SHARP Health Plan

Clinical Policy

SUBJECT: CLINICAL POLICIES – INJECTABLE MEDICATIONS_LEQVIO (INCLISIRAN) FOR THE TREATMENT OF HYPERCHOLESTEROLEMIA **POLICY NUMBER: HS-CP-MA_I3c** **EFFECTIVE DATE: 9/24/2025** **SERVICE/PRODUCT LINE: MEDICARE – MEDICAL**	Product Line (check all that apply): ☐ All ☐ Group HMO ☐ Individual HMO ☐ PPO ☐ POS ☒ Medicare ☐ N/A

These guidelines are used in conjunction with the independent judgment of a qualified licensed physician and do not constitute the practice of medicine or medical advice. This Clinical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This Clinical Policy is not intended to recommend treatment for members. Members should consult with their treating provider in connection with diagnosis and treatment decisions.

When coverage criteria are not fully established by Medicare including but not limited to National Coverage Decisions (NCD), Local Coverage Decisions (LCD), Medicare Manuals and National Coverage Articles, Sharp Health Plan develops Clinical Policies that serve as recommendations for medical necessity decisions. Sharp Health Plan utilizes evidence-based guidelines from nationally recognized professional organizations, peer reviewed medical and scientific literature and evidence-based consensus statements, which are all based on generally accepted standards of care.

I. BENEFIT STATEMENT: Any service reviewed and approved by this Sharp Health Plan Clinical Policy must be a covered benefit according to the member's evidence of coverage (EOC). Since benefit plans vary in coverage and some plans may not provide coverage for certain services discussed in this clinical policy, decisions are subject to all terms and conditions of the applicable benefit plan. Benefit determinations should be based in all cases on the member's contract benefits in effect at the time of service.

A. All reviewers must first identify member eligibility and all decisions of this clinical policy are subject to current state and/or federal law. This Clinical policy does not constitute plan authorization, nor is it an explanation of benefits. In the event of a conflict, a member's benefit plan, EOC, always supersedes the information in the Clinical Policies.

II. REGULATORY: N/A

III. DESCRIPTION

A. Before using this policy, please check the member specific benefit plan document and any federal mandates, if applicable.
B. This policy defines the Sharp Health Plan (Plan) coverage for Leqvio (inclisiran) when administered according to U.S. Food and Drug Administration (FDA) labeled indications.
C. This policy is to be used when there are no CMS criteria (NCD, LCF, NCA, Medicare Manual) for the drug in question.
D. Leqvio, a small interfering RNA (siRNA), is approved by the Federal Drug Administration (FDA) for

Indication	Dosing
Adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH) to reduce LDL-C.	284 mg subcutaneously once at 0 and 3 months then every 6 months thereafter

IV. DEFINITIONS

A. A Qualified Individual is a Sharp Health Plan (Plan) member.

B. Experimental and Investigational drugs and devices:
   1. Considered experimental if the FDA has not issued a specific indication or NDC number for the specific drug or device AND they are currently under investigation in a registered Clinical Trial.

   2. The Off-Label Use of an FDA approved prescription drug or device is not considered an experimental/investigational service if this off-label use is not currently being investigated in a registered Clinical Trial.

C. Biosimilars: A biosimilar is a biologic that is highly similar to, and has no clinically meaningful differences from, another biologic that is already approved by the FDA (known as the original biologic or reference product). Biosimilars are made with the same types of natural sources as the original medication they were compared to; they are given the same way, have the same strength and dosage, and have the same potential side effects. A biosimilar provides the same treatment benefits as the original biologic.

D. Injection: The introduction of a medicinal substance into the body; either subcutaneous, intramuscular, intravenous, intra-arterial or into other canals or cavities of the body. For purposes of this medical policy, a medication is provided either by a member (self-injectable) or by a medical provider. It is a “shot” or a dosage of medication given by way of a syringe and needle rather than over a period of time, though not to be given as part of a procedure.

E. Infusion: The slow diagnostic, prophylactic, or therapeutic introduction of fluid or medicinal substance into a vein or tissue given over a period of time.

F. Step Therapy: “Step therapy” is a process specifying the sequence in which different prescription drugs for a given medical condition and medically appropriate for a particular patient are prescribed. The health plan may require the enrollee to try one or more drugs to treat the enrollee's medical condition before the health plan will cover a particular drug for the condition pursuant to a step therapy request. If the enrollee's prescribing provider submits a request for step therapy exception, the health plans shall make exceptions to step therapy when the criteria is met.

V. MEDICAL NECESSITY

A. To be eligible for coverage under this policy, the member must be a Qualified Individual with active Plan membership. and

B. , The provision of physician samples does not guarantee coverage.and

C. Medications must be prescribed from a contracted Plan provider.

D. Leqvio (inclinsiran) for hypercholesterolemia:

1. Initial Criteria (must meet ALL):

a) Member at least 18 years of age, and

b) Member has one of the following documented diagnoses:

(1) Heterozygous Familial Hypercholesterolemia (HeFH) with:

(a) LDL-cholesterol is > 190 mg/dL pre-treatment plus tendon xanthomas, or evidence of these signs in a first or second-degree relative, or

(b) DNA-based evidence of an LDL- receptor mutation, apo-B100 or a PCSK9 mutation, or

(c) Other genetic typing indicating the presence of heterozygous familial hypercholesterolemia.

OR

(2) Atherosclerotic cardiovascular disease (ASCVD) (e.g., acute coronary syndrome, history of heart attack, stable or unstable angina, coronary or other arterial disease, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin), or an atherosclerotic cardiovascular disease risk equivalent (type 2 diabetes, familial hypercholesterolemia, or a 10-year risk of a cardiovascular event of ≥20% as assessed by the Framingham Risk Score for Cardiovascular Disease or equivalent), and

c) Member is being treated by a contracted cardiologist or endocrinologist; and

d) Member is intolerant, has contraindications, or has tried and failed two different treatment regimens used for at least two months (60 days) for each medication, consisting of a high-potency statin (atorvastatin, simvastatin, or rosuvastatin) at the maximum tolerated dose in combination with ezetimibe, along with a low-fat diet, despite optimal compliance with regimens; and

e) Medication will be used in combination with a statin used at the maximum tolerated dose OR member is intolerant to statins; and

f) No history of severe renal impairment (eGFR < 30ml/min) or severe hepatic impairment; and

g) Member is not pregnant or planning to become pregnant while on therapy.

h) A trial of evolocumab (Repatha) or alirocumab (Praluent) prior to inclisiran (Leqvio) is required.

i) Initial authorization will be for a 3-month period

2. Reauthorization criteria:

a) A reduction in LDL compared to baseline has been observed; and

b) For HeFH, evidence of ongoing concomitant lipid lowering therapy (statin, ezetimibe, LDL-apheresis) is available. (Note: Maximum dose of statin should be rosuvastatin 20mg or higher, atorvastatin 40mg or higher, or simvastatin 40mg or higher.)

c) Renewal for 1 year thereafter.

VI. NOT MEDICALLY NECESSARY

A. The Plan is not required to cover services or benefits that are not otherwise covered under the terms and conditions of the Plan contract.
B. PCSK9 Inhibitors, ANGPTL3 inhibitors, and siRNA agents are not medically necessary for all other indications.

VII. PROCEDURE/ATTACHMENTS

A. All requests for coverage of Injectable medications will be reviewed by the delegated Plan Medical Group (PMG) or by the Plan according to its regular and appropriate utilization management process, administered consistent with the Plan benefit and provided in a manner that limits disruptions in care per Health and Safety code 1363.5.

B. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this guideline. This Policy provides assistance in determining coverage under the member's benefit plan.

C. The terms of a member's benefit plan summary defined in the evidence of coverage document may differ from the standard benefit plans upon which this guideline is based. In the event of a conflict, the member's specific benefit document supersedes these guidelines.

D. The injectable medication(s) will be subject to step therapy exception per SHP Clinical Policy I3-Injectable Medications.

VIII. CODES: N/A

IX. REFERENCES:

A. Repatha® (evolocumab) package insert. Amgen. Revised November 2024.
B. Praluent® (alirocumab) package insert. Sanofi/Regeneron Pharmaceuticals, Revised September 2024.
C. Treatment of Drug resistant hypercholesterolemia, Robert Rosenson, et al; Up to Date. Literature review current through March 2020. Accessed 4/09/23.
D. PCSK-9 inhibitors: Pharmacology, adverse effects and use, Erik SG Stroes et al. Up to Date. Literature review current through March 2020. Accessed 4/09/23.
E. Evkeeza® (evinacumab-dgnb) package insert. Regeneron. Revised January 2025.
F. Raal, Frederick et al. Evinacumab for Homozygous Familial Hypercholesterolemia. N Engl J Med 2020; 383:711-720.
G. Leqvio® (inclisiran) package insert. Novartis Pharmaceuticals Co; East Hanover, NJ. Revised July 2024.
H. Lin GA, Kazi DS, Jih J, Agboola F, Chapman R, Pearson SD. Inclisiran and Bempedoic Acid for Patients with Heterozygous Familial Hypercholesterolemia and for Secondary Prevention of ASCVD: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review, March 2, 2021.
I. Ray K, Wright R, Kallend D, et al. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol [published online ahead of print March 18, 2020].
J. Raal FJ, Kallend D, Ray KK, et al. Inclisiran for heterozygous familial hypercholesterolemia. N Engl Med. 2020;382(16):1520-1530. doi:10.1056/NEJMoa1913805

X. REVISION HISTORY

Date	Modification (Original, Reviewed or Revised)
09/24/25	Original

Approved by: (Signature of VP /CMO) 	**Approval date:** **9/24/25**