability to tolerate any dose of a statin or partial intolerance, with inability to tolerate the dose necessary to achieve the individual-specific therapeutic objective. To classify an individual as having statin intolerance, a minimum of two statins should have been attempted, including at least one at the lowest approved daily dosage.

World Health Organization (WHO)/Dutch Lipid Clinic Network Criteria for Familial Hypercholesterolemia (FH) Diagnosis

Criteria	Points
Family History	
Known premature coronary and vascular disease (men <55 years, women <60 years) in first degree relative	1
Known LDL-C >95th percentile in first degree relative	1
Tendon xanthoma and/or corneal arcus in first degree relative	2
Children aged <18 years with LDL-C >95th percentile	2
Personal Clinical History	
Premature coronary artery disease (men <55 years, women <60 years)	2
Premature cerebral or peripheral vascular disease (men <55 years, women <60 years)	1
Clinical Exam	
Tendon xanthoma	6
Corneal arcus in individual aged <45 years	4

LDL-C Level	
> 329 mg/dL (>8.5 mmol/L)	8
250-329 mg/dL (6.5-8.4 mmol/L)	5
190-249 mg/dL (5.0-6.4 mmol/L)	3
155-189 mg/dL (4.0-4.9 mmol/L)	1
Genetic Testing	
Functional mutation in LDLR, ApoB or PCSK9 gene	8

Scoring: Definite FH:> 8 points; Probable FH: 6-8 points; Possible FH: 3-5 points; Unlikely FH: 0-2 points

Clinical criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Leqvio (inclisiran)

Initial requests for Leqvio (inclisiran) may be approved when the following criteria are met:

I. Individual is at high risk for atherosclerotic cardiovascular disease (ASCVD) events as identified by one of the following:
   A. Individual has Heterozygous Familial Hypercholesterolemia (HeFH) confirmed by (Singh 2015; WHO 1999):
      1. Presence of a mutation in LDLR, ApoB, PCSK9 or ARH adaptor protein (LDLRAP1) gene; **OR**
      2. WHO/Dutch Lipid Clinic Network criteria with score of greater than eight points; **OR**
   B. Individual has a history of clinical atherosclerotic cardiovascular disease (ASCVD) including one or more of the following (AHA/ACC 2018):
      1. Acute coronary syndrome;
      2. Coronary artery disease (CAD);
      3. History of myocardial infarction (MI);
      4. Stable or unstable angina;
      5. Coronary or other arterial revascularization;
      6. Stroke;
      7. Transient ischemic attack (TIA);
      8. Peripheral arterial disease (PAD);

AND

II. Individual meets one of the following:
   A. Individual is on high intensity statin therapy or statin therapy at the maximum tolerated dose (high intensity statin is defined as atorvastatin 40 mg or higher or rosuvastatin 20 mg or higher) (AHA/ACC 2018); **OR**
   B. Individual is statin intolerant based on one of the following:
      1. Inability to tolerate at least two statins, with at least one started at the lowest starting daily dose, demonstrated by adverse effects associated with statin therapy that resolve or improve with dose reduction or discontinuation (NLA 2022); **OR**
      2. Statin associated rhabdomyolysis or immune-mediated necrotizing myopathy (IMNM) after a trial of one statin; **OR**
   C. Individual has a contraindication for statin therapy including but not limited to active liver disease, unexplained persistent elevation of hepatic transaminases or pregnancy;

AND

III. Individual is on ezetimibe in addition to statin therapy (only applies to individuals on statin therapy) (AHA/ACC 2018);

AND

IV. Individual has achieved suboptimal lipid lowering response despite at least 90 days of compliant lipid lowering therapy and lifestyle modifications as defined (AHA/ACC 2018):
   A. For individuals where initial LDL-C is known:
      1. Less than 50% reduction in LDL-C; **OR**
   B. For individuals where initial LDL-C is unknown:
      1. ASCVD and LDL-C remains greater than or equal to 70 mg/dL; **OR**
      2. No history of ASCVD and LDL-C remains greater than or equal to 100 mg/dL.

Continuation requests for Leqvio (inclisiran) may be approved when the following criteria are met:

I. Individual continues to use in combination with maximally tolerated statin therapy (unless contraindication or individual is statin intolerant); **AND**
II. Confirmation of LDL-C reduction has been provided.

Leqvio (inclisiran) may not be approved for the following:

I. In combination with Praluent or Repatha; **OR**
II. When the above criteria are not met and for all other indications.

Initial Approval Duration: 6 months
Continuation Approval Duration: 1 year

Step Therapy

Note: When a PCSK9 inhibitor is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred[1] agent or agents.

Non-Preferred PCSK9 Inhibitor Step Therapy

A list of the preferred PCSK9 inhibitor agents is available here.

Requests for a non-preferred PCSK9 inhibitor may be approved if the following criteria are met:

I. Individual has had an adequate trial and titration of a preferred PCSK9 inhibitor and achieved suboptimal lipid lowering response despite at least 90 days of compliant therapy.

[1]Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

Quantity Limits

Leqvio (inclisiran) Quantity Limit

Drug	Limit
Leqvio (inclisiran) 284 mg/1.5 mL prefilled syringe	1 syringe per 6 months
Override Criteria	
Initiation of therapy: May approve one additional prefilled syringe within the first six months of initiating therapy.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1306	Injection, inclisiran, 1 mg [Leqvio]

ICD-10 Diagnosis

I25.10-I25.812	Atherosclerosis and atherosclerotic heart disease
I20.8	Other forms of angina pectoris
I20.9	Angina pectoris, unspecified
I23.7	Postinfarction angina
I24.0-I24.8	Acute coronary thrombosis not resulting in myocardial infarction
I25.2-I25.9	Coronary artery aneurysm

Document history

Revised: 8/19/2022
Document History:

- 03/27/2023 – Step therapy table udpates.

- 08/19/2022 – Annual Review: Update statin intolerance criteria. Wording and formatting changes. Coding Reviewed: No changes.
- 03/28/2022- Add step therapy section and table.
- 01/04/2022 – Select Review: Add clinical criteria and quantity limit for Leqvio. Coding Reviewed: Added HCPCS J3490. All diagnoses pend. Effective 7/1/2022 Added HCPCS J1306. Removed J3490. Added ICD-10-CM I25.10-I25.812, I20.8, I20.9, I23.7, I24.0-I24.8, I25.2-I25.9.

References

1. Cheeley MK, Saseen JJ, Agarwala A, et. al. NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. *J Clin Lipidol*. 2022. https://doi.org/10.1016/j.jacl.2022.05.068.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 13, 2022.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ ADA/AGS/APhA/ASPC/NLA/ PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:e285–350.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
6. Singh S, Bittner V. Familial hypercholesterolemia--epidemiology, diagnosis, and screening. *Curr Atheroscler Rep*. 2015; 17(2):482.
7. World Health Organization. Familial hypercholesterolemia—report of a second WHO Consultation. Geneva, Switzerland: World Health Organization, 1999. Available at: http://whqlibdoc.who.int/hq/1999/WHO_HGN_FH_CONS_99.2.pdf?ua=1. Accessed: July 17, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Commercial Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
07/01/2022	Praluent Repatha	Leqvio

Medicaid Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
04/01/2023 – DC, GA, MD, NJ, NY, WNY, SC 05/01/2023 - IN	Repatha	Leqvio