RX.PA.068.CCH LEQVIO (INCLISIRAN)

The purpose of this policy is to define the prior authorization process for Leqvio (inclisiran). Leqvio (inclisiran) is indicated, in adjunct to diet and maximally tolerated statin therapy, for patients who require additional lowering of low-density lipoprotein cholesterol (LDL-C) for the treatment of:

- Heterozygous familial hypercholesterolemia (HeFH)
- Clinical atherosclerotic cardiovascular disease (ASCVD)

DEFINITIONS

Acute Coronary Syndrome (ACS) – a spectrum of conditions with acute myocardial ischemia and/or infarction that are usually due to an abrupt reduction in coronary blood flow, including ST-elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina (UA)

ASCVD – atherosclerotic cardiovascular disease

ACC/AHA – American College of Cardiology/American Heart Association

Arcus Cornealis – white deposit of lipids in the outer rim of the iris due to high LDL-C levels

Clinical ASCVD – acute coronary syndromes, a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin

Dutch Lipid Clinic Network/WHO Criteria for Familial Hypercholesterolemia – scoring system developed to calculate a numeric score that predicts the probability of the diagnosis of familial hypercholesterolemia (FH). Diagnosis of FH is certain when the score is >8, probable when the score is 6-8, and possible when the score is 3-6.

Heterozygous FH (HeFH) – a common genetic cause of premature coronary heart disease due to lifelong elevated LDL-C

High Intensity Statin – daily dose lowers LDL-C by approximately ≥ 50%

Moderate Intensity Statin – daily dose lowers LDL-C by approximately 30% to < 50%

Tendon Xanthoma – cholesterol deposit formation on the Achilles tendon and/or extensor tendons of hands and feet, or on the knees and elbows, caused by increased LDL-C levels

Statin Intensity (Per 2013 ACC/AHA Guidelines)

High-intensity Statin (lowers cholesterol by ≥ 50%)	Moderate-intensity Statin (lowers cholesterol by 30-50%)	Low-intensity Statin (lowers cholesterol by <30%)
• Atorvastatin 40-80 mg a day • Rosuvastatin 20-40mg a day	• Atorvastatin 10-20 mg a day • Rosuvastatin 5-10 mg a day • Simvastatin 20-40 mg a day • Pravastatin 40-80 mg a day • Lovastatin 40mg a day • Fluvastatin XL 80mg a day • Fluvastatin 40mg twice a day • Pitavastatin 2-4mg a day	• Simvastatin 10 mg a day • Pravastatin 10-20 mg a day • Lovastatin 20 mg a day • Fluvastatin 20-40 mg a day • Pitavastatin 1 mg a day

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Medical Policy Committee.

The drug, Leqvio (inclisiran) is subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all the criteria below:

- Must be prescribed by or in consultation with a cardiologist, clinical lipidologist, or endocrinologist
- Must be age 18 years or older
- Must provide chart documentation indicating that the member has been counseled on the benefits of therapeutic lifestyle changes (i.e., diet, exercise, weight management, smoking cessation)
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
- Must have **ONE** of the following diagnoses:
    - **Clinical atherosclerotic cardiovascular disease (ASCVD)** – Chart documentation confirming the patient is Very High Risk ASCVD which includes a history of 2 or more major ASCVD events or 1 major ASCVD event and two or more high-risk conditions:

Major ASCVD Event	High-Risk Conditions
• Recent ACS (Within the past 12 months) • History of MI (other than recent ACS) • History of ischemic stroke • Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)	• Age ≥ 65 years old • Heterozygous familial hypercholesterolemia • History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD events • Diabetes Mellitus • Hypertension • CKD (eGFR 15-59 mL/min/1.73^2) • Current smoker • Persistently elevated LDL-C ≥ 100 despite max statin and ezetimibe therapy • History of Congestive Heart failure

- **<u>Heterozygous familial hypercholesterolemia (HeFH)</u>** – chart documentation must be provided showing at least ONE of the following to support the diagnosis:
  - Simon Broome criteria for definite familial hypercholesterolemia, as defined by meeting BOTH of the following:
    - Must have Total Cholesterol (TC) >290mg/dL OR LDL-C >190mg/dL AND
    - One of the following:
      - Tendon xanthomas must be present in patient or patient's parent, child, grandparent, sibling, uncle, or aunt OR
      - Confirmation by gene or receptor testing (presence of LDL-R, ApoB, or PCSK9 mutation)
  - Dutch Lipid Clinic Network/WHO criteria for probable familial hypercholesterolemia with a diagnostic score of 6 or greater based on the scoring chart below

	Clinical Signs	Score
Family History	First degree relative known with premature (men < 55 years; women < 60 years) coronary and vascular diseases	1
	First degree relative known with LDL-cholesterol >95th percentile	1
	First degree relative with tendon xanthomas and/or arcus cornealis	2
	Children below 18 years with LDL-C >95th percentile	2
Clinical History	Patient has premature (men < 55 years; women < 60 years) CAD	2
	Patient has premature (men < 55 years; women < 60 years) cerebral or peripheral vascular disease	1
Physical Examination	Tendon xanthomas	6
	Arcus cornealis below the age of 45 years	4
Laboratory Analysis	LDL-C > 330 mg/dL (8.5 mmol/L)	8
	LDL-C = 250-329 mg/dL (6.5-8.4 mmol/L)	5
	LDL-C = 190-249 mg/dL (5.0-6.4 mmol/L)	3
	LDL-C = 155-189 mg/dL (4.0-4.9 mmol/L)	1
DNA Analysis	Functional mutation LDL receptor gene present	8

- Must submit baseline (prior to lipid lowering therapy) lipid panel including LDL-C level demonstrating uncontrolled LDL-C beyond recommended goals
- Must be on concurrent therapy with a maximally tolerated dose of a HMG-CoA Reductase Inhibitor (statin) unless statin intolerant
- Must have an LDL-C above goal (LDL-C ≥ 70 for ASCVD or LDL-C ≥ 100 for HeFH) despite an adequate trial of a high intensity statin (rosuvastatin 20-40mg daily and atorvastatin 40-80mg daily) together concomitantly with ezetimibe for at least 2 continuous months with demonstrated adherence (based on chart documentation)
    - Note: If unable to tolerate high-intensity statins, a moderate-intensity statin must be tried together concomitantly with ezetimibe for at least 2 months, unless contraindicated. Will not accept separate trials of statin and ezetimibe. Both drugs must be taken at the same time.
    - If the member cannot use statins due to a contraindication, the following documentation is required:
        - The member must have documented active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels
        - Trial of ezetimibe or other cholesterol lowering medications (fibrates, bile acid sequestrants) for at least 2 continuous months with demonstrated adherence if a ≤ 20% decrease in LDL-C is required to achieve target levels

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon the following:

- Documentation of recent lipid panel (within last 3 months) indicating reduction in LDL-C with therapy
- Chart documentation/claims data demonstrating patient is continuing treatment with the maximally tolerated dose of a statin (when applicable)
- Chart documentation must demonstrate adherence to treatment recommendations (medication and lifestyle changes)

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 1 year
Reauthorization	Same as initial

If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.

Codes:

CPT Codes / HCPCS Codes / ICD-10 Codes		
Code	Brand	Description
J1306	Leqvio	Injection, inclisiran, 1 mg

References:

1. Leqvio [package insert]. East Hanover, New Jersey. Novartis Pharmaceuticals Corporation. December 2021.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001;285:2486-2497.
3. Scientific Steering Committee on behalf of the Simon Broome Register Group. Risk of fatal coronary heart disease in familial hypercholesterolemia. Br Med J 1991;303:893-6.
4. World Health Organization. Familial hypercholesterolemia. Report of a second WHO consultation. Geneva: World Health Organization; 1999.
5. Watts GF, Gidding S, Weirzbicki AS, et al. Integrated guidance on the care of familial hypercholesterolaemia from the International FH Foundation. Int J Cardiol 2014;171:309-325.
6. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient centered management of dyslipidemia: part 1 – full report. J Clin Lipidol 2014;8:473-488.
7. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC Guideline on the Management of Blood

Cholesterol: A Report on the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019; 139: e1082-e1143

Revision History

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Initial review	XX/XX

Record Retention

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

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