

DRUG POLICY

Redemplo® (plozasiran)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Redemplo is indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Initial Requests
 - a. Chart notes, medical records or genetic test(s) confirming diagnosis of FCS
 - b. Chart notes, medical records or laboratory values documenting fasting triglyceride (TG) level
2. Continuation Requests
 - a. Chart notes, medical records or laboratory values documenting positive clinical response

Prescriber Specialties

The requested medication must be prescribed by or in consultation with one of the following:

1. Endocrinologist
2. Cardiologist
3. Lipid specialist
4. Gastroenterologist

5. Geneticist

Criteria for Initial Approval

Familial Chylomicronemia Syndrome (FCS)

Authorization of 6 months may be granted for treatment of FCS (type 1 hyperlipoproteinemia) in members when all of the following criteria are met:

1. Member is 18 years of age or older
2. Member has a diagnosis of FCS as confirmed by ONE of the following:
 - A. Genetic confirmation of pathogenic variants in FCS-causing genes (e.g., LPL, GPIHBP1, APOA5, APOC2, LMF1)
 - B. ALL of the following:
 - i. North American Familial Chylomicronemia score (NAFCS) ≥ 45 (Appendix A) or Familial Chylomicronemia Syndrome (FCS) score ≥ 10 (Appendix B)
 - ii. History of recurrent pancreatitis or history of recurrent abdominal pain
 - iii. Secondary causes of hypertriglyceridemia have been ruled out (e.g., alcohol use, chronic kidney disease, uncontrolled diabetes, medications [e.g., atypical antipsychotics, beta-blockers, corticosteroids, oral estrogens])
3. Member has an untreated fasting triglyceride (TG) level of ≥ 880 mg/dL (≥ 10 mmol/L)
4. Member is adhering to a very low-fat diet (e.g., ≤ 20 g of total fat per day)
5. Traditional lipid lowering medications (e.g., fibrates, omega-3 fatty acids, statins) have been ineffective in lowering fasting triglyceride level

Continuation of Therapy

Familial Chylomicronemia Syndrome (FCS)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for FCS when both of the following criteria are met:

1. Member has demonstrated a positive clinical response with the requested medication (e.g., reduction in TG level from baseline, reduction in episodes of acute pancreatitis)
2. Member is adhering to a very low-fat diet (e.g., ≤ 20 g of total fat per day)

Other

Redemplo (plozasiran) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Members currently receiving the requested medication as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
Redemplo (plozasiran) 25 mg/0.5 mL prefilled syringe	1 prefilled syringe per 90 days	25 mg injected subcutaneously once every 3 months

Appendix A North American Familial Chylomicronemia Score (NAFCS)

Criteria	Points
----------	--------

Current age ≥ 1 to 9 years	+12
Current age ≥ 10 years AND hypertriglyceridemia onset at age < 10 years	+12
Current age ≥ 10 years AND hypertriglyceridemia onset at age ≥ 10 years	+0
Body Mass Index (percentile for children/adolescents) < 25 kg/m ² or < 85 th percentile	+9
Body Mass Index (percentile for children/adolescents) ≥ 25 kg/m ² or $\geq 85^{\text{th}}$ percentile	+0
History of pancreatitis	+16
Abdominal pain but no pancreatitis	+9
Neither abdominal pain nor pancreatitis	+0
Presence of NO secondary factors that may contribute to hypertriglyceridemia	+11
Presence of ≥ 1 secondary factor(s) that may contribute to hypertriglyceridemia	+0
All triglycerides > 880 mg/dL	+13
Ratio triglycerides/total cholesterol > 8	+8
Apolipoprotein B (apoB) < 1.0 g/L	+12
Additional Points	
If patient is ≥ 1 to 9 years old AND has no secondary factors	+7
If triglycerides/total cholesterol > 8 AND apoB < 1.0 g/L	+7
If triglycerides/total cholesterol > 8 AND has no secondary factors	+5

NAFCS Score:

- ≥ 60 : Strongly indicates definite FCS
- ≥ 45 : Suggests likely FCS rather than MCS
- ≥ 30 -44: Suggests rationale to confirm FCS with genetic testing
- < 30: deems unlikely FCS, but genetic testing may still be needed

Appendix B Familial Chylomicronemia Syndrome (FCS) Score

Criteria	Points
Fasting triglycerides > 10 mmole/L for 3 consecutive blood analyses	+5
Fasting triglycerides > 20 mmole/L at least once	+1
Previous triglycerides < 2 mmole/L	-5
No secondary factor (except pregnancy and ethinyl estradiol)	+2
History of pancreatitis	+1
Unexplained recurrent abdominal pain	+1
No history of familial combined hyperlipidemia	+1
No response (triglyceride decrease < 20%) to hypolipidemic treatment	+1
Onset of symptoms at age < 40 years	+1
Onset of symptoms at age < 20 years	+2
Onset of symptoms at age < 10 years	+3

FCS Score:

- ≥ 10 : FCS very likely
- ≤ 9 : FCS unlikely
- ≤ 8 : FCS very unlikely

CLINICAL RATIONALE

Redemplo (plogasiran) is an apolipoprotein-CIII (apoC-III)-directed small interfering RNA (siRNA) approved in November 2025 as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). FCS is a rare inherited disorder characterized by extremely high fasting triglycerides (≥ 880 mg/dL) and a high risk of acute pancreatitis. Redemplo is the second FDA-approved therapy for FCS.

and the first studied in both genetically confirmed and clinically diagnosed FCS populations, addressing diagnostic and access challenges inherent to the disease.

Redemplo (plozasiran) targets apoC-III mRNA, leading to its degradation through RNA interference and thereby reducing hepatic and circulating apoC-III protein. Lower apoC-III levels enhance clearance of triglyceride-rich lipoproteins, resulting in substantial triglyceride reduction. The approved dosing is 25 mg subcutaneously once every 3 months, which may be self-administered. Common adverse reactions occurring in $\geq 10\%$ of clinical trial participants and $>5\%$ more often than adverse reactions reported in the placebo treatment arm include hyperglycemia, headache, nausea, and injection-site reactions.

Clinical efficacy was demonstrated in the Phase 3 PALISADE trial (N=75), which enrolled adults with genetically confirmed or clinically diagnosed FCS. In the FDA-approved 25-mg arm, Redemplo (plozasiran) produced a median -80% reduction in fasting triglycerides at month 10 versus -17% with placebo, yielding a placebo-adjusted median difference of -58.7% (95% CI -89.6 to -27.9 ; $p < 0.0001$). Redemplo (plozasiran) also showed a numerical reduction in acute pancreatitis incidence over 12 months (8% vs. 20% with placebo). These results were consistent across patients regardless of genetic confirmation of FCS. Redemplo (plozasiran) represents a clinically meaningful, infrequently dosed therapeutic option for reducing triglycerides and pancreatitis risk in patients with FCS.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

REFERENCES

1. Redemplo [package insert]. Pasadena, CA: Arrowhead Pharmaceuticals, Inc.; November 2025.
2. Watts GF, et al. Plozasiran for managing persistent chylomicronemia and pancreatitis risk. *N Engl J Med*. 2024;392:127-137.
3. Javed F, et al. Familial chylomicronemia syndrome: an expert clinical review from the National Lipid Association. *J Clin Lipidol*. 2025;19(3):382-403.
4. Hegele RA, 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. Moulin P, Dufour R, Aversa M, et al. Identification and diagnosis of patients with familial chylomicronemia syndrome (FCS): expert panel recommendations and proposal of an “FCS score”. *Atherosclerosis*. 2018;274:265-272.
6. Handelsman Y, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Management of Dyslipidemia and Prevention of Cardiovascular Disease Algorithm – 2020 Executive Summary. *Endocr Pract*. 2020;26(10):1196-1224.
7. Williams L, et al. Familial chylomicronemia syndrome: bringing to life dietary recommendations throughout the life span. *J Clin Lipidol*. 2018;12(4):908-919.
8. Hegele RA, Boren J, Ginsberg HN, et al. Rare dyslipidaemias, from phenotype to genotype to management: a European Atherosclerosis Society task force consensus statement. *Lancet Diabetes Endocrinol*. 2020;8(1):50-67.
9. Spagnuolo CM, Hegele RA. Etiology and emerging treatments for familial chylomicronemia syndrome. *Expert Rev Endocrinol Metab*. 2024;19(4):299-306.

POLICY HISTORY

Policy #: 05.06.15

Original Effective Date: March 10, 2026

Reviewed: January 2026

Revised:

Current Effective Date: March 10, 2026