Drug Coverage Policy

Effective Date.....9/1/2026
Coverage Policy Number.....IP0773
Policy Title.....Redemplo

Hypertriglyceridemia - Redemplo

- Redemplo® (plozasiran subcutaneous injection - Arrowhead)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Redemplo, an apolipoprotein C-III (apoC-III)-directed small interfering ribonucleic acid (siRNA), is indicated as an adjunct to diet to reduce triglycerides (TGs) for familial chylomicronemia syndrome

(FCS) in adults.[1] It is recommended to maintain a low-fat diet (≤ 20 grams of fat per day) in conjunction with Redemplo.

Disease Overview
FCS is an ultra-rare, genetic form of severe hypertriglyceridemia that impacts 1 to 10 per 1,000,000 persons in the US. Patients with FCS may have triglyceride levels in the thousands.[2-4] Of note, normal triglyceride levels are < 150 mg/dL with levels above 500 mg/dL categorized as severe hypertriglyceridemia. In general, patients with FCS do not have adequate responses to triglyceride-lowering therapies (e.g., fibrates, omega-3 fatty acids). The high triglyceride levels lead to symptoms such as severe abdominal pain, inflammation of the pancreas (acute pancreatitis), and fatty deposits in the skin. Lipemia retinalis may occur, a condition in which the retinal veins of the eyes appear milky. Patients may develop symptoms of FCS in infancy but may not have the disease be known until adulthood. FCS is caused by biallelic pathogenic variants in five known genes (i.e., lipoprotein lipase [*LPL*], glycosylphosphatidylinositol-anchored high-density lipoprotein [HDL]-binding protein 1 [*GPIHBP1*], apolipoprotein A-V [*APOA5*], apolipoprotein C-II [*APOC2*], or lipase maturation factor 1 [*LMF1*]).[2-4] Tryngolza® (olezarsen subcutaneous injection), an apoC-III-directed antisense oligonucleotide, is indicated as an adjunct to diet to reduce triglyceride levels in adults with FCS.[5]

Clinical Efficacy
The efficacy of Redemplo was evaluated in a randomized, placebo-controlled, double-blind, Phase III trial in adults with genetically identified or clinically diagnosed.[1,6] A fasting triglyceride level ≥ 880 mg/dL was required. At study entry, patients who received the FDA-approved dose of Redemplo (n = 26) had baseline mean triglyceride levels of 2,008 mg/dL; the value in patients who received placebo (n = 25) was 2,053 mg/dL. Patients were treated with statins (43%), omega-3 fatty acids (29%), and fibrates (69%). In total, 25% of patients were not receiving background TG-lowering therapies. The difference between Redemplo 25 mg and placebo in the percent change in fasting triglycerides from baseline to Month 10 was -59%.

Guidelines
An expert clinical review from the National Lipid Association states that Redemplo and Tryngolza show great promise in the treatment of FCS.[3] There are recommendations regarding the diagnosis and/or identification of FCS.[3,4] An expert panel (2018) states the FCS is characterized by very high plasma triglyceride concentrations (> 885 mg/dL) in the untreated state.[3] Patients with FCS experience physical complications including incapacitating abdominal pain, and severe recurrent acute pancreatitis. Other clinical symptoms include eruptive xanthomas, lipemia retinalis, and lower body weight. Neurologic symptoms may be present (e.g., irritability, memory problems, dementia). Pathogenic variants are also present in FCS-genes (i.e., *LPL*, *GPIHBP1*, *APOA5*, *APOC2*, or *LMF1*). An FCS score ≥ 10 (often referred to as the Moulin et al scoring criteria) is a strong predictor of the condition.[3] Also, patients with a North America Familial Chylomicronemia Syndrome (NAFCS) score ≥ 45 are very likely to have classical FCS.[4] Refer to Appendix A and Appendix B for FCS scoring and NAFCS scoring.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Redemplo. Because of the specialized skills required for evaluation and diagnosis of patients treated with Redemplo as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Redemplo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, prescription receipts and/or other information. All documentation must include patient-specific identifying information.

Redemplo is considered medically necessary when the following are met (1):

FDA-Approved Indication

1. **Familial Chylomicronemia Syndrome.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has a fasting triglyceride level ≥ 880 mg/dL at baseline **[documentation required]**; AND
       Note: This refers to baseline prior to treatment with a triglyceride-lowering medication. Examples of triglyceride-lowering medications include statins, niacin, fibrates, and omega-3 fatty acids.
     - **iii.** Patient meets at least ONE of the following (a, b, orc):
       - **a)** Molecular genetic test results demonstrate biallelic pathogenic variants in at least one gene causing familial chylomicronemia syndrome **[documentation required]**; OR
         Note: Examples of genes causing Familial Chylomicronemia Syndrome include lipoprotein lipase (*LPL*), glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 (*GPIHBP1*), apolipoprotein A-V (*APOA5*), apolipoprotein C-II (*APOC2*), or lipase maturation factor 1 (*LMF1*).
       - **b)** Molecular genetic test results are inconclusive, and the patient has ONE of the following ([1] or[2]) **[documentation required]**; OR
         - **(1)** Patient has a Moulin familial chylomicronemia syndrome score ≥ 10; OR
         - **(2)** Patient has a North American familial chylomicronemia syndrome score ≥ 45; OR
       - **c)** Patient has received a clinical diagnosis of familial chylomicronemia syndrome based on the presence of ALL of the following ([1], [2], and [3]):
         - **(1)** Patient meets ONE of the following (i or ii):
           (i) History of acute pancreatitis not caused by alcohol or cholelithiasis; OR
           (ii) History of recurrent hospitalizations for severe abdominal pain without other explainable cause; AND
         - **(2)** Absence of secondary hypertriglyceridemia (e.g., obesity, uncontrolled diabetes); AND
         - **(3)** Lack of response to a traditional triglyceride-lowering medication; AND
           Note: Examples of triglyceride-lowering medications include statins, niacin, fibrates, and omega-3 fatty acids.
     - **iv.** The medication will be used concomitantly with a low-fat diet; AND
     - **v.** Medication is prescribed by a cardiologist, an endocrinologist, a lipidologist, or a physician who focuses in the treatment of disorders related to severe hypertriglyceridemia.
     - **vi.** Preferred product criteria are met for the product as listed in the below table.
   - **B)** Patient is Currently Receiving Redemplo. Approve for 1 year if the patient has experienced a response to therapy.
     Note: Examples of a response to therapy include lowering triglycerides or a reduced number of pancreatitis episodes.

Employer Plans

Product	Criteria
Redemplo (plozasiran subcutaneous injection)	**1.** Approve if the patient meets ONE of the following (A or B): **A)** Patient meets ONE of the following criteria (i or ii): **i.** Patient has received Tryngolza for ≥ 1 year, unless not tolerated **[documentation required]**; OR **ii.** According to the prescriber, the patient has thrombocytopenia or is at risk for thrombocytopenia.

Conditions Not Covered

Redemplo for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Hypertriglyceridemia (in the absence of a confirmed diagnosis of familial chylomicronemia syndrome).** A trial evaluated Redemplo in patients with severe hypertriglyceridemia.[7] However, Redemplo is not FDA-approved for this use.[1]

References

1. Redemplo® subcutaneous injection [prescribing information]. Pasadena, CA: Arrowhead; November 2025.
2. Javed F, Saadatagah S, Larouche M, Naderian M, et al. Recognition and management of persistent chylomicronemia: a Joint Expert Clinical Consensus by the National Lipid Association and the American Society for Preventative Cardiology. *J Clin Lipidol*. 2025;19:723-736.
3. Moulin P, Dufour R, Averna M, et al. Identification and diagnosis of patients with familial chylomicronemia syndrome (FCS): expert panel recommendations and proposal of an "FCS score." *Atherosclerosis*. 2018;275:265-272.
4. Hegele RA, Ahmad Z, Ashraf A, et al. Development and validation of clinical criteria to identify familial chylomicronemia syndrome (FCS) in North America. *J Clin Lipidol*. 2025;19(1):83-94.
5. Tryngolza® subcutaneous injection [prescribing information]. Carlsbad, CA: Ionis; January 2025.
6. Watts GF, Rosenson RS, Hegele RA, et al, for the PALISADE Study Group. Plozasiran for managing persistent chylomicronemia and pancreatic risk. *N Engl J Med*. 2025;392(2):127-137.
7. Gaudet D, Pall D, Watts GF, et al. Plozasiran (ARO-APOC3) for severe hypertriglyceridemia: The SHASTA-2 randomized clinical trial. *JAMA Cardiol*. 2024;9(7):620-630.

Revision Details

Summary of Changes	Review Date	Effective Date
New policy.	4/16/2026	6/1/2026
The name of the policy was changed to as listed. Previously, it was Familial Chylomicronemia Syndrome – Redemplo Prior Authorization policy. **Familial Chylomicronemia Syndrome**: The duration of approval for Initial Therapy was changed to 6 months. Previously, it was 1 year.	7/23/2026	9/1/2026

Continuation of therapy was added for a patient who is currently receiving Redemplo and has experienced a response to therapy. A Note of examples of a response was included. **Redemplo preferred product criteria updated:** The prerequisite requirement was revised from "tried Tryngolza" to "received Tryngolza for ≥ 1 year, unless not tolerated [documentation required]." The exception criterion was also updated by replacing "decreased platelets" with "thrombocytopenia."		

The policy effective date is in force until updated or retired.

Appendix A. Familial Chylomicronemia Syndrome Score Diagnostic Criteria (for Patients with Fasting TGs > 885 mg/dL).[3*]

Fasting TG levels > 885 mg/dL for three consecutive blood analyses (measured at least 1 month apart; presence of eruptive xanthoma may be used as a surrogate for high TG levels): **+5** • Fasting TG levels > 1,770 mg/dL at least once: **+1**
Previous TG levels < 177 mg/dL: **-5**
No secondary factor (i.e., alcohol, diabetes, metabolic syndrome, hypothyroidism, steroid therapy, and additional drugs; exceptions include pregnancy and ethinyl estradiol; if diagnosis is made during pregnancy, a second assessment is necessary to confirm diagnosis postpartum): **+2**
History of pancreatitis: **+1**
Unexplained recurrent abdominal pain: **+1**
No history of familial combined hyperlipidemia: **+1**
No response (TG decrease < 20%) to hypolipidemic treatment: **+1**
Onset of symptoms age: • < 40 years: **+1** • < 20 years: **+2** • < 10 years: **+3**

TG(s) – Triglyceride(s); * The FCS score is the sum of all items cited above and a score ≥ 10 suggests that FCS is very likely.

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